

Contents

Lorazepam	200	THAM acetate	292
Methadone	202	Tropicamide (Ophthalmic) ...	293
Midazolam.....	204	Vitamins/Minerals	295
Morphine	208	AquADEKs™ Pediatric	
Naloxone	210	Liquid	296
Neostigmine	211	Calcium - Oral	297
Pancuronium	212	Calcium chloride 10%	298
Pentobarbital	214	Calcium gluconate 10%	300
Phenobarbital	216	Ferrous sulfate	302
Phenytoin	218	INFUVITE® Pediatric	304
Rocuronium	220	Iron Dextran	306
Sucrose	222	Potassium chloride	307
Vecuronium	224	Pyridoxine	308
Diuretics	227	Vitamin A	309
Bumetanide	228	Vitamin D	310
Chlorothiazide	230	Vitamin E	312
Furosemide	232	Vitamin K ₁	314
Hydrochlorothiazide	234	Vi-Daylin® Multivitamin	
Spironolactone.....	235	Products	316
GI Drugs	237	Vi-Sol® Multivitamin	
Cimetidine	238	Products	317
Famotidine	240	Nutritionals	319
Lansoprazole	242	Dilution Table	320
Metoclopramide	244	Human Milk (Mature)	321
Nizatidine.....	245	Preterm Human Milk +	
Omeprazole	246	Similac® Human Milk	
Ranitidine	248	Fortifier	322
Ursodiol	250	Preterm Human Milk +	
Respiratory Drugs	251	Enfamil® Human Milk	
Albuterol	252	Fortifier	323
Aminophylline	254	Preterm Human Milk +	
Caffeine Citrate	256	Prolact+ H ² MF™	
Dexamethasone	258	Human Milk Fortifier	324
Dornase alfa	261	Enfamil® Human Milk	
Ipratropium	262	Fortifier	325
Nitric Oxide	264	Similac® Human Milk	
Surfactant (Natural, animal-derived)	266	Fortifier	326
Curosurf®	268	Prolact+ H ² MF™ Human	
Infasurf®	270	Milk Fortifier	327
Survanta®	271	Preterm Human Milk +	
Miscellaneous Drugs	273	Similac® Special Care®	
Cyclopentolate (Ophthalmic)	274	30 (1:1 ratio)	328
Diazoxide	275	Similac® Special Care® 30	
EMLA®	276	with Iron	329
Glucagon	277	Term Human Milk +	
Hyaluronidase	278	Similac® NeoSure®	
Hydrocortisone	280	Powder	330
Insulin.....	282	Term Human Milk +	
Levothyroxine (T ₄)	284	EnfaCare® LIPIL®	
Octreotide	286	Powder	331
Phenylephrine (Ophthalmic)	288	Similac® Special Care® 20 ..	332
Sodium Bicarbonate	290	Similac® Special Care® 24 ..	333

Contents

Similac® Special Care® 24 High Protein	335	Enfamil® Premature LIPIL® 20	353
Similac® Special Care® 24 High Protein + Similac® Special Care® with Iron 30	336	Enfamil® Premature LIPIL® 24	354
Similac® Advance® EarlyShield™	337	Enfamil LIPIL® with Iron 20	355
Similac® PM 60/40	338	Enfamil A.R.® LIPIL® 20	356
Similac Sensitive™	339	Enfamil® LactoFree® LIPIL® 20	357
Similac Sensitive R.S.™	340	Enfamil® ProSobee® LIPIL® 20	358
Similac® Organic	341	Pregestimil® LIPIL® 20	359
EleCare®	342	Pregestimil® LIPIL® 24	360
Dilution Table - EleCare® Powder	343	Pregestimil® LIPIL® Powder 20	361
Similac® Isomil® Advance®	344	Enfamil® Gentlelease® LIPIL®	362
Similac® Alimentum®	345	Enfaport® LIPIL®	363
Similac® NeoSure®	346	Nutramigen® LIPIL® 20	364
PediaSure®	347	Nutramigen® AA™ LIPIL®	365
PediaSure® Enteral	348	Good Start® DHA & ARA	366
Enfamil® EnfaCare® LIPIL® 22	349	Neocate® 20	367
Enfamil® EnfaCare® LIPIL® + Enfamil® LIPIL® Concentrate 24	350	MCT Oil	368
Enfamil® EnfaCare® LIPIL® + Enfamil® LIPIL® Concentrate 27	351	Microlipid®	369
Enfamil® Premature LIPIL® 24 + Enfamil® LIPIL® Concentrate 30	352	Fat Emulsion	370
Recommended Concentrations for Administration 373			
Newborn Metric Conversion Tables 379			

Abbreviations

The abbreviations listed below are used in the text.

a/A	arterial-alveolar (gradient)
a/ApO ₂	arterial-alveolar oxygen tension ratio
ABGs	arterial blood gases
ACTH	adrenocorticotrophic hormone
ALT	alanine aminotransferase
AMP	adenosine monophosphate
ANC	absolute neutrophil count
APTT	activated partial thromboplastin time
AST	aspartate aminotransferase
ATP	adenosine triphosphate
ATPase	adenosine triphosphatase
A-V	atrioventricular
BUN	blood urea nitrogen
BPD	bronchopulmonary dysplasia
bpm	beats per minute
CBC	complete blood count
CSF	cerebrospinal fluid
CHF	congestive heart failure
CNS	central nervous system
CVP	central venous pressure
DIC	disseminated intravascular coagulation
DNA	deoxyribonucleic acid
D ₅ NS	5% dextrose in normal saline solution
DPPC	dipalmitoyl phosphatidylcholine
D ₅ W	5% dextrose in water solution
D ₁₀ W	10% dextrose in water solution
D ₁₅ W	15% dextrose in water solution
D ₂₀ W	20% dextrose in water solution
DT	diphtheria, tetanus [vaccine]
DTP	diphtheria, tetanus, pertussis [vaccine]
EEG	electroencephalogram
EKG	electrocardiogram
ET	endotracheal
FiO ₂	fractional inspired oxygen concentration
FRC	functional residual capacity
GABA	gamma-aminobutyric acid
GCSF	granulocyte colony stimulating factor
GE	gastroesophageal
GFR	glomerular filtration rate
GI	gastrointestinal
HBeAg	hepatitis B e antigen
HBIG	hepatitis B immune globulin
HBsAg	hepatitis B surface antigen
Hib	Haemophilus influenzae b
HIV	human immunodeficiency virus

IC	intracardiac
IgG	immunoglobulin G
IM	intramuscular
IPV	inactivated polio vaccine (Salk)
IV	intravenous
IVH	intraventricular hemorrhage
IVIG	intravenous immune globulin (human)
Lf	potency of a given weight of an internationally accepted standard preparation of antiserum or antigen
LR	lactated Ringer's solution
NEC	necrotizing enterocolitis
NS	normal saline solution (0.9% sodium chloride)
OPV	oral polio vaccine
PMA	postmenstrual age
PCO ₂	partial pressure of carbon dioxide in the blood
PDA	patent ductus arteriosus
PO	by mouth (per os)
PO ₂	partial pressure of oxygen in the blood
ppm	parts per million
PR	by rectum
PVC	premature ventricular contraction
Q	every (quaque)
RDI	Reference Daily Intakes (replaces US RDAs)
RDS	respiratory distress syndrome
RNA	ribonucleic acid
ROP	retinopathy of prematurity
S-A	sinoatrial node, "pacemaker" of the heart
subQ	subcutaneously
SGA	small for gestational age
SVT	supraventricular tachycardia
⁹⁹ Tc-IDA	technetium 99m-image display and analysis
TPN	total parenteral nutrition
TSH	thyroid-stimulating hormone
UAC	umbilical artery catheter
US RDAs	US Recommended Daily Allowances
VLBW	very-low-birth-weight

ANTIMICROBIALS

An explanatory note about antimicrobial dosing charts:

The antibiotic dosing charts reflect the fact that the renal function and drug elimination are most strongly correlated with Postmenstrual Age ("PMA", equivalent to Gestational Age plus Postnatal Age). Postmenstrual age is therefore used as the primary determinant of dosing interval, with Postnatal Age as the secondary qualifier.

Example: A baby born at 28 weeks gestation is now 21 days old. To determine the dosing interval for cefotaxime, first go to the row on the chart containing his Postmenstrual Age of 31 weeks (30 to 36), and then his Postnatal Age of 21 days (>14) to yield a dosing interval of 8 hours.

Dose & Administration

20 mg/kg per dose Q8 hours IV infusion by syringe pump over 1 hour. Prolong the dosing interval in premature infants <34 weeks PMA, or in patients with significant renal impairment or hepatic failure. Treat localized herpes simplex infections for 14 days, disseminated or CNS infections for 21 days.

Chronic suppression: 75 mg/kg per dose PO Q12 hours.

Uses

Treatment of neonatal herpes simplex infections, varicella zoster infections with CNS and pulmonary involvement, and herpes simplex encephalitis.

Monitoring

Periodic CBC. Serum concentrations two hours after a dose should be approximately 2 mcg/mL. Follow renal and hepatic function. Monitor IV site for phlebitis—if noted, make infusion solution more dilute.

Adverse Effects/Precautions

Neutropenia occurs in approximately 20% of patients - decrease dose or treat with GCSF if ANC remains less than 500/mm³. Phlebitis may occur at IV site due to alkaline pH of 10. Risk of transient renal dysfunction and crystalluria is minimized by slow infusion rates and adequate patient hydration. Resistant viral strains may emerge during long-term therapy; these patients are at high risk for progressive life-threatening disease.

Pharmacology

Antiviral drug that is preferentially taken up by infected cells; inhibits viral DNA synthesis. CSF concentrations are 30 to 50% of serum concentrations. Oral absorption is 15 to 30%. Most of administered dose is excreted unchanged in urine, primarily via glomerular filtration. Protein binding and metabolism are minimal. Serum half-life is 3 to 4 hours in patients with normal renal and hepatic function.

Special Considerations/Preparation

Intravenous formulations available as solution (50 mg/mL) or as powder for solution in 500-mg and 1-g vials. Prepare powder for solution by dissolving contents of 500-mg vial in 10 mL sterile water for injection. Reconstituted solution is stable at room temperature for 12 hours. **Do not refrigerate.**

Infusion solution concentration should be no greater than 7 mg/mL.

A 5-mg/mL dilution may be made by adding 1 mL of 50 mg/mL concentration to 9 mL of preservative-free normal saline. Dilution should be used within 24 hours.

Oral suspension available in 200 mg/5 mL concentration. Store at room temperature. Shake well before administration.

Acyclovir

Solution Compatibility: D₅W, D₁₀W, and NS.

Solution Incompatibility: Dex/AA.

Terminal Injection Site Compatibility: Amikacin, ampicillin, aminophylline, cefazolin, cefotaxime, cefoxitin, ceftazidime, ceftriaxone, chloramphenicol, cimetidine, clindamycin, dexamethasone, erythromycin lactobionate, famotidine, fluconazole, gentamicin, heparin, hydrocortisone succinate, imipenem/cilastatin, linezolid, lorazepam, meropenem, metoclopramide, metronidazole, milrinone, morphine, nafcillin, oxacillin, penicillin G, pentobarbital, piperacillin, potassium chloride, propofol, ranitidine, remifentanil, sodium bicarbonate, theophylline, ticarcillin/clavulanate, tobramycin, trimethoprim-sulfamethoxazole, vancomycin, and zidovudine.

Incompatibility: Fat emulsion. Aztreonam, caffeine citrate, cefepime, dobutamine, dopamine, and piperacillin-tazobactam.

Selected References

- ◆ Tiffany KF, Benjamin DK Jr, Palansthiran P, et al: Improved neurodevelopmental outcomes following long-term high-dose acyclovir therapy in infants with central nervous system and disseminated herpes simplex disease. *J Perinatol* 2005;25:156-161.
- ◆ Kimberlin DW, Lin C-Y, Jacobs RF, et al: Safety and efficacy of high-dose intravenous acyclovir in the management of neonatal herpes simplex infections. *Pediatrics* 2001;108:230-238.
- ◆ American Academy of Pediatrics. Herpes simplex. In: Pickering LK, ed. *2003 Red Book: Report of the Committee on Infectious Diseases*. 26th ed. Elk Grove Village, IL: American Academy of Pediatrics;2003: p 347.
- ◆ Rudd C, Rivadeneira ED, Gutman LT: Dosing considerations for oral acyclovir following neonatal herpes disease. *Acta Paediatr* 1994;83:1237-43.
- ◆ Whitley R, Arvin A, Prober C, et al: A controlled trial comparing vidarabine with acyclovir in neonatal herpes simplex virus infection. *N Engl J Med* 1991;324:444.
- ◆ Englund JA, Zimmerman BS, Swierkosz EM, et al: Herpes simplex virus resistant to acyclovir: A study in a tertiary care center. *Ann Intern Med* 1990;112:416.
- ◆ McDonald L, Tartaglione TA, Mendelman PM, et al: Lack of toxicity in two cases of neonatal acyclovir overdose. *Pediatr Infect Dis J* 1989;8:529.
- ◆ Sullender WM, Arvin AM, Diaz PS, et al: Pharmacokinetics of acyclovir suspension in infants and children. *Antimicrob Agents Chemother* 1987;31:1722.
- ◆ Hintz M, Connor JD, Spector SA, et al: Neonatal acyclovir pharmacokinetics in patients with herpes virus infections. *Am J Med* 1982;73(suppl):210.
- ◆ Product Information, Abraxis Pharmaceutical Products, 2006
- ◆ Product Information, GlaxoSmithKline, 2005

Text updated 03/2008

References updated 3/2006

Compatibilities updated 3/2005

Dose & Administration

IV infusion by syringe pump over 30 minutes. Administer as a separate infusion from penicillin-containing compounds. IM injection is associated with variable absorption, especially in the very small infant.

To use dosing chart, please refer to explanatory note on page 1.

Dosing Chart

PMA (weeks)	Postnatal (days)	Dose (mg/kg)	Interval (hours)
$\leq 29^*$	0 to 7	18	48
	8 to 28	15	36
	≥ 29	15	24
30 to 34	0 to 7	18	36
	≥ 8	15	24
≥ 35	ALL	15	24

* or significant asphyxia, PDA, or treatment with indomethacin

Uses

Restricted to treatment of infections caused by gram-negative bacilli that are resistant to other aminoglycosides. Usually used in combination with a β -lactam antibiotic.

Monitoring

Measure serum concentrations when treating for more than 48 hours. Obtain peak concentration 30 minutes after end of infusion, and trough concentration just prior to the next dose. When treating patients with serious infections or significantly changing fluid or renal status consider measuring the serum concentration 24 hours after a dose, and use the chart below for the suggested dosing interval. Blood samples obtained to monitor serum drug concentrations should be spun and refrigerated or frozen as soon as possible.

Therapeutic serum concentrations:

Peak: 20 to 30 mcg/mL (or C_{max} /MIC ratio greater than 8:1)
(Draw 30 minutes after end of infusion, 1 hour after IM injection.)

Trough: 2 to 5 mcg/mL

Suggested Dosing Intervals

Level at 24 hrs (mcg/mL)	Half-life (hours)	Suggested Dosing Interval (hours)
≤ 5	≈ 9	24
5.1 to 8.0	≈ 12	36
8.1 to 10.5	≈ 16	48
≥ 10.6		Measure level in 24 hours

Adverse Effects/Precautions

Black Box Warning

According to the manufacturer's black box warning, aminoglycoside therapy has been associated with potential neurotoxicity, ototoxicity, and nephrotoxicity. Patients with impaired renal function, dehydration, and those who receive high dosage or prolonged therapy are at an increased risk of toxicity. Discontinue therapy or adjust dose if there is evidence of ototoxicity or nephrotoxicity. Aminoglycoside ototoxicity is usually irreversible.

Transient and reversible renal tubular dysfunction may occur, resulting in increased urinary losses of sodium, calcium, and magnesium. Vestibular and auditory ototoxicity may occur. The addition of other nephrotoxic and/or ototoxic medications (e.g. furosemide, vancomycin) may increase these adverse effects. Increased neuromuscular blockade (i.e. neuromuscular weakness and respiratory failure) may occur when used with pancuronium or other neuromuscular blocking agents and in patients with hypermagnesemia.

Pharmacology

Dosing recommendations are based on: (1) Higher peak concentrations increase concentration-dependent bacterial killing; (2) There is a post-antibiotic effect on bacterial killing, especially when treating concurrently with a β -lactam antibiotic; (3) There may be less toxicity with less frequent dosing, due to less renal drug accumulation. Volume of distribution is increased and clearance is decreased in patients with PDA. Serum half-life is prolonged in premature and asphyxiated newborns. Inactivation of amikacin by penicillin-containing compounds appears to be a time-, temperature-, and concentration-dependent process. This is probably clinically significant only when penicillin-containing compounds are mixed in IV solutions or when the blood is at room temperature for several hours before the assay is performed.

Special Considerations/Preparation

Available in concentrations of 50 mg/mL and 250 mg/mL. For IV use, dilute with a compatible solution to a concentration of 5 mg/mL.

Solution Compatibility: D₅W, D₁₀W, D₂₀W, and NS.

Terminal Injection Site Compatibility: Dex/AA solutions. Acyclovir, aminophylline, amiodarone, aztreonam, caffeine citrate, calcium chloride, calcium gluconate, cefazolin, cefepime, cefotaxime, cefoxitin, ceftazidime, ceftriaxone, chloramphenicol, cimetidine, clindamycin, dexamethasone, enalaprilat, epinephrine, esmolol, fluconazole, furosemide, heparin (concentrations ≤ 1 unit/mL), hydrocortisone succinate, hyaluronidase, linezolid, lorazepam, metronidazole, midazolam, milrinone, morphine, nicardipine, pentobarbital, phenobarbital, potassium chloride, ranitidine, remifentanil, sodium bicarbonate, vancomycin, vitamin K₁, and zidovudine.

Incompatibility: Fat emulsion. Amphotericin B, ampicillin, azithromycin, carbenicillin, heparin (concentrations > 1 unit/mL), imipenem/cilastatin, methicillin, mezlocillin, nafcillin, oxacillin, penicillin G, phenytoin, propofol, thiopental, and ticarcillin/clavulanate.

continued...

Selected References

- ◆ Contopoulos-Ioannidis DG, Giotis ND, Baliatsa DV, Ioannidis JPA: Extended-interval aminoglycoside administration for children: a meta-analysis. *Pediatrics* 2004;114:e111-e118.
- ◆ Langhendries JP, Battisti O, Bertrand JM, et al: Adaptation in neonatology of the once-daily concept of aminoglycoside administration: Evaluation of a dosing chart for amikacin in an intensive care unit. *Biol Neonate* 1998;74:351-362.
- ◆ Product Information, Bedford Laboratories, 2004

Adverse Effects/Precautions updated 1/2009

Monitoring, Compatibilities and References updated 3/2005

It is also a good idea to have
a few small pieces of paper
in your backpack or briefcase
so you can quickly write down
any important numbers or
information you may need.

Remember, time is money!

Dose & Administration

0.5 to 1 mg/kg Q24 hours IV infusion over 2 to 6 hours.

Dosage modification for renal dysfunction is only necessary if serum creatinine increases >0.4 mg/dL during therapy - hold dose for 2 to 5 days.

Uses

Treatment of systemic fungal infections and severe superficial mycoses.

Monitoring

Monitor CBC, electrolytes, urine output, BUN, and serum creatinine at least every other day. Observe IV site for irritation—phlebitis is common. Serum amphotericin concentrations are not routinely followed.

Adverse Effects/Precautions

Decreases renal blood flow and GFR by 20% to 60%. Injures tubular epithelium with resultant urinary loss of potassium and magnesium, decreased reabsorption of sodium, and renal tubular acidosis. Sodium intake > 4 mEq/kg per day may prevent or decrease nephrotoxicity. Anemia, thrombocytopenia, hypokalemia, nausea/vomiting, and fever/chills. Consider analgesia before beginning infusion. Cardiac arrest has occurred in patients who received 10 times the recommended dose.

Black Box Warning According to the manufacturer's black box warning, it is recommended that the product name and dosage are verified if the prescribed dose exceeds 1.5 mg/kg.

Pharmacology

Amphotericin B binds to ergosterol in the membrane of sensitive fungi and may be fungicidal or fungistatic. The therapeutic concentration range is not well-defined. Highly protein-bound (greater than 90%). Elimination half-life is approximately 15 days. Drug may accumulate in tissues to a significant concentration and be excreted renally for months.

Special Considerations/Preparation

Available as powder for injection in 50-mg vials. Reconstitute using D₅W or Preservative free SW to a concentration of 5 mg/mL, then dilute further using D₅W to a concentration no greater than 0.1 mg/mL for infusion. Reconstituted solution stable for 24 hours at room temperature or 7 days in refrigerator. **Do not flush IV or mix amphotericin with saline solution**—precipitation will occur. May filter if necessary; mean pore diameter should not be less than 1 micron. **Protect from light.**

Solution Compatibility: D₅W, D₁₀W, D₁₅W, and D₂₀W.

Solution Incompatibility: Dex/AA solutions and NS.

Terminal Injection Site Compatibility: Amiodarone, heparin, hydrocortisone, sodium bicarbonate, and zidovudine.

Incompatibility: Fat emulsion. Amikacin, aztreonam, calcium chloride, calcium gluconate, cefepime, cimetidine, ciprofloxacin, dopamine, enalaprilat, fluconazole, gentamicin, linezolid, magnesium sulfate, meropenem, netilmicin, penicillin G, piperacillin-tazobactam, potassium chloride, propofol, ranitidine, remifentanil, and tobramycin.

continued...

Amphotericin B

Selected References

- ◆ Holler B, Omar SA, Farid MD, Patterson MJ: Effects of fluid and electrolyte management on amphotericin B-induced nephrotoxicity among extremely low birth weight infants. *Pediatrics* 2004;113:e608-e616.
- ◆ Chapman RL: *Candida* infections in the neonate. *Curr Opin Pediatr* 2003;15:97-102.
- ◆ Bliss JM, Wellington M, Gigliotti F: Antifungal pharmacotherapy for neonatal candidiasis. *Semin Perinatol* 2003;27:365-374.
- ◆ Lyman CA, Walsh TJ: Systemically administered antifungal agents: A review of their clinical pharmacology and therapeutic applications. *Drugs* 1992;44:9.
- ◆ Baley JE, Meyers C, Kliegman RM, et al: Pharmacokinetics, outcome of treatment, and toxic effects of amphotericin B and 5-fluorocytosine in neonates. *J Pediatr* 1990;116:791.
- ◆ Starke JR, Mason EL, Kramer WG, Kaplan SL: Pharmacokinetics of amphotericin B in infants and children. *J Infect Dis* 1987;155:766.
- ◆ Dodds Ashley ES, Lewis R, Lewis JS, et al. Pharmacology of systemic antifungal agents. *Clin Infect Dis* 2006;43:S29-39.
- ◆ Product Information, Bristol-Myers Squibb, 2006.

Adverse Effects/Precautions updated 1/2009

References updated 3/2007

Compatibilities updated 3/2005

Dose & Administration

5 mg/kg per dose Q24 hours IV infusion by syringe pump over 2 hours.

Uses

Treatment of systemic fungal infections resistant to conventional amphotericin B therapy or in patients with renal or hepatic dysfunction.

Monitoring

Serum amphotericin B concentrations are not routinely followed. Monitor urine output. Periodic CBC for thrombocytopenia, electrolytes for hypokalemia, BUN, serum creatinine, and hepatic transaminases.

Adverse Effects/Precautions

Anemia, thrombocytopenia, hypokalemia, nausea/vomiting, and fever/chills.

Pharmacology

ABELCET® consists of amphotericin B complexed with two phospholipids in a 1:1 drug-to-lipid ratio. Acts by binding to the sterol component of a cell membrane leading to alterations in the cell wall permeability and death. Penetrates the cell wall of susceptible fungi. Concentrates in the liver and spleen. Less nephrotoxic than conventional amphotericin B. Mean serum half-life in adults 24 to 38 hours. The pharmacokinetics of amphotericin B lipid complex is nonlinear.

Special Considerations/Preparation

Available as a ready-to-use admixture containing 100-mg ABELCET® in 20-mL suspension (5 mg/mL). Shake the vial gently until there is no evidence of any yellow sediment on the bottom. Withdraw the appropriate dose into a syringe using an 18 gauge needle. Remove the needle and replace with the supplied 5 micron filter needle. Inject the drug into a different syringe containing a measured amount of D₅W so that the **final infusion concentration is 1 to 2 mg/mL**. Shake until thoroughly mixed. Check for complete dispersion. The diluted admixture is stable for 48 hours refrigerated and an additional 6 hours at room temperature.

Do not freeze. Protect from light.

Do not flush IV or mix ABELCET® with saline solutions - precipitation will occur.

Solution Compatibility: D₅W at 1 to 2 mg/mL, D₁₀W and D₁₅W at 1 mg/mL dilution.

Solution Incompatibility: Dex/AA and NS.

Terminal Injection Site Compatibility: No available data.

Selected References

- ◆ Adler-Shohet F, Waskin H, Lieberman J M: Amphotericin B lipid complex for neonatal invasive candidiasis . *Arch Dis Child Fetal Neonatal Ed* 2001;84:F131-F133.
- ◆ Walsh TJ, Seibel NL, Arndt C, et al: Amphotericin B lipid complex in pediatric patients with invasive fungal infections. *Pediatr Infect Dis J* 1999;18:702-708.
- ◆ Wong-Beringer A, Jacobs RA, Guglielmo BJ: Lipid formulations of amphotericin B: Clinical efficacy and toxicities. *Clin Infect Dis* 1998;27:603-618.
- ◆ Dodds Ashley ES, Lewis R, Lewis JS, et al. Pharmacology of systemic antifungal agents. *Clin Infect Dis* 2006;43:S29-39.
- ◆ Product Information, Enzon, 2002

Compatibilities updated 3/2005,
Dose and References updated 3/2007.

Amphotericin B Liposome

Dose & Administration

5 to 7 mg/kg per dose Q24 hours IV infusion by syringe pump over 2 hours.

Uses

Treatment of systemic fungal infections resistant to conventional amphotericin B therapy or in patients with renal or hepatic dysfunction.

Monitoring

Serum amphotericin B concentrations are not routinely followed. Monitor urine output. Periodic CBC for thrombocytopenia, electrolytes for hypokalemia, BUN, serum creatinine, and hepatic transaminases.

Adverse Effects/Precautions

Anemia, thrombocytopenia, hypokalemia, nausea/vomiting, and fever/chills.

Pharmacology

Ambisome® consists of amphotericin B intercalated within a single bilayer liposomal drug delivery system. Acts by binding to the sterol component of a cell membrane leading to alterations in the cell wall permeability and death. Penetrates the cell wall of susceptible fungi. Concentrates in the liver and spleen but penetrates the CNS less than conventional amphotericin B. Less nephrotoxic than conventional amphotericin B. Mean serum half-life in adults 24 to 38 hours. The pharmacokinetics of amphotericin B liposome is nonlinear.

Special Considerations/Preparation

Available as powder for injection in 50 mg vials. Reconstitute by adding 12 mL of sterile water for injection to a yield a concentration of 4 mg/mL. Immediately shake vial vigorously for 30 seconds. Check for complete dispersion. Reconstituted suspension stable for 24 hours refrigerated.

Do not freeze. Protect from light.

Before administration, Ambisome® must be diluted with D₅W to a final concentration less than 2 mg/mL. A 1 mg/mL dilution may be made by filtering (using 5 micron filter) 1 mL of reconstituted solution into 3 mL of D₅W. Use one filter per vial of Ambisome®. Use dilution immediately.

Do not flush IV or mix Ambisome® with saline solutions-precipitation will occur.

Solution Compatibility: D₅W.

Solution Incompatibility: Dex/AA and NS.

Terminal Injection Site Compatibility: No available data.

Selected References

- ◆ Juster-Reicher A, Flidel-Rimon O, Amitay M, et al: High dose liposomal amphotericin B in the therapy of systemic candidiasis in neonates. *Eur J Clin Microbiol Infect Dis* 2003;22:603-07.
- ◆ Scarella A, Pasquariello MB, Giugliano B, et al: Liposomal amphotericin B treatment for neonatal fungal infections. *Pediatr Infect Dis J* 1998;17:146-148.
- ◆ Evdoridou J, Roilides E, Bibashi E, Kremenopoulos G: Multifocal osteoarthritis due to Candida albicans in a neonate: Serum level monitoring of liposomal amphotericin B and literature review. *Infection* 1997;25:112.
- ◆ Weitkamp JH, Poets CF, Sievers R, et al: Candida infection in very low birthweight infants: Outcome and nephrotoxicity of treatment with liposomal amphotericin B (Ambisome®). *Infection* 1998;26:11-15.
- ◆ Dodds Ashley ES, Lewis R, Lewis JS, et al. Pharmacology of systemic antifungal agents. *Clin Infect Dis* 2006;43:S29-39.
- ◆ Product Information, Gilead Sciences, 2005

References updated 3/2007.



AMIC BIAL

Dose & Administration

25 to 50 mg/kg per dose by IV slow push, or IM.

Some experts recommend 100 mg/kg/dose when treating meningitis and severe group B streptococcal sepsis.

To use dosing chart, please refer to explanatory note on page 1.

Dosing Interval Chart

PMA (weeks)	PostNatal (days)	Interval (hours)
≤29	0 to 28 ≥28	12 8
30 to 36	0 to 14 ≥14	12 8
37 to 44	0 to 7 ≥7	12 8
≥45	ALL	6

Uses

Broad-spectrum antibiotic useful against group B *streptococcus*, *Listeria monocytogenes*, and susceptible *E coli* species.

Monitoring

Serum concentration can be measured but is not usually necessary.

Adverse Effects/Precautions

Very large doses may result in CNS excitation or seizure activity. Hypersensitivity reactions (maculopapular rash, urticarial rash, or fever) are rare in neonates.

Pharmacology

Ampicillin is a semisynthetic penicillin that is bactericidal. Clearance is primarily by the renal route and is inversely related to postnatal age. Serum half-life in term infants younger than 7 days is approximately 4 hours.

Special Considerations/Preparation

Available as powder for injection in 125-, 250-, 500-mg, 1-g, and 2-g vials. Reconstitute using sterile water for injection. Maximum concentration for IV infusion is 100 mg/mL. Mix to a final concentration of 250 mg/mL for IM administration. Reconstituted solution must be used within 1 hour of mixing because of loss of potency.

Solution Compatibility: D₅W and NS.

Solution Incompatibility: Dex/AA.

Terminal Injection Site Compatibility: Fat emulsion. Acyclovir, aminophylline, aztreonam, calcium gluconate, cefepime, chloramphenicol, cimetidine, clindamycin, dopamine, enalaprilat, epinephrine, famotidine, furosemide, heparin, hydrocortisone succinate, insulin, lidocaine, linezolid, metronidazole, milrinone, morphine, phytonadione, potassium chloride, propofol, ranitidine, remifentanil, sodium bicarbonate, and vancomycin.

Incompatibility: Amikacin, amiodarone, erythromycin lactobionate, fluconazole, gentamicin, hydralazine, metoclopramide, midazolam, nicardipine, and tobramycin.

Selected References

- ◆ Shaffer CL, Davey AM, Ransom JL, et al: Ampicillin-induced neurotoxicity in very-low-birth-weight neonates. *Ann Pharmacother* 1998;32:482-484.
- ◆ Prober CG, Stevenson DK, Benitz WE: The use of antibiotics in neonates weighing less than 1200 grams. *Pediatr Infect Dis J* 1990;9:111.
- ◆ Kaplan JM, McCracken GH, Horton LJ, et al: Pharmacologic studies in neonates given large dosages of ampicillin. *J Pediatr* 1974;84:571.
- ◆ Boe RW, Williams CPS, Bennett JV, Oliver TK Jr: Serum levels of methicillin and ampicillin in newborn and premature infants in relation to postnatal age. *Pediatrics* 1967;39:194.
- ◆ Axline SG, Yaffe SJ, Simon HJ: Clinical pharmacology of antimicrobials in premature infants: II. Ampicillin, methicillin, oxacillin, neomycin, and colistin. *Pediatrics* 1967;39:97.
- ◆ Product Information, Sandoz 2004

Updated 3/2001

Compatibilities updated 3/2005

Dose & Administration

Treatment of Pertussis infections: 10 mg/kg per dose orally, once daily for 5 days.

Treatment of Chlamydia trachomatis conjunctivitis and pneumonitis: 20 mg/kg per dose orally, once daily for 3 days.

Intravenous treatment is limited to those who cannot be treated orally. To date no clinical studies have been conducted to evaluate the safety or efficacy of IV azithromycin in the pediatric population. Suggested IV dose: 5 mg/kg per dose once daily.

Uses

Treatment and postexposure prophylaxis against *Bordetella pertussis*. As a substitute for penicillin in situations of significant allergic intolerance.

Monitoring

Assess gastrointestinal tolerance.

Adverse Effects/Precautions

Limited data in neonates. Diarrhea and/or vomiting occur in 5% to 12% of patients. Irritability, rash, and blood in stool have also been reported. There is one new case report of pyloric stenosis in 2 of 3 triplets treated with azithromycin for pertussis.

Pharmacology

Azithromycin is classified as an azalide, a subclass of macrolide antibiotics. In vitro activity has been demonstrated against *Bordetella pertussis*, as well as Streptococci (Groups C, F, G and Viridans), *Ureaplasma urealyticum*, and Peptostreptococcus species. Eradication of *B. pertussis* in unimmunized individuals (e.g., neonates) takes longer and requires higher doses than immunized individuals. Oral bioavailability is 38% in adults and children and is not affected by food. Primarily excreted unchanged in the bile, with some hepatic metabolism to inactive metabolites. The prolonged terminal half-life (approximately 80 hours) is thought to be due to extensive uptake and subsequent release of drug from tissues.

Special Considerations/Preparation

Oral suspension is available in 300, 600, 900, and 1,200 mg bottles. Reconstitute 300 mg bottle with 9 mL of water to provide a final concentration of 100 mg per 5 mL (20 mg/mL). Shake well before administration. Do not refrigerate. Use within 10 days once bottle has been opened. Azithromycin for intravenous injection is supplied in single use vials containing 500 mg lyophilized powder. Reconstitute by adding 4.8 mL Sterile Water for Injection, then shake the vial until all the drug is dissolved. The concentration of the reconstituted solution is 100 mg/mL. It is stable at room temperature for 24 hours. **Dilute prior to administration** using a compatible solution to a final concentration of 1 to 2 mg/mL. Diluted solution stable for 24 hours at room temperature or 7 days in refrigerator. Do not use higher concentrations due to local IV site reactions. **Infuse over at least 60 minutes.**

Solution Compatibility: D₅W, NS, 5% Dextrose in 0.45%NaCl with 20 mEq/L KCl, and Lactated Ringer's.

Terminal Injection Site Compatibility: Do not infuse other drugs through the same IV line.

Incompatibility: Amikacin, aztreonam, cefotaxime, ceftazidime, ceftriaxone, cefuroxime, clindamycin, famotidine, fentanyl, furosemide, gentamicin, imipenem-cilastatin, morphine, piperacillin-tazobactam, potassium chloride, ticarcillin-clavulanate, and tobramycin.

Selected References

- ◆ American Academy of Pediatrics. Chlamydia trachomatis, and Pertussis. In: Pickering LK, Baker CJ, Long SS, McMillan JA, eds. *Red Book: 2006 Report of the Committee on Infectious Diseases*. 27th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2006: pp 255, and 500-502.
- ◆ Centers for Disease Control and Prevention. Recommended antimicrobial agents for the treatment and postexposure prophylaxis of pertussis. 2005 CDC guidelines. *MMWR* 2005;54(No. RR-14):pp. 4, 10.
- ◆ Friedman DS, Curtis CR, Schauer SL, et al. Surveillance for transmission and antibiotic adverse events among neonates and adults exposed to a healthcare worker with pertussis. *Infect Control Hosp Epidemiol* 2004;25:967-73.
- ◆ Langley JM, Halperin SA, Boucher FD, et al. Azithromycin is as effective and better tolerated than erythromycin estolate for the treatment of pertussis. *Pediatrics* 2004;114:96-101.
- ◆ Jacobs RF, Maples HD, Aranda JV, et al. Pharmacokinetics of intravenously administered azithromycin in pediatric patients. *Pediatr Infect Dis J* 2005;24:34-39.
- ◆ Morrison W. Infantile hypertrophic pyloric stenosis in infants treated with azithromycin. *Pediatr Infect Dis J* 2007;26:186-188.
- ◆ Product Information, Pfizer, Inc., 2007.

Updated 3/2007

Dose & Administration

30 mg/kg per dose IV slow push over 5 to 10 minutes, or IM.

To use dosing chart, please refer to explanatory note on page 1.

Dosing Interval Chart

PMA (weeks)	PostNatal (days)	Interval (hours)
≤29	0 to 28 >28	12 8
30 to 36	0 to 14 >14	12 8
37 to 44	0 to 7 >7	12 8
≥45	ALL	6

Uses

Treatment of neonatal sepsis caused by susceptible gram-negative organisms (e.g. *E coli*, *H influenzae*, *Klebsiella*, *Pseudomonas*, and *Serratia*). Generally used in combination with ampicillin (empirical treatment of sepsis) or an aminoglycoside (for synergism against *Pseudomonas* and *Enterobacteriaceae*).

Monitoring

Check serum glucose one hour after administration. Measuring serum concentration is not usually necessary. Periodic CBC, AST, ALT.

Adverse Effects/Precautions

Aztreonam contains 780 mg L-arginine per gram of drug (23.4 mg/kg body weight per dose). Adequate amounts of glucose must be provided to prevent hypoglycemia. Side effects are rare but include eosinophilia, elevation of serum transaminases, and phlebitis at the injection site.

Pharmacology

Aztreonam is a synthetically-produced monocyclic β-lactam antibiotic. Although bactericidal against aerobic gram-negative bacteria, it has virtually no activity against aerobic gram-positive and anaerobic bacteria, thereby producing little alteration of bowel flora. Good tissue and fluid penetration has been demonstrated in adults, along with protein-binding of 50 to 65%. Eliminated renally, primarily as unchanged drug. Serum half-life in neonates is 3 to 9 hours. Aztreonam does not interfere with bilirubin-albumin binding.

Special Considerations/Preparation

Available as powder for injection in 1-g, and 2-g vials. Reconstitute 1-g vial with 10 mL of either sterile water for injection or NS (100 mg/mL).

Shake immediately and vigorously. Reconstituted solution stable for 48 hours at room temperature, 7 days refrigerated.

Solution Compatibility: D₅W, D₁₀W, and NS.

Terminal Injection Site Compatibility: Dex/AA and fat emulsion. Amikacin, aminophylline, ampicillin, bumetanide, calcium gluconate, cefazolin, ceftazidime, ceftriaxone, cimetidine, clindamycin, dexamethasone, dobutamine, dopamine, enalaprilat, famotidine, fluconazole, furosemide, gentamicin, heparin, hydrocortisone succinate, imipenem, insulin, linezolid, metoclopramide, mezlocillin, morphine, netilmicin, nicardipine, piperacillin, piperacillin/tazobactam, potassium chloride, propofol, quinupristin/dalfopristin, ranitidine, remifentanil, sodium bicarbonate, ticarcillin/clavulanate, tobramycin, vancomycin, and zidovudine.

Incompatibility: Acyclovir, amphotericin B, azithromycin, ganciclovir, lorazepam, metronidazole, and nafcillin.

Selected References

- ◆ Uauy R, Mize C, Argyle C, McCracken GH: Metabolic tolerance to arginine: Implications for the safe use of arginine salt-aztreonam combination in the neonatal period. *J Pediatr* 1991;118:965.
- ◆ Cuzzolin L, Fanos V, Zambreri D, et al: Pharmacokinetics and renal tolerance of aztreonam in premature infants. *Antimicrob Agents Chemother* 1991;35:1726.
- ◆ Prober CG, Stevenson DK, Benitz WE: The use of antibiotics in neonates weighing less than 1200 grams. *Pediatr Infect Dis J* 1990;9:111.
- ◆ Likitnukul S, McCracken GH, Threlkeld N, et al: Pharmacokinetics and plasma bactericidal activity of aztreonam in low-birth-weight infants. *Antimicrob Agents Chemother* 1987;31:81.
- ◆ Product Information, Bristol-Myers Squibb, 2007

Added 3/96

Compatibilities updated 3/2007

Dose & Administration

25 mg/m² (or approximately 2 mg/kg) per dose Q24h, IV infusion via syringe pump over at least 1 hour.

Uses

Treatment of patients with refractory Candidemia, intra-abdominal abscesses, peritonitis and pleural space infections, and those patients intolerant of amphotericin B. Treatment of invasive Aspergillosis in patients who are refractory to or intolerant of other therapies.

There are case reports, but not controlled clinical trials, treating endocarditis, osteomyelitis, and meningitis due to *Candida*.

Monitoring

Assess IV site for signs of irritation. Periodic measurement of serum potassium, calcium, and hepatic transaminases.

Adverse Effects/Precautions

Adverse effects reported in neonates (small number of patients): thrombophlebitis, hypercalcemia, hypokalemia, elevated liver enzymes, and isolated direct hyperbilirubinemia. In adult studies the primary adverse effects are fever, headache, vomiting, diarrhea, signs of histamine release and irritation at the injection site. These occurred less frequently than with amphotericin B or with AmBisome®.

Pharmacology

Caspofungin is the first of a new class of antifungal agents (echinocandins) that inhibit the synthesis of β -(1,3)-D-glucan, an integral component of the fungal cell wall. It is fungicidal against *Candida* species, but fungistatic against *Aspergillus*. The echinocandins are excreted primarily by the liver, presumably metabolized through an O-methyltransferase. They are not metabolized through the CYP enzyme system and therefore have significantly fewer drug-drug interactions than the azoles. Dexamethasone, phenytoin, carbamazepine, nevirapine, and rifampin all induce caspofungin drug clearance, lowering serum concentrations.

Special Considerations/Preparation

Cancidas® is supplied as a white to off-white powder cake in single use vials, containing either 50- or 70 mg. To prepare the 50 mg Cancidas® infusion: 1) Equilibrate the refrigerated vial to room temperature. 2) Aseptically add 10.5 mL Normal Saline or Sterile Water for Injection to the vial. The powder cake will dissolve completely with gentle mixing. This reconstituted solution can be stored at room temperature for up to one hour. Visually inspect the reconstituted solution for particulate matter or discoloration. Do not use if the solution is cloudy or has precipitated. 3) Aseptically transfer 10 ml of the reconstituted solution to 250 mL bag or bottle of 0.9%, 0.45%, or 0.225% Sodium Chloride Injection, or Lactated Ringer's Injection. This final patient infusion solution has a concentration of 0.2 mg/mL caspofungin, and can be stored for up to 24 hours at room temperature or up to 48 hours refrigerated. May also be diluted in 100 mL of compatible diluent for fluid restricted patients. **Do not use diluents containing dextrose.**

fl (50 mg) + 10,5 ml SF 0,9% \Rightarrow dil.
 dil. I \rightarrow 10 ml be transferred in 250 ml
Concentrație finală 0,2 mg/ml SF 0,9%
 (dacă e restricție de fluid)

125.

SF 0,9%

100 ml

Solution Compatibility: Normal Saline, Lactated Ringer's.

Solution Incompatibility: All solutions containing dextrose.

Terminal Injection Site Compatibility: Do not co-infuse with any other medications. (No data).

Selected References

- ◆ Saez-Llorens X, Macias M, Maiya P, et al. Pharmacokinetics and safety of caspofungin in neonates and infants less than 3 months of age. *Antimicrob Agents Chemother* 2009;53:869-875.
- ◆ Smith PB, Steinbach WJ, Cotton CM, et al. Caspofungin for the treatment of azole resistant candidemia in a premature infant. *J Perinatol* 2007;27:127-129.
- ◆ Manzar S, Kamat M, Pyati S. Caspofungin for refractory candidemia in neonates. *Pediatr Infect Dis J* 2006;25:282-283.
- ◆ Odio CM, Araya R, Pinto Le, et al. Caspofungin therapy of neonates with invasive candidiasis. *Pediatr Infect Dis J* 2004;23:1093-1097.
- ◆ Steinbach WJ, Benjamin DK. New agents under development in children and neonates. *Curr Opin Infect Dis* 2005;18:484-489.
- ◆ Pannaraj PS, Walsh TJ, Baker CJ. Advances in antifungal therapy. *Pediatr Infect Dis J* 2005;10:921-923.
- ◆ Walsh TJ, Adamson PC, Seibel NL, et al. Pharmacokinetics, safety, and tolerability of caspofungin in children and adolescents. *Antimicrob Agents Chemother* 2005;49:4536-4545.
- ◆ Dodds Ashley ES, Lewis R, Lewis JS, et al. Pharmacology of systemic antifungal agents. *Clin Infect Dis* 2006;43:S29-39.
- ◆ Product Information, Merck & Co., 2008.

Dose and References updated 03/2009

Added 3/2007

Dose & Administration

25 mg/kg per dose IV slow push, or IM.

To use dosing chart, please refer to explanatory note on page 1.

Dosing Interval Chart

PMA (weeks)	PostNatal (days)	Interval (hours)
≤ 29	0 to 28	12
	>28	8
30 to 36	0 to 14	12
	>14	8
37 to 44	0 to 7	12
	>7	8
≥ 45	ALL	6

Uses

Use in neonates is generally limited to perioperative infection prophylaxis and treatment of urinary tract and soft tissue infections caused by susceptible organisms, e.g. penicillin-resistant *Staph. aureus*, *Klebsiella*, and *Proteus*.

Monitoring

Serum concentrations are not routinely monitored.

Adverse Effects/Precautions

Adverse effects are rare, but include phlebitis and eosinophilia.

Pharmacology

First generation cephalosporin that is bactericidal against many gram-positive and a few gram-negative organisms. Inactivated by β -lactamase producing organisms. Poor CNS penetration. Renally excreted as unchanged drug. Half-life in neonates is 3 to 5 hours.

Special Considerations/Preparation

Available as powder for injection in 500-mg, and 1000-mg vials. Reconstitute 500-mg vial using 2 mL of NS or sterile water for injection to a concentration of 225 mg/mL. Reconstituted solution stable for 24 hours at room temperature or 10 days in refrigerator. A 20 mg/mL dilution may be made by adding 1-mL of reconstituted solution to 10 mL sterile water for injection, or D₅W.

Solution Compatibility: D₅W, D₁₀W, and NS.

Terminal Injection Site Compatibility: Dex/AA and fat emulsion. Acyclovir, amikacin, aminophylline, aztreonam, calcium gluconate, clindamycin, enalaprilat, esmolol, famotidine, fluconazole, heparin, insulin, lidocaine, linezolid, midazolam, milrinone, morphine, metronidazole, multivitamins, nicardipine, pancuronium bromide, propofol, prostaglandin E₁, ranitidine, remifentanil, and vecuronium.

Incompatibility: Amiodarone, cimetidine, pentobarbital, and vancomycin. No data are currently available for potassium chloride.

Selected References

- ◆ Saez-Llorens X, McCracken GH: Clinical pharmacology of antibacterial agents. In: Remington JS, Klein JO (eds): *Infectious Diseases of the Fetus and Newborn Infant*, ed 5. Philadelphia: WB Saunders Co, 2001.
- ◆ Pickering LK, O'Connor DM, Anderson D, et al: Clinical and pharmacologic evaluation of cefazolin in children. *J Infect Dis* 1973;128:S407.
- ◆ Product Information, Orchid Healthcare, 2006

Added 3/96

Compatibilities updated 3/2005

Solution Compatibility: D₅W, D₁₀W, and NS.

Terminal Injection Site Compatibility: Dex/AA and fat emulsion. Acyclovir, amikacin, aminophylline, aztreonam, calcium gluconate, clindamycin, enalaprilat, esmolol, famotidine, fluconazole, heparin, insulin, lidocaine, linezolid, midazolam, milrinone, morphine, metronidazole, multivitamins, nicardipine, pancuronium bromide, propofol, prostaglandin E₁, ranitidine, remifentanil, and vecuronium.

Incompatibility: Amiodarone, cimetidine, pentobarbital, and vancomycin. No data are currently available for potassium chloride.

Selected References

- ◆ Saez-Llorens X, McCracken GH: Clinical pharmacology of antibacterial agents. In: Remington JS, Klein JO (eds): *Infectious Diseases of the Fetus and Newborn Infant*, ed 5. Philadelphia: WB Saunders Co, 2001.
- ◆ Pickering LK, O'Connor DM, Anderson D, et al: Clinical and pharmacologic evaluation of cefazolin in children. *J Infect Dis* 1973;128:S407.
- ◆ Product Information, Orchid Healthcare, 2006

Added 3/96

Compatibilities updated 3/2005

Dose & Administration

Term and preterm infants >28 days of age: 50 mg/kg per dose Q12 hr.

Term and preterm infants ≤28 days of age: 30 mg/kg per dose Q12 hr.

Meningitis and severe infections due to *Pseudomonas aeruginosa* or *Enterobacter* spp.: 50 mg/kg per dose Q 12 hr.

Administer via IV infusion by syringe pump over 30 minutes, or IM. To reduce pain at IM injection site, cefepime may be mixed with 1% lidocaine without epinephrine.

Uses

Treatment of serious infections caused by susceptible gram-negative organisms (e.g. *E. coli*, *H. influenzae*, *Enterobacter*, *Klebsiella*, *Morganella*, *Neisseria*, *Serratia*, and *Proteus* species), especially *Pseudomonas aeruginosa* that are resistant to 3rd generation cephalosporins. Treatment of serious infections caused by susceptible Gram-positive organisms (e.g. *Strep. pneumoniae*, *Strep. pyogenes*, *Strep. agalactiae*, and *Staph. aureus*).

Monitoring

Measuring serum concentration is not usually necessary.

Adverse Effects/Precautions

Safety has been documented to be the same as commonly used second- and third-generation cephalosporins. Reported adverse effects are uncommon but include rash, diarrhea, elevated hepatic transaminases, eosinophilia, and positive Coombs' test.

Pharmacology

Cefepime is a fourth-generation cephalosporin with treatment efficacy equivalent to third-generation cephalosporins. Potential advantages include: more rapid penetration through the cell wall of Gram-negative pathogens; enhanced stability to hydrolysis by β-lactamases; and enhanced affinity for penicillin-binding proteins. The drug distributes widely in body tissues and fluids (i.e. CSF, bile, bronchial secretions, lung tissue, ascitic fluid, middle ear). Protein binding is low ($\approx 20\%$), and it is primarily excreted unchanged in the urine. Serum half-life in infants older than 2 months of age is approximately 2 hours.

Cefepime

Special Considerations/Preparation

Available as powder for injection in 500-mg and 1-g, and 2-g vials. Reconstitute 500-mg vial with 5 mL of sterile water for injection to a concentration of 100 mg/mL. Maximum concentration for IV administration is 160 mg/mL, and for IM administration 280 mg/mL. Reconstituted solution stable for 24 hours at room temperature, 7 days refrigerated.

Solution Compatibility: D₅W, D₁₀W, D₅LR, and NS.

Terminal Injection Site Compatibility: Dex/AA solutions. Amikacin, ampicillin, aztreonam, bumetanide, calcium gluconate, clindamycin, dexamethasone, fluconazole, furosemide, heparin, hydrocortisone succinate, imipenem/cilastatin, lorazepam, methylprednisolone, metronidazole, milrinone, piperacillin-tazobactam, potassium chloride, ranitidine, sodium bicarbonate, ticarcillin/clavulanate, trimethoprim/sulfamethoxazole, and zidovudine.

Incompatibility: Acyclovir, aminophylline, amphotericin B, cimetidine, diazepam, dobutamine, dopamine, enalaprilat, famotidine, ganciclovir, gentamicin, magnesium sulfate, metoclopramide, morphine, netilmicin, tobramycin, and vancomycin.

Selected References

- ◆ Lima-Rogel V, Medina-Rojas EL, del Carmen Milan-Segovia R, et al: Population pharmacokinetics of cefepime in neonates with severe nosocomial infections. *J Clin Pharm Ther* 2008;33:295-306.
- ◆ Capparelli E, Hochwald C, Rasmussen M, et al: Population pharmacokinetics of cefepime in the neonate. *Antimicrob Agents Chemother* 2005;49:2760-2766.
- ◆ Gutierrez K: Newer antibiotics: cefepime. *NeoReviews* 2004;5:e382-386.
- ◆ Blumer JL, Reed MD, Knupp C: Review of the pharmacokinetics of cefepime in children. *Pediatr Infect Dis J* 2001;20:337-342.
- ◆ Bradley JS, Arrieta A: Empiric use of cefepime in the treatment of lower respiratory tract infections in children. *Pediatr Infect Dis J* 2001;20:343-349.
- ◆ Saez-Llorens XO, O'Ryan M: Cefepime in the empiric treatment of meningitis in children. *Pediatr Infect Dis J* 2001;20:356-361.
- ◆ Kessler RE: Cefepime microbiologic profile and update. *Pediatr Infect Dis J* 2001; 20:331-336.
- ◆ Product Information, Bristol-Myers Squibb, 2007

Dose and References updated 1/2009
Added 3/2002



Dose & Administration

50 mg/kg per dose IV infusion by syringe pump over 30 minutes, or IM.

Gonococcal infections: 25 mg/kg per dose IV over 30 minutes, or IM.

Gonococcal ophthalmia prophylaxis in newborns whose mothers have gonorrhea at the time of delivery: 100 mg/kg IV over 30 minutes or IM, single dose. (Note: topical antibiotic therapy alone is inadequate and is unnecessary if systemic treatment is administered.)

To use dosing chart, please refer to explanatory note on page 1.

Dosing Interval Chart

PMA (weeks)	PostNatal (days)	Interval (hours)
≤29	0 to 28 >28	12 8
30 to 36	0 to 14 >14	12 8
37 to 44	0 to 7 >7	12 8
≥45	ALL	6

Uses

Treatment of neonatal meningitis and sepsis caused by susceptible gram-negative organisms (e.g. *E coli*, *H influenzae*, and *Klebsiella*). Treatment of disseminated gonococcal infections.

Monitoring

Measuring serum concentration is not usually necessary. Periodic CBC.

Adverse Effects/Precautions

Side effects are rare but include rash, phlebitis, diarrhea, leukopenia, granulocytopenia, and eosinophilia.

Pharmacology

Cefotaxime is one of many third-generation cephalosporin antibiotics. The mechanism of action appears to be by bacterial cell wall disruption. Metabolized in the liver to an active compound, desacetylcefotaxime. The drug distributes widely (i.e. CSF, bile, bronchial secretions, lung tissue, ascitic fluid, middle ear). Excreted renally.

Serum half-life in the premature infant is approximately 3 to 6 hours.

Cefotaxime

Special Considerations/Preparation

Available as powder for injection in 500-mg, 1-g, and 2-g vials.

The 500-mg vial is reconstituted with 10 mL sterile water for injection to yield a concentration of 50 mg/mL. Reconstituted solution stable for 24 hours at room temperature, 7 days refrigerated.

Solution Compatibility: D₅W, D₁₀W, and NS.

Terminal Injection Site Compatibility: Dex/AA solutions, fat emulsion. Acyclovir, amikacin, aztreonam, caffeine citrate, clindamycin, famotidine, heparin, lorazepam, metronidazole, midazolam, milrinone, morphine, potassium chloride, propofol, and remifentanil.

Incompatibility: Aminophylline, azithromycin, fluconazole, sodium bicarbonate, and vancomycin.

Selected References

- ◆ Centers for Disease Control and Prevention: Sexually transmitted diseases treatment guidelines 2006. *MMWR* 2006;55(No. RR-11):47-48.
- ◆ Prober CG, Stevenson DK, Benitz WE: The use of antibiotics in neonates weighing less than 1200 grams. *Pediatr Infect Dis J* 1990;9:111.
- ◆ Kearns GL, Jacobs RF, Thomas BR, et al: Cefotaxime and desacetylcefotaxime pharmacokinetics in very low birth weight neonates. *J Pediatr* 1989;114:461.
- ◆ de Louvois J, Mulhall A, Hurley R: The safety and pharmacokinetics of cefotaxime in the treatment of neonates. *Pediatr Pharmacol* 1982;2:275.
- ◆ Kafetzis DA, Brater DC, Kapiki AN: Treatment of severe neonatal infections with cefotaxime: Efficacy and pharmacokinetics. *J Pediatr* 1982;100:483.
- ◆ Product Information, Abraxis Pharmaceutical Products, 2006

References updated 3/2007

Compatibilities updated 3/2007

Dose & Administration

25 to 33 mg/kg per dose IV infusion by syringe pump over 30 minutes.

To use dosing chart, please refer to explanatory note on page 1.

Dosing Interval Chart

PMA (weeks)	PostNatal (days)	Interval (hours)
≤29	0 to 28 >28	12 8
30 to 36	0 to 14 >14	12 8
37 to 44	0 to 7 >7	12 8
≥45	ALL	6

Uses

Use in neonates is generally limited to treatment of skin, intra-abdominal and urinary tract infections caused by susceptible bacteria - anaerobes (e.g. *Bacteroides fragilis*), gram positives (e.g. *Staphylococcus aureus*, *Streptococcus pneumoniae*, and other streptococci except enterococcus) and gram negatives (e.g. *Haemophilus influenzae*, *Klebsiella* sp., *E. coli*, *Proteus vulgaris*, and *Neisseria gonorrhoeae*).

Monitoring

Serum concentrations are not routinely monitored.

Adverse Effects/Precautions

Adverse effects are rare. Transient eosinophilia and elevation of hepatic transaminases have been reported in < 3% of treated patients. Severe overdose can cause tachypnea, pallor, hypotonia, and metabolic acidosis.

Pharmacology

Broad spectrum bactericidal second generation cephalosporin that has enhanced activity against anaerobic bacteria. Inhibits bacterial cell wall synthesis by binding to one or more penicillin-binding proteins. Not inactivated by β -lactamase. Poor CNS penetration. Highly protein bound. Renally excreted as unchanged drug (85 to 90%). Half-life in term neonates is approximately 1.4 hours, and 2.3 hours in preterm neonates —considerably longer than children (0.6 hours) and adults (0.8 hours).

Dose & Administration

25 to 33 mg/kg per dose IV infusion by syringe pump over 30 minutes.

To use dosing chart, please refer to explanatory note on page 1.

Dosing Interval Chart

PMA (weeks)	PostNatal (days)	Interval (hours)
≤ 29	0 to 28	12
	>28	8
30 to 36	0 to 14	12
	>14	8
37 to 44	0 to 7	12
	>7	8
≥ 45	ALL	6

Uses

Use in neonates is generally limited to treatment of skin, intra-abdominal and urinary tract infections caused by susceptible bacteria - anaerobes (e.g. *Bacteroides fragilis*), gram positives (e.g. *Staphylococcus aureus*, *Streptococcus pneumoniae*, and other streptococci except enterococcus) and gram negatives (e.g. *Haemophilus influenzae*, *Klebsiella* sp., *E. coli*, *Proteus vulgaris*, and *Neisseria gonorrhoeae*).

Monitoring

Serum concentrations are not routinely monitored.

Adverse Effects/Precautions

Adverse effects are rare. Transient eosinophilia and elevation of hepatic transaminases have been reported in < 3% of treated patients. Severe overdose can cause tachypnea, pallor, hypotonia, and metabolic acidosis.

Pharmacology

Broad spectrum bactericidal second generation cephalosporin that has enhanced activity against anaerobic bacteria. Inhibits bacterial cell wall synthesis by binding to one or more penicillin-binding proteins. Not inactivated by β -lactamase. Poor CNS penetration. Highly protein bound. Renally excreted as unchanged drug (85 to 90%). Half-life in term neonates is approximately 1.4 hours, and 2.3 hours in preterm neonates —considerably longer than children (0.6 hours) and adults (0.8 hours).

Special Considerations/Preparation

Available as powder for injection in 1-g, and 2-g vials.

IV administration: Reconstitute 1-g vial with 9.5 mL sterile water for injection to a concentration of 100 mg/mL. A 40 mg/mL dilution may be made by adding 4 mL of reconstituted solution to 6 mL sterile water for injection, or D₅W. Stable for 18 hours at room temperature or 7 days refrigerated.

Solution Compatibility: D₅W, D₁₀W, and NS.

Terminal Injection Site Compatibility: Dex/AA and fat emulsion. Acyclovir, amikacin, aztreonam, cimetidine, clindamycin, famotidine, fluconazole, gentamicin, heparin, insulin, lidocaine, linezolid, magnesium sulfate, metronidazole, morphine, multivitamins, potassium chloride, propofol, ranitidine, remifentanil, sodium bicarbonate, tobramycin and vecuronium.

Incompatibility: Vancomycin

Selected References

- ◆ Regazzi MB, Chirico G, Cristiani D, et al: Cefoxitin in newborn infants. *Eur J Clin Pharmacol* 1983;25:507-509.
- ◆ Yoge R, Delaplane D, Wiringa K: Cefoxitin in a neonate. *Ped Infect Dis J* 1983;2:342-343.
- ◆ Farmer K: Use of cefoxitin in the newborn. *New Zealand Med J* 1982;95:398.
- ◆ Marget W: Tenfold overdose of cefoxitin in a newborn. *Infection* 1982;10:243.
- ◆ Brogden RN, Heel RC, Speight TM, et al: Cefoxitin: A review of its antibacterial activity, pharmacological properties and therapeutic use. *Drugs* 1979;17:1-37.
- ◆ Feldman WE, Moffitt S, Sprow N: Clinical and pharmacokinetic evaluation of parenteral cefoxitin in infants and children. *Antimicrob Agents Chemother* 1980;17:669-674.
- ◆ Product Information, Abraxis Pharmaceutical Produts, 2006

Added 3/2001

Compatibilities updated: 3/2003

Text updated 3/2008

Dose & Administration

30 mg/kg per dose IV infusion by syringe pump over 30 minutes, or IM.
To reduce pain at IM injection site, ceftazidime may be mixed with 1% lidocaine without epinephrine.

To use dosing chart, please refer to explanatory note on page 1.

Dosing Interval Chart

PMA (weeks)	PostNatal (days)	Interval (hours)
≤29	0 to 28 >28	12 8
30 to 36	0 to 14 >14	12 8
37 to 44	0 to 7 >7	12 8
≥45	ALL	8

Uses

Treatment of neonatal meningitis and sepsis caused by susceptible gram-negative organisms (e.g. *E. coli*, *H. influenzae*, *Neisseria*, *Klebsiella*, and *Proteus* species), especially *Pseudomonas aeruginosa*. Resistance among strains of *Serratia* and *Enterobacteriaceae* is increasing.

Monitoring

Measuring serum concentration is not usually necessary.

Adverse Effects/Precautions

Reported adverse effects are uncommon but include rash, diarrhea, elevated hepatic transaminases, eosinophilia, and positive Coombs' test.

Pharmacology

Ceftazidime is one of many third-generation cephalosporins. The drug distributes widely in body tissues and fluids (i.e. CSF, bile, bronchial secretions, lung tissue, ascitic fluid, middle ear). Protein binding is low, and it is excreted unchanged in the urine. Ceftazidime is synergistic with aminoglycosides. Serum half-life in neonates is 3 to 12 hours.

Special Considerations/Preparation

Available as powder for injection in 500-mg and 1-g, 2-g, and 6-g vials.

Intravenous solution: Reconstitute 500-mg vial with 10 mL of sterile water for injection to make a concentration of 50 mg/mL. Reconstituted solution stable for 12 hours at room temperature, 3 days refrigerated.

Intramuscular solution: Prepared by reconstituting 500-mg vial with 2.2 mL of 1% lidocaine without epinephrine or Sterile Water to a concentration of 200 mg/mL. Solution is stable for 12 hours at room temperature, 3 days refrigerated.

All dosage forms approved for pediatric use contain sodium carbonate; when reconstituted, carbon dioxide bubbles will form. Using a vented needle may help reduce spraying and leaking.

Solution Compatibility: D₅W, D₁₀W, and NS.

Terminal Injection Site Compatibility: Dex/AA solutions, fat emulsion. Acyclovir, amikacin, aminophylline, aztreonam, cimetidine, ciprofloxacin, clindamycin, enalaprilat, esmolol, famotidine, furosemide, gentamicin, heparin, linezolid, metronidazole, milrinone, morphine, potassium chloride, propofol, ranitidine, remifentanil, sodium bicarbonate, tobramycin, and zidovudine.

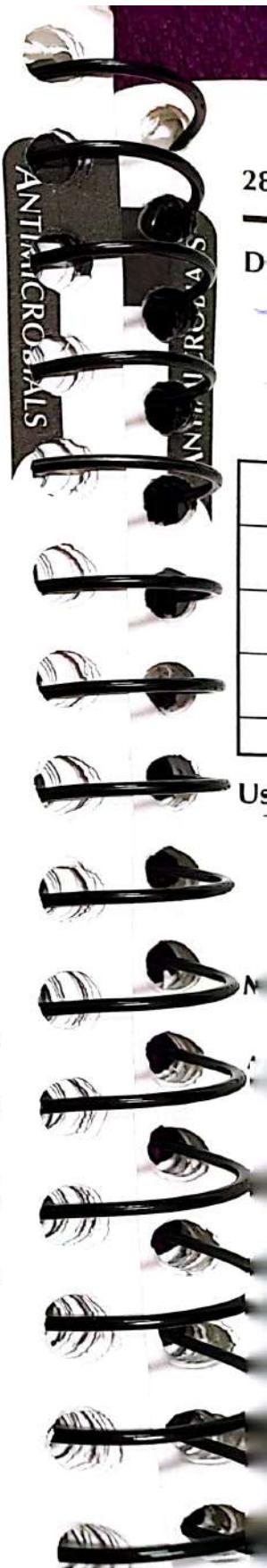
Incompatibility: Amiodarone, azithromycin, erythromycin lactobionate, fluconazole, midazolam, nicardipine, and vancomycin.

Selected References

- ◆ Prober CG, Stevenson DK, Benitz WE: The use of antibiotics in neonates weighing less than 1200 grams. *Pediatr Infect Dis J* 1990;9:111.
- ◆ Tessin I, Thiringer K, Trollfors B, Brorson JE: Comparison of serum concentrations of ceftazidime and tobramycin in newborn infants. *Eur J Pediatr* 1988;147:405.
- ◆ Odio CM, Umana MA, Saenz A, et al: Comparative efficacy of ceftazidime vs. carbenicillin and amikacin for treatment of neonatal septicemia. *Pediatr Infect Dis* 1987;6:371.
- ◆ McCracken GH, Threlkeld N, Thomas ML: Pharmacokinetics of ceftazidime in newborn infants. *Antimicrob Agents Chemother* 1984;26:583.
- ◆ Product Information, GlaxoSmithKline, 2007

Updated 1/93

Compatibilities updated 3/2007



Dose & Administration

Sepsis and disseminated gonococcal infection: 50 mg/kg Q24 hours.

Meningitis: 100 mg/kg loading dose, then 80 mg/kg Q24 hours.

Uncomplicated gonococcal ophthalmia: 50 mg/kg (maximum 125 mg) single dose. (Note: topical antibiotic therapy alone is inadequate and is unnecessary if systemic treatment is administered.)

IV administration: Infusion by syringe pump over 30 minutes. Avoid administration of calcium-containing solutions or products within 48 hours of the last administration of ceftriaxone.

IM administration: To reduce pain at the injection site, reconstitute with 1% lidocaine without epinephrine.

Uses

Treatment of neonatal sepsis and meningitis caused by susceptible gram-negative organisms (e.g. *E. coli*, *Pseudomonas*, *Klebsiella*, *H. influenzae*). Treatment of gonococcal infections.

Monitoring

CBC for eosinophilia, thrombocytosis, leukopenia. Serum electrolytes, BUN, creatinine. AST, ALT, bilirubin. Consider abdominal ultrasonography.

Adverse Effects/Precautions

Not recommended for use in neonates with hyperbilirubinemia. Displaces bilirubin from albumin binding sites, resulting in higher free bilirubin serum concentrations. **Concurrent administration of ceftriaxone and calcium-containing solutions or products in newborns is not recommended.** Fatal reactions with calcium-ceftriaxone precipitates have been reported in neonates (lung and kidney). Administration of calcium-containing solutions or products within 48 hours of the last administration of ceftriaxone is not recommended. Eosinophilia, thrombocytosis, leukopenia. Increase in bleeding time. Diarrhea. Increase in BUN and serum creatinine. Increase in AST and ALT. Skin rash. Transient gallbladder precipitations occasionally associated with colicky abdominal pain, nausea, and vomiting.

Pharmacology

Ceftriaxone is one of many third-generation cephalosporin antibiotics. The drug distributes widely (i.e. CSF, bile, bronchial secretions, lung tissue, ascitic fluid, middle ear). It is eliminated unchanged by both biliary (40%) and renal mechanisms. Serum half-life in premature infants is 5 to 16 hours. Dosage adjustment is necessary only for patients with combined hepatic and renal failure.

Ceftriaxone

Special Considerations/Preparation

Intravenous solution: Available as a powder for injection in 250-mg, 500-mg, 1-g, and 2-g vials. Prepared by reconstituting powder with compatible solution (sterile water for injection, D₅W, or D₁₀W) to a concentration of 100 mg/mL. Reconstituted solution is stable for 2 days at room temperature, 10 days refrigerated. A dark color may appear after reconstitution; however, potency is retained.

To make 40-mg/mL solution add 6.2 mL to the 250-mg vial.

Intramuscular solution: Prepared by reconstituting 250-mg vial with 0.9 mL of 1% lidocaine without epinephrine to a concentration of 250 mg/mL. Solution is stable for 24 hours at room temperature, 3 days refrigerated.

Solution Compatibility: D₅W, D₁₀W, and NS.

Solution Incompatibility: Any calcium-containing solution.

Terminal Injection Site Compatibility: Dex/AA solutions, fat emulsion. Acyclovir, amikacin, amiodarone, aztreonam, clindamycin, famotidine, gentamicin, heparin, lidocaine, linezolid, metronidazole, morphine, potassium chloride, propofol, remifentanil, sodium bicarbonate, and zidovudine.

Incompatibility: Aminophylline, azithromycin, calcium chloride, calcium gluconate, fluconazole and vancomycin.

Selected References

- ◆ Centers for Disease Control and Prevention: Sexually transmitted diseases treatment guidelines 2006. *MMWR* 2006;55(No. RR-11):47-48.
- ◆ Prober CG, Stevenson DK, Benitz WE: The use of antibiotics in neonates weighing less than 1200 grams. *Pediatr Infect Dis J* 1990;9:111.
- ◆ Schaad UB, Suter S, Gianella-Borradori A, et al: A comparison of ceftriaxone and cefuroxime for the treatment of bacterial meningitis in children. *N Engl J Med* 1990;332:141.
- ◆ Fink S, Karp W, Robertson A: Ceftriaxone effect on bilirubin-albumin binding. *Pediatrics* 1987;80:873.
- ◆ Laga M, Naamara W, Brunham RC, et al: Single-dose therapy of gonococcal ophthalmia neonatorum with ceftriaxone. *N Engl J Med* 1986;315:1382.
- ◆ Yoge R, Shulman ST, Chadwick E, et al: Once daily ceftriaxone for central nervous system infections and other serious pediatric infections. *Pediatr Infect Dis J* 1986;5:298.
- ◆ Martin E, Koup JR, Paravicini U, Stoeckel K: Pharmacokinetics of ceftriaxone in neonates and infants with meningitis. *J Pediatr* 1984;105:475.
- ◆ Schaad UB, Stoeckel K: Single-dose pharmacokinetics of ceftriaxone in infants and young children. *Antimicrob Agents Chemother* 1982;21:248.
- ◆ Product Information, Roche, 2007.

Text and References updated 7/2007

Compatibilities updated 7/2007



Dose & Administration

Loading dose: 20 mg/kg IV infusion by syringe pump over 30 minutes.

Maintenance dose: (Begin 12 hours after loading dose.)

Premature infants under 1 month of age: 2.5 mg/kg per dose Q6 hours.

Fullterm infants under 1 week of age and premature infants over 1 month of age: 5 mg/kg per dose Q6 hours.

Fullterm infants over 1 week of age: 12.5 mg/kg per dose Q6 hours.

(Absorption of oral chloramphenicol palmitate is erratic in newborns.)

Uses

A wide-spectrum antimicrobial bacteriostatic agent. May be bactericidal to species such as *H influenzae* and *Neisseria meningitidis*.

Monitoring

Close monitoring of serum concentration is mandatory. Small changes in dose and interval can lead to disproportionately large changes in serum concentration. Therapeutic peak serum concentration: 10 to 25 mcg/mL. Monitor CBC and reticulocyte counts. Assess hepatic and renal function.

Adverse Effects/Precautions

Reversible bone marrow suppression, irreversible aplastic anemia. Serum concentration greater than 50 mcg/mL has been associated with the "gray baby" syndrome (i.e. abdominal distention, pallid cyanosis, vasomotor collapse; may lead to death within hours of onset). Fungal overgrowth.

Black Box Warning

According to the manufacturer's black box warning, serious and fatal blood dyscrasias (aplastic anemia, hypoplastic anemia, thrombocytopenia, and granulocytopenia) are known to occur. There have been reports of aplastic anemia which later terminated in leukemia. Blood dyscrasias have occurred after both short-term and prolonged therapy with this drug. It is essential that adequate blood studies be made during treatment.

Pharmacology

Both esters (succinate and palmitate) are biologically inactive prodrugs. Hydrolysis to the active compound is erratic in newborns. Metabolized by hepatic glucuronyl transferase. Hepatically and renally eliminated. Inhibits metabolism of phenobarbital, phenytoin, and other agents.

Special Considerations/Preparation

Chloramphenicol succinate is available as powder for injection in a 1-g vial. Reconstitute with 10 mL sterile water for injection, or D₅W to a concentration of 100 mg/mL.

Solution Compatibility: D₅W, D₁₀W, and NS.

Terminal Injection Site Compatibility: Dex/AA solutions, fat emulsion. Acyclovir, amikacin, aminophylline, ampicillin, calcium chloride, calcium gluconate, dopamine, enalaprilat, erythromycin lactobionate, esmolol, heparin, hydrocortisone succinate, lidocaine, magnesium sulfate, methicillin, metronidazole, morphine, nafcillin, nicardipine, oxacillin, penicillin G, pentobarbital, potassium chloride, ranitidine, sodium bicarbonate, and vitamin K₁.

Incompatibility: Fluconazole, metoclopramide, phenytoin, and vancomycin.

Selected References

- ◆ Roberts RJ: *Drug Therapy in Infants*. Philadelphia: WB Saunders Co, 1984, p 70.
- ◆ Rajchgot P, Prober CG, Soldin S: Initiation of chloramphenicol therapy in the newborn infant. *J Pediatr* 1982;101:1018.
- ◆ Glazer JP, Danish MA, Plotkin SA, Yaffe SJ: Disposition of chloramphenicol in low birth weight infants. *Pediatrics* 1980;66:573.
- ◆ Product Information, Abraxis, 2006

Adverse Effects/Precautions updated 1/2009

Compatibilities updated 3/2005



Dose & Administration

5 to 7.5 mg/kg per dose IV infusion by syringe pump over 30 minutes, or PO.

Increase dosing interval in patients with significant liver dysfunction.

To use dosing chart, please refer to explanatory note on page 1.

Dosing Interval Chart

PMA (weeks)	PostNatal (days)	Interval (hours)
≤29	0 to 28 >28	12 8
30 to 36	0 to 14 >14	12 8
37 to 44	0 to 7 >7	12 8
≥45	ALL	6

Uses

Bacteriostatic antibiotic used for the treatment of bacteremia and pulmonary and deep tissue infections caused by anaerobic bacteria and some gram-positive cocci. Clindamycin should not be used in the treatment of meningitis.

Monitoring

Assess liver function. Monitor GI status closely. Therapeutic serum concentration ranges from 2 to 10 mcg/mL (bioassay yields variable results).

Adverse Effects/Precautions**Black Box Warning**

According to the manufacturer's black box warning, diarrhea, colitis, and pseudomembranous colitis have been reported, and may begin up to several weeks following cessation of therapy.

Discontinue clindamycin if any of these signs or symptoms occur, begin bowel rest and TPN, and consider treatment with oral metronidazole.

Pharmacology

Clindamycin inhibits bacterial protein synthesis and is primarily bacteriostatic at therapeutically attainable concentrations. Widely distributed into most tissues, especially the lung. Poor CSF penetration. Oral clindamycin is completely absorbed from the GI tract. Highly protein bound. Almost complete metabolism in the liver, with excretion via bile and feces. Available data in neonates suggest extremely variable clearance, especially in premature infants. No data are available regarding conversion of ester to active drug.

Clindamycin

Special Considerations/Preparation

Oral preparation (clindamycin palmitate) is reconstituted with sterile water for injection, yielding a 75 mg per 5 mL solution.

Do not refrigerate. Stable at room temperature for 2 weeks.

IV preparation (clindamycin phosphate) is available as a 150 mg/mL solution in 2-mL, 4-mL, and 6-mL vials containing 9.45 mg/mL benzyl alcohol. It should be diluted using D₅W, NS, or LR to a maximum concentration of 18 mg/mL, and infused at a rate no greater than 30 mg/min. Also available in premixed bags (50 mL) without benzyl alcohol containing 300 mg, 600 mg or 900 mg of clindamycin.

Solution Compatibility: D₅W, D₁₀W, and NS.

Terminal Injection Site Compatibility: Dex/AA solutions, fat emulsion. Acyclovir, amikacin, amiodarone, ampicillin, aztreonam, caffeine citrate, cefazolin, cefepime, cefotaxime, cefoxitin, ceftazidime, ceftriaxone, cimetidine, enalaprilat, esmolol, gentamicin, heparin, hydrocortisone succinate, linezolid, magnesium sulfate, metoclopramide, metronidazole, midazolam, milrinone, morphine, netilmicin, nicardipine, penicillin G, piperacillin, piperacillin/tazobactam, potassium chloride, propofol, prostaglandin E₁, ranitidine, remifentanil, sodium bicarbonate, tobramycin, and zidovudine.

Incompatibility: Aminophylline, azithromycin, barbiturates, calcium gluconate, ciprofloxacin, fluconazole, and phenytoin.

Selected References

- ◆ Koren G, Zarfin Y, Maresky D, et al: Pharmacokinetics of intravenous clindamycin in newborn infants. *Pediatr Pharmacol* 1986;5:287.
- ◆ Bell MJ, Shackelford P, Smith R, Schroeder K: Pharmacokinetics of clindamycin phosphate in the first year of life. *J Pediatr* 1984;105:482.
- ◆ Feigin RD, Pickering LK, Anderson D, et al: Clindamycin treatment of osteomyelitis and septic arthritis in children. *Pediatrics* 1975;55:213.
- ◆ Lwin N, Collipp PJ: Absorption and tolerance of clindamycin 2-palmitate in infants below 6 months of age. *Curr Ther Res Clin Exp* 1970;12:648.
- ◆ Product Information, Pfizer, 2003

Adverse Effects/Precautions updated 1/2009

Special Considerations updated 3/2008

Compatibilities updated 3/2007



Dose & Administration

Treatment of pneumonitis and conjunctivitis due to *Chlamydia trachomatis*: 12.5 mg/kg per dose PO Q6 hours for 14 days.

Other infections and prophylaxis: 10 mg/kg per dose PO Q6 hours.

Oral treatment with E. ethylsuccinate (e.g., E. E. S.[®], EryPed[®]).

Treatment and prophylaxis of pertussis: 12.5 mg/kg per dose PO Q6 hours for 14 days. The drug of choice in infants younger than 1 month of age is azithromycin. Administer with infant formula to enhance absorption of the ethylsuccinate and reduce possible GI side effects.

Severe infections when PO route unavailable: 5 to 10 mg/kg per dose IV infusion by syringe pump over at least 60 minutes Q6 hours.

Do not administer IM.

Prophylaxis of ophthalmia neonatorum: Ribbon of 0.5% ointment instilled in each conjunctival sac.

Treatment of feeding intolerance due to dysmotility: 10 mg/kg per dose PO every 6 hours for 2 days, followed by 4 mg/kg per dose PO every 6 hours for 5 days.

Uses

Treatment of infections caused by *Chlamydia*, *Mycoplasma*, and *Ureaplasma*. Treatment for and prophylaxis against *Bordetella pertussis*. As a substitute for penicillin in situations of significant allergic intolerance. As a prokinetic agent in cases of feeding intolerance.

Monitoring

Watch for diarrhea and signs of abdominal discomfort. CBC for eosinophilia. **Monitor heart rate and blood pressure closely during IV administration.** Observe IV site for signs of infiltration.

Adverse Effects/Precautions

The risk of hypertrophic pyloric stenosis is increased 10-fold in neonates under 2 weeks of age who receive oral erythromycin for pertussis prophylaxis (1 additional case per every 42 infants treated). No studies of premature infants with feeding intolerance have been large enough to assess safety. Two reported cases of severe bradycardia and hypotension occurring during IV administration of erythromycin lactobionate. Intrahepatic cholestasis. Loose stools occur infrequently. Bilateral sensorineural hearing loss has been reported rarely in adults, usually associated with intravenous administration and renal or hepatic dysfunction. The hearing loss occurred after the first few doses and was reversible after discontinuing the drug. Venous irritation is common when using the IV dosage form.

Pharmacology

Erythromycin may be bacteriostatic or bactericidal depending on the tissue concentration of drug and the microorganism involved. IV administration of E. lactobionate to preterm infants, using doses of 6.25 to 10 mg/kg, yielded peak serum concentrations of 1.9 to 3.7 mcg/mL and a half-life of 2 hours. The drug penetrates poorly into the CNS, is concentrated in the liver and bile, and is excreted via the bowel. It is a motilin receptor agonist and induces stomach and small intestine motor activity. Plasma clearance of midazolam is reduced by 50%. Digoxin, midazolam, theophylline and carbamazepine serum concentrations may be significantly increased because of prolongation of their half-life.

continued...

Special Considerations/Preparation

E. ethylsuccinate oral suspension is available in concentrations of 200 mg- and 400 mg per 5 mL. Refrigeration not required except to preserve taste. Shake suspension well before administering.

Available as powder for injection in 500-mg and 1-g vials. Reconstitute 500-mg vial with 10 mL of sterile water for injection to concentration of 50 mg/mL. Reconstituted solution stable for 24 hours at room temperature or 2 weeks in refrigerator. After reconstitution, dilute to a concentration of 1 to 5 mg/mL for infusion. To make a 5-mg/mL dilution, add 1 mL of reconstituted solution to 9 mL sterile water for injection. Use diluted drug within 8 hours.

Solution Compatibility: NS and sterile water for injection.

Solution Incompatibility: D₅W and D₁₀W (unless buffered with 4% sodium bicarbonate to maintain stability).

Terminal Injection Site Compatibility: Dex/AA solutions, fat emulsion. Acyclovir, aminophylline, amiodarone, chloramphenicol, cimetidine, enalaprilat, esmolol, famotidine, heparin, hydrocortisone succinate, lidocaine, lorazepam, magnesium sulfate, methicillin, midazolam, morphine, nicardipine, penicillin G, pentobarbital, potassium chloride, ranitidine, sodium bicarbonate, and zidovudine.

Incompatibility: Ampicillin, ceftazidime, fluconazole, furosemide, linezolid, and metoclopramide.

Selected References

- ◆ American Academy of Pediatrics. Chlamydia trachomatis. In: Pickering LK, Baker CJ, Long SS, McMillan JA, eds. *Red Book: 2006 Report of the Committee on Infectious Diseases*. 27th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2006: p255.
- ◆ Centers for Disease Control and Prevention: Sexually transmitted diseases treatment guidelines 2006. *MMWR* 2006;55(No. RR-11).
- ◆ Nuntnarumit P, Kiatchoosakun P, Tantiprapa W, Boonkasidecha S: Efficacy of oral erythromycin for treatment of feeding intolerance in preterm infants. *J Pediatr* 2006;148:600-605.
- ◆ Patole S, Rao S, Doherty D: Erythromycin as a prokinetic agent in preterm neonates: a systematic review. *Arch Dis Child Fetal Neonatal Ed* 2005;90:F301-F306.
- ◆ Oei J, Lui K: A placebo-controlled trial of low-dose erythromycin to promote feed tolerance in preterm infants. *Acta Paediatr* 2001;90:904-908.
- ◆ Pai MP, Graci DM, Amsden GW: Macrolide drug interactions: an update. *Ann Pharmacother* 2000;34:495-513.
- ◆ Honein MA, Paulozzi LJ, Himelright IM, et al: Infantile hypertrophic pyloric stenosis after pertussis prophylaxis with erythromycin: a case review and cohort study. *Lancet* 1999;354:2101-2105.
- ◆ Waites KB, Sims PJ, Crouse DT, et al: Serum concentrations of erythromycin after intravenous infusion in preterm neonates treated for *Ureaplasma urealyticum* infection. *Pediatr Infect Dis J* 1994;13:287.
- ◆ Farrar HC, Walsh-Sukys MC, Kyllonen K, Blumer JL: Cardiac toxicity associated with intravenous erythromycin lactobionate: Two case reports and a review of the literature. *Pediatr Infect Dis J* 1993;12:688.
- ◆ Ginsburg CM: Pharmacology of erythromycin in infants and children. *Pediatr Infect Dis* 1986;5:124.
- ◆ Gouyon JB, Benoit A, Betremieux P, et al: Cardiac toxicity of intravenous erythromycin lactobionate in preterm infants. *Pediatr Infect Dis J* 1994;13:840-841.
- ◆ Eichenwald H: Adverse reactions to erythromycin. *Pediatr Infect Dis* 1986;5:147.
- ◆ Product Information, Abbott, 2003

Updated 3/2007

Compatibilities updated 3/2005



Dose & Administration

Systemic infections, including meningitis: 12 mg/kg loading dose, then 6 mg/kg per dose IV infusion by syringe pump over 30 minutes, or PO.

Prophylaxis: 3 mg/kg per dose via IV infusion twice weekly.

(Consider only in VLBW infants cared for in NICUs with high rates of invasive fungal disease).

Thrush: 6 mg/kg on Day 1, then 3 mg/kg per dose Q24 hours PO.

To use dosing chart, please refer to explanatory note on page 1.

Systemic Infections Dosing Interval Chart

PMA (weeks)	PostNatal (days)	Interval (hours)
≤29	0 to 14 ≥14	72 48
30 to 36	0 to 14 ≥14	48 24
37 to 44	0 to 7 ≥7	48 24
≥45	ALL	24

Uses

Treatment of systemic infections, meningitis, and severe superficial mycoses caused by *Candida* species. Resistance has been reported with *C glabrata* and *C krusei* and in patients receiving long-term suppressive therapy.

Monitoring

Serum fluconazole concentrations are not routinely followed. Assess renal function. Follow AST, ALT, and CBC for eosinophilia.

Adverse Effects/Precautions

Data in neonates are limited. Reversible elevations of transaminases have occurred in 12% of children. A retrospective study using historical controls reports direct hyperbilirubinemia in the absence of elevated transaminases in some infants treated prophylactically for 6 weeks. Interferes with metabolism of barbiturates and phenytoin. May also interfere with metabolism of aminophylline, caffeine, theophylline, and midazolam.

Contraindicated in patients receiving **cisapride** due to precipitation of life-threatening arrhythmias.

Pharmacology

Water-soluble triazole antifungal agent. Inhibits cytochrome P-450-dependent ergosterol synthesis. Well absorbed after oral administration, with peak serum concentrations reached within 1 to 2 hours. Less than 12% protein binding. Good penetration into CSF after both oral and IV administration. Serum half-life is 30 to 180 hours in severely ill VLBW infants in the first 2 weeks of life and approximately 17 hours in children. Primarily excreted unchanged in the urine.

Special Considerations/Preparation

Available as a premixed solution for IV injection in concentrations of 200 mg/100 mL and 400 mg/200 mL in Viaflex® bags (2 mg/mL).

Oral dosage form is available as powder for suspension in concentrations of 10mg/mL and 40 mg/mL. Prepare both concentrations by adding 24 mL distilled water to bottle of powder and shaking vigorously. Suspension is stable at room temperature for 2 weeks. Do not freeze.

Solution Compatibility: D₅W and D₁₀W.

Terminal Injection Site Compatibility: Dex/AA solutions, fat emulsion.

Acyclovir, amikacin, aminophylline, amiodarone, aztreonam, cefazolin, cefepime, cefoxitin, cimetidine, dexamethasone, dobutamine, dopamine, famotidine, gentamicin, heparin, hydrocortisone succinate, intravenous immune globulin (human), linezolid, lorazepam, meropenem, metoclopramide, metronidazole, midazolam, morphine, nafcillin, nitroglycerin, oxacillin, pancuronium bromide, penicillin G, phenytoin, piperacillin/tazobactam, potassium chloride, propofol, quinupristin/dalfopristin, ranitidine, remifentanil, ticarcillin/clavulanate, tobramycin, vancomycin, vecuronium, and zidovudine.

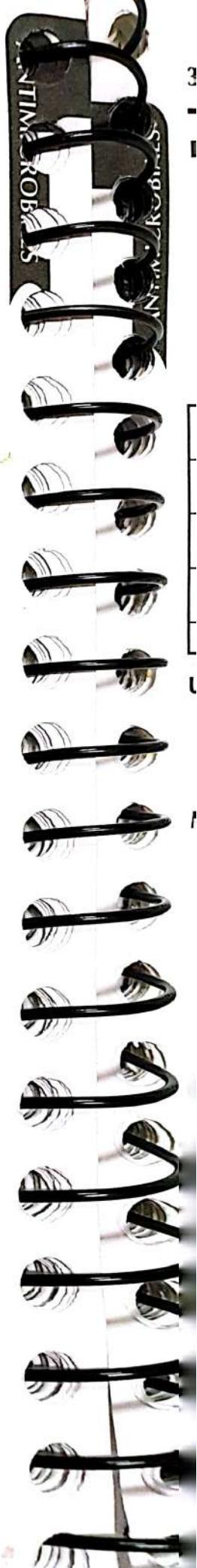
Incompatibility: Amphotericin B, ampicillin, calcium gluconate, cefotaxime, ceftazidime, ceftriaxone, chloramphenicol, clindamycin, digoxin, erythromycin lactobionate, furosemide, imipenem, piperacillin, ticarcillin, and trimethoprim-sulfamethoxazole.

Selected References

- ◆ Manzoni P, Stolfi I, Pugni L, et al: A multicenter, randomized trial of prophylactic fluconazole in preterm neonates. *N Eng J Med* 2007;356:2483-95.
- ◆ Kaufman D, Boyle R, Hazen KC, et al: Twice weekly fluconazole prophylaxis for prevention of invasive Candida infection in high-risk infants of <1000 grams birth weight. *J Pediatr* 2005;147:172-179.
- ◆ Aghai ZH, Mudduluru M, Nakhla TA, et al. Fluconazole prophylaxis in extremely low birth weight infants: association with cholestasis. *J Perinatol* 2006;26:550-555.
- ◆ Huttova M, Hartmanova I, Kralinsky K, et al: Candida fungemia in neonates treated with fluconazole: report of forty cases, including eight with meningitis. *Pediatr Infect Dis J* 1998;17:1012-1015.
- ◆ Driessen M, Ellis JB, Cooper PA, et al: Fluconazole vs. amphotericin B for the treatment of neonatal fungal septicemia: a prospective randomized trial. *Pediatr Infect Dis J* 1996;15:1107.
- ◆ Flynn PM, Cunningham CK, Kerker T, et al: Oropharyngeal candidiasis in immunocompromised children: a randomized, multicenter study of orally administered fluconazole suspension versus nystatin. The Multicenter Fluconazole Study Group. *J Pediatr* 1995;127:322.
- ◆ Fasano C, O'Keefe J, Gibbs D: Fluconazole treatment of neonates and infants with severe fungal infections not treatable with conventional agents. *Eur J Clin Microbiol Infect Dis* 1994;13:351.
- ◆ Saxen H, Hoppu K, Pohjavuori M: Pharmacokinetics of fluconazole in very low birth weight infants during the first two weeks of life. *Clin Pharmacol Ther* 1993;54:269.
- ◆ Dodds Ashley ES, Lewis R, Lewis JS, et al. Pharmacology of systemic antifungal agents. *Clin Infect Dis* 2006;43:S29-39.
- ◆ Product information, Pfizer, 2004

References updated 3/2008

Compatibilities updated 3/2005



Dose & Administration

12.5 to 37.5 mg/kg per dose Q6 hours PO. Increase dosing interval if renal dysfunction is present.

Uses

Antifungal agent used in combination with amphotericin B or fluconazole for treatment of infections caused by *Candida*, *Cryptococcus*, and other sensitive fungi.

Monitoring

Desired peak serum concentration ranges from 50 to 80 mcg/mL. Assess renal function. Follow GI status closely. Twice-weekly CBC and platelet counts. Periodic AST, ALT.

Adverse Effects/Precautions

Toxicities are related to serum concentration above 100 mcg/mL, and are usually reversible if the drug is stopped or the dose is reduced. Fatal bone marrow depression (related to fluorouracil production), hepatitis, severe diarrhea, rash. Amphotericin B may increase toxicity by decreasing renal excretion.

Black Box Warning

According to the manufacturer's black box warning, extreme caution is recommended in patients with impaired renal function. Close monitoring of hematologic, renal, and hepatic status of all patients is essential.

Pharmacology

Well absorbed orally. Transformed within cell to fluorouracil, which interferes with RNA synthesis. Excellent penetration into CSF and body tissues. 90% renal elimination of unchanged drug, proportional to GFR. Serum half-life in adults is 3 to 5 hours if renal function is normal, but 30 to 250 hours if renal impairment is present. Limited pharmacokinetic data in premature infants. Resistance develops frequently if used alone. Synergistic with amphotericin even if treating resistant strain.

Special Considerations/Preparation

Flucytosine is available only in 250 and 500-mg capsules. A pediatric suspension (10 mg/mL) may be prepared using distilled water; adjust pH from 5 to 7 with dilute sodium hydroxide. The capsule contains talc, which forms large-particle precipitates of inactive compound. The remaining suspension, containing the active drug, may be decanted. Shake well before use. The suspension is stable for 7 days at room temperature.

Flucytosine

Selected References

- ◆ Marr B, Gross S, Cunningham C, et al: Candidal sepsis and meningitis in a very-low-birth-weight infant successfully treated with fluconazole and flucytosine. *Clin Infect Dis* 1994;19:795.
- ◆ Smego RA, Perfect JR, Durack DT: Combined therapy with amphotericin B and 5-fluorocytosine for *Candida* meningitis. *Rev Infect Dis* 1984;6:791.
- ◆ Johnson DE, Thompson TR, Green TP, Ferrieri P: Systemic candidiasis in very low-birth-weight infants(<1500 grams). *Pediatrics* 1984;73:138.
- ◆ Koldin MH, Medoff G: Antifungal chemotherapy. *Pediatr Clin North Am* 1983;30:49.
- ◆ Product Information, Valeant Pharmaceuticals, 2005

Adverse Effects/Precautions updated 1/2009

Dose & Administration

6 mg/kg per dose Q12 hours IV infusion by syringe pump over 1 hour. Treat for a minimum of 6 weeks if possible. Reduce the dose by half for significant neutropenia (<500 cells/mm³).

Chronic oral suppression: 30 to 40 mg/kg per dose Q8 hours PO.

Uses

Prevention of progressive hearing loss in babies with symptomatic congenital CMV infection.

Monitoring

CBC every 2 to 3 days during first 3 weeks of therapy, weekly thereafter if stable.

Adverse Effects/Precautions**Black Box Warning**

According to the manufacturer's black box warning, the clinical toxicity of ganciclovir includes granulocytopenia, anemia, and thrombocytopenia.

Significant neutropenia will occur in the majority of treated patients. Discontinue treatment if the neutropenia does not resolve after reducing the dosage by half.

Pharmacology

Ganciclovir is an acyclic nucleoside analog of guanine that inhibits replication of herpes viruses *in vivo*. There is large interpatient variability in pharmacokinetic parameters. Mean half-life in infants less than 49 days postnatal age is 2.4 hours. Metabolism is minimal; almost all drug is excreted unchanged in the urine via glomerular filtration and active tubular secretion.

Ganciclovir

Special Considerations/Preparation

Cytovene® is supplied as lyophilized powder for injection, 500 mg per vial. Reconstitute by injecting 10 mL of Sterile Water for Injection into the vial. Do not use bacteriostatic water for injection containing parabens; it is incompatible with ganciclovir and may cause precipitation. Shake the vial to dissolve the drug. Visually inspect the reconstituted solution for particulate matter and discoloration prior to proceeding with infusion solution. Discard the vial if particulate matter or discoloration is observed.

Reconstituted solution in the vial is stable at room temperature for 12 hours. Do not refrigerate, may cause precipitation. The pH is approximately 11: use caution when handling. Osmolarity is 320 mOsm/kg.

Based on patient weight, remove the appropriate volume of the reconstituted solution (ganciclovir concentration 50 mg/mL) from the vial and add to a compatible diluent fluid to make a final infusion concentration less than 10 mg/mL. Although stable for 14 days, the infusion solution must be used within 24 hours of dilution to reduce the risk of bacterial contamination. Refrigerate the infusion solution. Do not freeze.

Available as 250-mg and 500-mg capsules. Do not open or crush ganciclovir capsules. Prepare oral suspension in a vertical-flow laminar hood. Oral suspension (100 mg/mL) may be prepared by emptying eighty (80) 250-mg capsules into a glass mortar wetted and triturated with Oral-Sweet® to a smooth paste. Add 50-mL of Oral-Sweet® to the paste, mix, and transfer contents to an amber polyethylene terephthalate bottle. Rinse the mortar with another 50 mL of Oral-Sweet® and transfer contents to the bottle. Add enough Oral-Sweet® to make a final volume of 200 mL. Stable for 123 days when stored at 23° to 25° C. Protect from light.

Solution Compatibility: NS, D₅W, and LR.

Solution Incompatibility: Dex/AA.

Terminal Injection Site Compatibility: Enalaprilat, fluconazole, linezolid, propofol, and remifentanil.

Incompatibility: Aztreonam, cefepime, and piperacillin-tazobactam.

Selected References

- ◆ Kimberlin DW, Lin C-Y, Sanchez PJ, et al: Effect of ganciclovir therapy on hearing in symptomatic congenital cytomegalovirus disease involving the central nervous system: a randomized, controlled trial. *J Pediatr* 2003;143:16-25.
- ◆ Michaels MG, Greenberg DP, Sabo DL, Wald ER: Treatment of children with cytomegalovirus infection with ganciclovir. *Pediatr Infect Dis J* 2003;22:504-08.
- ◆ Frenkel LM, Capparelli EV, Dankner WM, et al: Oral ganciclovir in children: pharmacokinetics, safety, tolerance, and antiviral effects. *J Infect Dis* 2000;182:1616-24.
- ◆ Anaizi NH, Swenson CF, and Dentinger PJ: Stability of ganciclovir in extemporaneously compounded oral liquids. *Am J Health Syst Pharm* 1999;56:1738-41.
- ◆ Product Information, Roche, 2006

Adverse Effects/Precautions updated 1/2009
Compatibilities undated 3/2005



Dose & Administration

IV infusion by syringe pump over 30 minutes. Administer as a separate infusion from penicillin-containing compounds. IM injection is associated with variable absorption, especially in the very small infant.

To use dosing chart, please refer to explanatory note on page 1.

Dosing Chart

PMA (weeks)	Postnatal (days)	Dose (mg/kg)	Interval (hours)
$\leq 29^*$	0 to 7	5	48
	8 to 28	4	36
	≥ 29	4	24
30 to 34	0 to 7	4.5	36
	≥ 8	4	24
≥ 35	ALL	4	24

* or significant asphyxia, PDA, or treatment with indomethacin

Uses

Treatment of infections caused by aerobic gram-negative bacilli (e.g. *Pseudomonas*, *Klebsiella*, *E coli*). Usually used in combination with a β -lactam antibiotic.

Monitoring

Measure serum concentrations when treating for more than 48 hours. Obtain peak concentration 30 minutes after end of infusion, and trough concentration just prior to the next dose. When treating patients with serious infections or significantly changing fluid or renal status consider measuring the serum concentration 24 hours after a dose, and use the chart below for the suggested dosing interval. Blood samples obtained to monitor serum drug concentrations should be spun and refrigerated or frozen as soon as possible.

Therapeutic serum concentrations:

Peak: 5 to 12 mcg/mL (or C_{max} /MIC ratio greater than 8:1)

Trough: 0.5 to 1 mcg/mL

Suggested Dosing Intervals

Level at 24 hours (mcg/mL)	Half-life (hours)	Suggested Dosing Interval (hours)
≤ 1	≈ 8	24
1.1 to 2.3	≈ 12	36
2.4 to 3.2	≈ 15	48
≥ 3.3		Measure level in 24 hours

Adverse Effects/Precautions

Black Box Warning

According to the manufacturer's black box warning, aminoglycoside therapy has been associated with potential neurotoxicity, ototoxicity, and nephrotoxicity. Patients with impaired renal function, dehydration, and those who receive high dosage or prolonged therapy are at an increased risk of toxicity. Discontinue therapy or adjust dose if there is evidence of ototoxicity or nephrotoxicity. Aminoglycoside ototoxicity is usually irreversible.

Transient and reversible renal tubular dysfunction may occur, resulting in increased urinary losses of sodium, calcium, and magnesium. Vestibular and auditory ototoxicity may occur. The addition of other nephrotoxic and/or ototoxic medications (e.g. furosemide, vancomycin) may increase these adverse effects. Increased neuromuscular blockade (i.e. neuromuscular weakness and respiratory failure) may occur when used with pancuronium or other neuromuscular blocking agents and in patients with hypermagnesemia.

Pharmacology

Dosing recommendations are based on: (1) Higher peak concentrations increase concentration-dependent bacterial killing; (2) There is a post-antibiotic effect on bacterial killing, especially when treating concurrently with a β -lactam antibiotic; (3) There may be less toxicity with less frequent dosing, due to less renal drug accumulation. Volume of distribution is increased and clearance is decreased in patients with PDA. Serum half-life is prolonged in premature and asphyxiated newborns. Inactivation of gentamicin by penicillin-containing compounds appears to be a time-, temperature-, and concentration-dependent process. This is probably clinically significant only when penicillin-containing compounds are mixed in IV solutions or when the blood is at room temperature for several hours before the assay is performed.

Special Considerations/Preparation

Pediatric injectable solution available in a concentration of 10 mg/mL.

Solution Compatibility: D₅W, D₁₀W, and NS.

Terminal Injection Site Compatibility: Dex/AA solutions, fat emulsion. Acyclovir, amiodarone, aztreonam, caffeine citrate, cefoxitin, ceftazidime, ceftriaxone, cimetidine, clindamycin, dopamine, enalaprilat, esmolol, famotidine, fluconazole, heparin (concentrations ≤ 1 unit/mL), insulin, lorazepam, linezolid, magnesium sulfate, meropenem, metronidazole, midazolam, milrinone, morphine, nicardipine, pancuronium bromide, prostaglandin E₁, ranitidine, remifentanil, vecuronium, and zidovudine.

Incompatibility: Amphotericin B, ampicillin, azithromycin, cefepime, furosemide, imipenem/cilastatin, heparin (concentrations > 1 unit/mL), indomethacin, methicillin, mezlocillin, nafcillin, oxacillin, penicillin G, propofol, and ticarcillin/clavulanate.



Selected References

- ◆ Contopoulos-Ioannidis DG, Giotis ND, Baliatsa DV, Ioannidis JPA: Extended-interval aminoglycoside administration for children: a meta-analysis. *Pediatrics* 2004;114:e111-e118.
- ◆ Stolk LML, Degraeuwe PLJ, Nieman FHM, et al: Population pharmacokinetics and relationship between demographic and clinical variables and pharmacokinetics of gentamicin in neonates. *Ther Drug Monit* 2002;24:527-31.
- ◆ Avent ML, Kinney JS, Istre GR, Whitfield JM: Gentamicin and tobramycin in neonates: comparison of a new extended dosing regimen with a traditional multiple daily dosing regimen. *Am J Perinatol* 2002;8:413-19.
- ◆ Giapros VI, Andronikou S, Cholevas VI, Papadopoulou ZL: Renal function in premature infants during aminoglycoside therapy. *Pediatr Nephrol* 1995;9:163.
- ◆ Daly JS, Dodge RA, Glew RH, et al: Effect of time and temperature on inactivation of aminoglycosides by ampicillin at neonatal dosages. *J Perinatol* 1997;17:42-45.
- ◆ Williams BS, Ransom JL, Gal P, et al: Gentamicin pharmacokinetics in neonates with patent ductus arteriosus. *Crit Care Med* 1997;25:273-75.
- ◆ Product Information, Hospira, 2004

Adverse Effects/Precautions updated 1/2009

Text, Compatibilities, and References updated 3/2007

Select

- ◆ Contaminants e118
- ◆ Stochastic relations
- ◆ Average communication regions
- ◆ Giapponese preprint
- ◆ Dahlmann amide
- ◆ Wilhelmi plate
- ◆ Provenance

Adverse
Text,



Dose & Administration

20 to 25 mg/kg per dose Q12 hours IV infusion over 30 minutes.

Uses

Restricted to treatment of non-CNS infections caused by bacteria, primarily Enterobacteriaceae and anaerobes, resistant to other antibiotics.

Monitoring

Periodic CBC and hepatic transaminases. Assess IV site for signs of phlebitis.

Adverse Effects/Precautions

Seizures occur frequently in patients with meningitis, preexisting CNS pathology, and severe renal dysfunction. Local reactions at the injection site and increased platelet counts are the most frequent adverse effects. Others including eosinophilia, elevated hepatic transaminases, and diarrhea also occur in more than 5% of patients.

Pharmacology

Imipenem is a broad-spectrum carbapenem antibiotic combined in a 1:1 ratio with cilastatin, a renal dipeptidase inhibitor with no intrinsic antibacterial activity. Bactericidal activity is due to inhibition of cell wall synthesis. Clearance is directly related to renal function. Serum half-life of imipenem in neonates is 2.5 hours; the half-life of cilastatin is 9 hours.

Special Considerations/Preparation

Available as powder for injection in 250-mg, and 500-mg vials. Reconstitute with 10 mL of compatible diluent. When reconstituted with compatible diluent, solution is stable for 4 hours at room temperature, 24 hours refrigerated. Maximum concentration for infusion is 5 mg/mL.

Solution Compatibility: D₅W, D₁₀W, and NS.

Terminal Injection Site Compatibility: Fat emulsion. Acyclovir, aztreonam, cefepime, famotidine, insulin, linezolid, midazolam, propofol, remifentanil, and zidovudine.

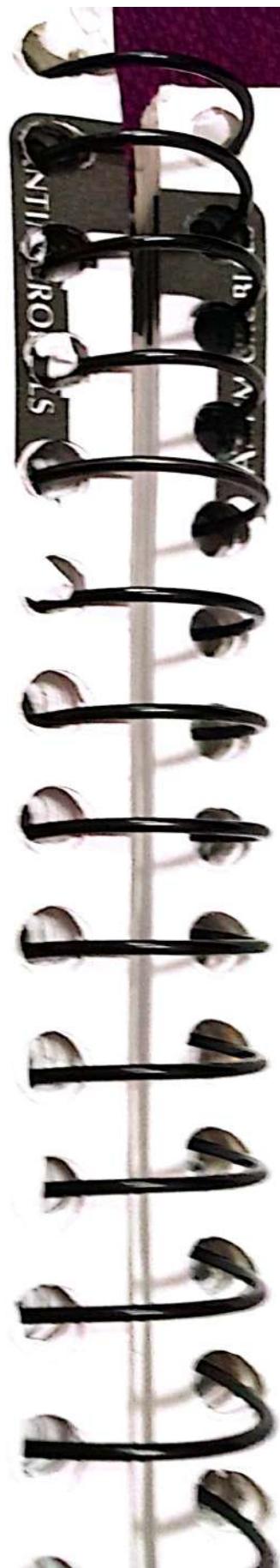
Incompatibility: Amikacin, amiodarone, azithromycin, fluconazole, gentamicin, lorazepam, milrinone, sodium bicarbonate, and tobramycin.

Selected References

- ◆ Garges HP, Alexander KA: Newer antibiotics: imipenem/cilastatin and meropenem. *NeoReviews* 2003;4:e364-68.
- ◆ Stuart RL, Turnidge J, Grayson ML: Safety of imipenem in neonates. *Pediatr Infect Dis J* 1995;14:804.
- ◆ Reed MD, Kliegman RM, Yamashita TS, et al: Clinical pharmacology of imipenem and cilastatin in premature infants during the first week of life. *Antimicrob Agents Chemother* 1990;34:1172.
- ◆ Ahonkhai VI, Cyhan GM, Wilson SE, Brown KR: Imipenem-cilastatin in pediatric patients: an overview of safety and efficacy in studies conducted in the United States. *Pediatr Infect Dis J* 1989;8:740.
- ◆ Nalin DR, Jacobsen CA: Imipenem/cilastatin therapy for serious infections in neonates and infants. *Scand J Infect Dis* 1987;Suppl.2:46.
- ◆ Product Information, Merck, 2006

Added 3/97

Compatibilities updated 3/2007



Dose

20

Uses

Res

pri

ant

Mon

Per

phi

Adve

Sei

pat

inj

ad

tra

Pha

In

1s

ap

w

h

i

Sp

Dose & Administration

PO: 2 mg/kg per dose Q12 hours for one week following birth.

Uses

Prevention of mother-to-child HIV transmission in neonates born to HIV-infected women who have had no therapy during pregnancy (has received intrapartum therapy only). The use of lamivudine with zidovudine may be considered in neonates who received single-dose nevirapine, to potentially reduce the risk for nevirapine resistance. The decision to use combination infant antiretroviral prophylaxis, or the treatment of infected infants with combination antiretroviral therapy, should be done in consultation with a pediatric infectious disease expert.

Monitoring

Specific monitoring unnecessary due to short treatment course.

Adverse Effects/Precautions

Generally well tolerated - limited data in neonates.

Black Box Warning

According to the manufacturer's black box warning, lactic acidosis and severe hepatomegaly with steatosis, including fatal cases, have been reported (in adults).

Pharmacology

Lamivudine (3TC) is a synthetic nucleoside analog "prodrug" that inhibits HIV replication by interfering with viral reverse transcriptase. It is intracellularly converted in several steps to the active compound, then renally excreted. Poor CNS penetration, CSF:plasma ratio is 1:100. The oral solution is well-absorbed, with 66% bioavailability in children. The serum half-life in preterm infants less than 33 weeks gestation is approximately 14 hours. Viral resistance develops rapidly to monotherapy with lamivudine (3TC). TMP-SMX increases lamivudine blood levels (significance unknown).

Special Considerations/Preparation

Available as an oral solution in concentrations of 5 mg/mL (Epivir-HBV®) and 10 mg/mL (Epivir®). Store at room temperature.

Lamivudine (3TC)

Selected References

- ◆ Perinatal HIV Guidelines Working Group. Public Health Service Task Force Recommendations for Use of Antiretroviral Drugs in Pregnant HIV-1 Infected Women for Maternal Health and Interventions to Reduce Perinatal HIV-1 Transmission in the United States. July 8, 2008. Available at <http://aidsinfo.nih.gov/ContentFiles/PerinatalGL.pdf>.
- ◆ Mueller BU, Lewis LL, Yuen GJ, et al: Serum and cerebrospinal fluid pharmacokinetics of intravenous and oral lamivudine in human immunodeficiency virus-infected children. *Antimicrob Agents Chemother* 1998;42:3187-3192.
- ◆ Moodley J, Moodley D, Pillay K, et al: Pharmacokinetics and antiretroviral activity of lamivudine alone or when coadministered with zidovudine in human immunodeficiency virus type 1-infected pregnant women and their offspring. *J Infect Dis* 1998;178:1327-1333.
- ◆ Paediatric European Network for Treatment of AIDS: A randomized double-blind trial of the addition of lamivudine or matching placebo to current nucleoside analogue reverse transcriptase inhibitor therapy in HIV-infected children: the PENTA-4 trial. *AIDS* 1998;12:F151-F160.
- ◆ Horneff G, Adams O, Wahn V: Pilot study of zidovudine-lamivudine combination therapy in vertically HIV-infected antiretroviral-naive children. *AIDS* 1998;12:489-494.
- ◆ Product Information, GlaxoSmithKline, 2008

Adverse Effects/Precautions updated 1/2009

References and Uses updated 3/2008

Dose & Administration

10 mg/kg per dose Q8 hours by IV infusion over 30 to 120 minutes.

Preterm newborns < 1 week of age: 10 mg/kg per dose Q12 hours.

Oral dosing is the same as IV.

Uses

Limited to treatment of non-CNS infections, including endocarditis, caused by gram positive organisms resistant to other antibiotics, e.g. methicillin-resistant *Staph. aureus*, penicillin-resistant *Strep. pneumoniae*, and vancomycin-resistant *Enterococcus faecium*. Treatment of VRE endocarditis that has failed conventional therapy. Do not use as empiric treatment or in any patient with infections caused by gram-negative organisms.

Monitoring

Weekly CBC, AST, ALT. Blood pressure if receiving sympathomimetics.

Adverse Effects/Precautions

Elevated transaminases and diarrhea occur in 6 to 10% of treated patients; thrombocytopenia, anemia, and rash occur in 1 to 2%. The FDA issued an alert regarding Zyvox (linezolid) on March 16, 2007. Patients in an open-label, randomized trial comparing linezolid to vancomycin, oxacillin, or dicloxacillin in the treatment of seriously ill patients with intravascular catheter-related bloodstream infections had a higher chance of death than did patients treated with any comparator antibiotic, and the chance of death was related to the type of organism causing the infection. Patients with Gram positive infections had no difference in mortality according to their antibiotic treatment. In contrast, mortality was higher in patients treated with linezolid who were infected with Gram negative organisms alone, with both Gram positive and Gram negative organisms, or who had no infection when they entered the study. See "<http://www.fda.gov/cder/drug/InfoSheets/HCP/linezolidHCP.htm>"

Pharmacology

Linezolid is an oxazolidinone agent that has a unique mechanism of inhibition of bacterial protein synthesis. It is usually bacteriostatic, although it may be bactericidal against *S. pneumoniae*, *B. fragilis*, and *C. perfringens*. Rapidly penetrates osteoarticular tissues and synovial fluid. CSF concentrations were 70% of plasma concentrations in older patients with non-inflamed meninges. Completely and rapidly absorbed when administered orally to adults and children. Metabolized by oxidation without cytochrome CYP induction. Excreted in the urine as unchanged drug (30%) and two inactive metabolites. Serum half-life in most neonates is 2 to 3 hours, with the exception of preterm neonates less than one week of age, who have a serum half-life of 5 to 6 hours.

Linezolid

Special Considerations/Preparation

Linezolid IV injection is supplied as a 2 mg/mL solution in single-use, ready-to-use 100-mL, 200-mL, and 300-mL plastic infusion bags in a foil laminate overwrap. Keep in the overwrap until use. Store at room temperature. Protect from freezing. IV injection may exhibit a yellow color that can intensify over time without affecting potency. An oral suspension is available, 100 mg per 5 mL. Store at room temperature. Use within 21 days after reconstitution. Protect from light.

Solution Compatibility: D₅W, NS, Lactated Ringers.

Terminal Injection Site Compatibility: Dex/AA. Acyclovir, amikacin, aminophylline, ampicillin, aztreonam, calcium gluconate, cefazolin, cefoxitin, ceftazidime, ceftriaxone, cefuroxime, cimetidine, clindamycin, dexamethasone, digoxin, dobutamine, dopamine, enalaprilat, esmolol, famotidine, fentanyl, fluconazole, furosemide, ganciclovir, gentamicin, heparin, hydrocortisone succinate, imipenem/cilastatin, lidocaine, lorazepam, magnesium, meropenem, methylprednisolone, metoclopramide, metronidazole, mezlocillin, midazolam, morphine, naloxone, netilmicin, nicardipine, nitroglycerin, pentobarbital, phenobarbital, piperacillin, piperacillin-tazobactam, potassium chloride, propranolol, ranitidine, remifentanil, sodium bicarbonate, theophylline, ticarcillin, tobramycin, trimethoprim-sulfamethoxazole, vancomycin, vecuronium, and zidovudine.

Incompatibility: Amphotericin B, chlorpromazine, diazepam, erythromycin lactobionate, pentamidine isethionate, and phenytoin.

Selected References

- ◆ Tan TQ: Update on the use of linezolid: a pediatric perspective. *Pediatr Infect Dis J* 2004;23:955-956.
- ◆ Jungbluth GL, Welshman IR, Hopkins NK: Linezolid pharmacokinetics in pediatric patients: an overview. *Pediatr Infect Dis J* 2003;23:S153-157.
- ◆ Kearns GL, Jungbluth GL, Abdel-Rahman SM, et al: Impact of ontogeny on linezolid disposition in neonates and infants. *Clin Pharmacol Ther* 2003;74:413-22.
- ◆ DeVille JG, Adler S, Azimi PH: Linezolid versus vancomycin in the treatment of known or suspected resistant Gram-positive infections in neonates. *Pediatr Infect Dis J* 2003;22:S158-63.
- ◆ Saiman L, Goldfarb J, Kaplan SA, et al: Safety and tolerability of linezolid in children. *Pediatr Infect Dis J* 2003;22:S193-200.
- ◆ Garges HP, Alexander KA: Newer antibiotics: Linezolid. *NeoReviews* 2003;4:e128-32.
- ◆ Trissel LA, Williams KY, Gilbert DL: Compatibility screening of linezolid injection during simulated Y-site administration with other drugs and infusion solutions. *J Amer Pharm Assoc* 2000;40:515-519.
- ◆ Product information, Pfizer 2007.

Text updated 3/2007

References updated 3/2005

Dose & Administration

Sepsis: 20 mg/kg per dose Q12 hours IV infusion over 30 minutes.

Meningitis and infections caused by *Pseudomonas* species: 40 mg/kg per dose Q8 hours IV infusion over 30 minutes.

Uses

Limited to treatment of pneumococcal meningitis and other serious infections caused by susceptible gram-negative organisms resistant to other antibiotics, especially extended-spectrum beta-lactamase producing *Klebsiella pneumoniae*.

Monitoring

Periodic CBC (for thrombocytosis and eosinophilia) and hepatic transaminases. Assess IV site for signs of inflammation.

Adverse Effects/Precautions

Diarrhea (4%), nausea/vomiting (1%) and rash (2%). May cause inflammation at the injection site. The use of carbapenem antibiotics can result in the development of cephalosporin resistance in *Enterobacter*, *Pseudomonas*, *Serratia*, *Proteus*, *Citrobacter*, and *Acinetobacter* species. The risks of pseudomembranous colitis and fungal infections are also increased.

Pharmacology

Meropenem is a broad-spectrum carbapenem antibiotic that penetrates well into the CSF and most body tissues. It is relatively stable to inactivation by human renal dehydropeptidase. Plasma protein binding is minimal. Clearance is directly related to renal function, and 70% of a dose is recovered intact in the urine. Hepatic function does not affect pharmacokinetics. Serum half-life of meropenem is 3 hours in preterm and 2 hours in full term neonates.

Special Considerations/Preparation

Available (USA) as powder for injection in 500-mg, and 1000-mg vials. Reconstitute with 10 mL of compatible diluent (500 mg vial) or 20 mL (1000 mg vial). When reconstituted with sterile water for injection, stable for up to 2 hours at room temperature or up to 12 hours when refrigerated. When reconstituted with NS to a final concentration between 2.5-50 mg/mL, the solution is stable for up to 2 hours at room temperature or 18 hours when refrigerated. When reconstituted with D5W to final concentration between 2.5-50 mg/mL, the solution is stable for up to 1 hour at room temperature or 8 hours when refrigerated. Solutions prepared in sterile water for injection or NS at concentrations of 1-20 mg/mL are stable in plastic syringes for up to 48 hours when refrigerated. Solutions prepared in D5W at concentrations of 1-20 mg/mL are stable in plastic syringes for up to 6 hours when refrigerated. Solutions prepared for infusion in NS at concentrations of 1-20 mg/mL are stable in plastic IV bags for 4 hours at room temperature or 24 hours when refrigerated. Solutions prepared for infusion in D5W at concentrations of 1-20 mg/mL are stable in plastic IV bags for 1 hour at room temperature or 4 hours when refrigerated.

continued...

Dose & Administration

Loading dose: 15 mg/kg PO or IV infusion by syringe pump over 60 minutes.

Maintenance dose: 7.5 mg/kg per dose PO or IV infusion over 60 minutes. Begin one dosing interval after initial dose.

To use dosing chart, please refer to explanatory note on page 1.

Dosing Interval Chart

PMA (weeks)	Postnatal (days)	Interval (hours)
≤29	0 to 28 >28	48 24
30 to 36	0 to 14 >14	24 12
37 to 44	0 to 7 >7	24 12
≥45	ALL	8

Uses

Reserved for treatment of meningitis, ventriculitis, and endocarditis caused by *Bacteroides fragilis* and other anaerobes resistant to penicillin; treatment of serious intra-abdominal infections; and treatment of infections caused by *Trichomonas vaginalis*. Treatment of *C. difficile* colitis.

Monitoring

Measure CSF drug concentrations when treating CNS infections. Trough drug concentration should be greater than minimum inhibitory concentration for organism.

Adverse Effects/Precautions

Seizures and sensory polyneuropathy have been reported in a few adult patients receiving high doses over a prolonged period. Drug metabolites may cause brownish discoloration of the urine.

Black Box Warning

According to the manufacturer's black box warning, metronidazole has been shown to be carcinogenic in mice and rats.

Pharmacology

Metronidazole is bactericidal for many anaerobic organisms. It is well absorbed after oral administration, with peak serum concentrations attained in 1 to 3 hours. Distribution in all tissues throughout the body is excellent. It is less than 20% protein bound. Hydroxylation in the liver occurs in term infants and premature infants exposed to antenatal betamethasone. Unchanged drug and the active metabolite are excreted renally. Elimination half-life is strongly related to gestational age, ranging from 22 to 109 hours.

Metronidazole

Special Considerations/Preparation

Available in 5 mg/mL concentration in 100 mL single-dose plastic ready-to-use solution containers. Store at controlled room temperature.

Do not refrigerate (crystals form, but redissolve on warming to room temperature). Osmolarity is 310 mOsm/L, pH is 5 to 7. Each container contains 14 mEq of sodium.

Supplied as 250 mg and 500 mg for oral administration. Suspension may be prepared by crushing five 250-mg tablets (1250 mg), dissolving powder in 10 mL purified water, then adding cherry syrup to make a total volume of 83 mL. Final concentration is 15 mg/mL.

Protect from light. Shake well. Suspension is stable for 30 days refrigerated.

Solution Compatibility: D₅W, and NS.

Solution Incompatibility: Manufacturer recommends that if metronidazole is used with a primary IV fluid system, the primary solution should be discontinued during metronidazole infusion.

Terminal Injection Site Compatibility: Dex/AA solutions, fat emulsion. Acyclovir, amikacin, aminophylline, amiodarone, ampicillin, cefazolin, cefepime, cefotaxime, cefoxitin, ceftazidime, ceftriaxone, chloramphenicol, clindamycin, dopamine, enalaprilat, esmolol, fluconazole, gentamicin, heparin, hydrocortisone succinate, linezolid, lorazepam, magnesium sulfate, midazolam, miltromine, morphine, netilmicin, nicardipine, penicillin G, piperacillin-tazobactam, prostaglandin E₁, remifentanil, and tobramycin.

Incompatibility: Aztreonam, and meropenem.

Selected References

- ◆ Wenisch C, Parschalk B, Hasenhundl M, et al: Comparison of vancomycin, teicoplanin, metronidazole, and fusidic acid for the treatment of *Clostridium difficile*-associated diarrhea. *Clin Infect Dis* 1996;22:813.
- ◆ Allen LV, Erickson MA: Stability of ketocconazole, metolazone, metronidazole, procainamide hydrochloride, spironolactone in extemporaneously compounded oral liquids. *Am J Health Syst Pharm* 1996;53:2073-2078.
- ◆ Feder HM Jr: *Bacteroides fragilis* meningitis. *Rev Infect Dis* 1987;9:783.
- ◆ Roberts RL: *Drug Therapy in Infants*. Philadelphia: WB Saunders Co, 1984, p 76.
- ◆ Hall P, Kaye CM, McIntosh N, Steele J: Intravenous metronidazole in the newborn. *Arch Dis Child* 1983;58:529.
- ◆ Oldenburg B, Speck WT: Metronidazole. *Pediatr Clin North Am* 1983;30:71.
- ◆ Jager-Roman E, Doyle PE, Baird-Lambert J, et al: Pharmacokinetics and tissue distribution of metronidazole in the newborn infant. *J Pediatr* 1982;100:651.
- ◆ Product Information, BBraun, 2004

Adverse Effects/Precautions updated 1/2009
Updated 3/2007
Compatibilities updated 3/2005



Meropenem

Solution Compatibility: D₅W, D₁₀W, and NS.

Terminal Injection Site Compatibility: Dex/AA and fat emulsion. Acyclovir, aminophylline, atropine, calcium gluconate, cimetidine, dexamethasone, digoxin, dobutamine, dopamine, enalaprilat, fluconazole, furosemide, gentamicin, heparin, insulin, linezolid, metoclopramide, milrinone, morphine, norepinephrine, phenobarbital, ranitidine, sodium bicarbonate, vancomycin, and zidovudine.

Incompatibility: Amphotericin B and metronidazole.

Selected References

- ◆ Garges HP, Alexander KA: Newer antibiotics: imipenem/cilastatin and meropenem. *NeoReviews* 2003;4:e364-68.
- ◆ Bradley JS: Meropenem: a new, extremely broad spectrum β-lactam antibiotic for serious infections in pediatrics. *Pediatr Infect Dis J* 1997;16:263-68.
- ◆ Blumer JL: Pharmacokinetic determinants of carbapenem therapy in neonates and children. *Pediatr Infect Dis J* 1996;15:733-37.
- ◆ Patel PR: Compatibility of meropenem with commonly used injectable drugs. *Am J Health-Syst Pharm* 1996;53:2853-55.
- ◆ Blumer JL, Reed MD, Kearns GL, et al: Sequential, single-dose pharmacokinetic evaluation of meropenem in hospitalized infants and children. *Antimicrob Agents Chemother* 1995;39:1721-25.
- ◆ Hurst M, Lamb HM: Meropenem: a review of its use in patients in intensive care. *Drugs* 2000;59:653-680.
- ◆ Product Information, Astra-Zeneca, 2007

References updated 3/2008
Compatibilities updated 3/2004
Text updated 3/2008

Micafungin

Dose & Administration

10 mg/kg per dose Q24 hours, IV infusion via syringe pump over at least 1 hour.

Uses

Treatment of patients with fungal septicemia, peritonitis, and disseminated infections due to *Candida* species including *C.albicans*, azole-resistant *C.albicans*, and non-albicans species including *C.krusei*, *C.glabrata*, *C.tropicalis* and *C.parapsilosis*.

There are case reports, but no controlled clinical trials, of patients treated for endocarditis and osteomyelitis due to *Candida*. Clinical studies are ongoing for use in neonatal hematogenous *Candida* meningoencephalitis (no data reported yet).

Monitoring

Assess IV site for signs of irritation. Periodic measurement of serum potassium, calcium, BUN, and creatinine (isolated renal dysfunction reported in adults).

Adverse Effects/Precautions

Limited data in neonates. The most common reportable adverse reactions in adults are diarrhea, vomiting, pyrexia, hypokalemia, thrombocytopenia, and histamine-mediated symptoms (including rash, pruritus, facial swelling, and vasodilatation). Rapid infusion rates may result in more frequent histamine-mediated reactions.

Pharmacology

Micafungin is a semisynthetic lipopeptide echinocandin antifungal agent with broad-spectrum fungicidal activity against many *Candida* species. It inhibits the synthesis of 1, 3-beta-D-glucan, an integral component of the fungal cell wall. Plasma protein binding is high, primarily to albumin, but it does not displace bilirubin. Pharmacokinetics are linear. Metabolism occurs primarily in the liver through both noncytochrome and cytochrome P450 pathways to 2 biologically inactive metabolites that are eliminated in the feces. Serum half-life ranges from 7.4 to 9.2 hours in neonates (compared to 12 hours in adults). Mutant strains of *Candida* with reduced susceptibility have been identified in some adult patients during treatment suggesting the potential development of drug resistance. Animal studies suggest distribution of micafungin to liver, spleen, kidney, and lungs indicative of tissue penetration to common sites of invasive fungal infections. No cerebrospinal fluid levels were detected but brain tissue levels were measurable suggesting tissue penetration.

Micafungin

Special Considerations/Preparation

Available in single-use lyophilized powder for injection in vials containing 50 and 100 mg. Add 5 mL of 0.9% sodium chloride injection (without bacteriostatic agent) to each 50 mg or 100 mg vial yielding approximately 10 mg or 20 mg per mL, respectively. Inspect reconstituted vials for particulate matter and discoloration prior to administration. Gently dissolve lyophilized powder by swirling the vial to avoid excessive foaming. Do not shake. Protect from light. Reconstituted vials may be stored at room temperature for up to 24 hours before use.

Reconstituted drug should be further diluted in NS or D₅W to a final concentration between 0.5 to 1.5 mg/mL prior to administration. Diluted infusion should be protected from light and may be stored at room temperature for up to 24 hours before use. An existing IV line should be flushed with NS prior to administration.

Solution Compatibility: D₅W and NS.

Terminal Injection Site Compatibility: Aminophylline, bumetanide, calcium chloride, calcium gluconate, dopamine, esmolol, heparin, lidocaine, milrinone, potassium chloride, and sodium nitroprusside.

Incompatibility: Albumin, amiodarone, dobutamine, epinephrine, insulin, midazolam, morphine, nicardipine, octreotide, phenytoin, rocuronium, and vecuronium.

Selected References

- ◆ Trusley C, Kupiec T, Trissel LA: Compatibility of micafungin injection with other drugs during simulated Y-site co-administration. *International Journal of Pharmaceutical Compounding* 2006;10:230-233.
- ◆ Heresi GP, Gerstmann DR, Reed MD, et al: The pharmacokinetics and safety of micafungin, a novel echinocandin, in premature infants. *Pediatr Infect Dis J* 2006;25:1110-1115.
- ◆ Groll AH, Mickiene D, Petraitis V, et al: Compartmental pharmacokinetics and tissue distribution of the antifungal echinocandin lipopeptide micafungin (FK463) in rabbits. *Antimicrob Agents Chemother* 2001;45:3322-3327.
- ◆ Hope WW, Mickiene D, Petraitis V, et al: The pharmacokinetics and pharmacodynamics of micafungin in experimental hematogenous Candida meningoencephalitis: Implications for echinocandin therapy in neonates. *J Infect Dis* 2008;197:163-171.
- ◆ Bliss JM, Wellington M, Gigliotti F: Antifungal pharmacotherapy for neonatal candidiasis. *Semin Perinatol* 2003;27:365-374.
- ◆ Steinbach WJ, Benjamin DK: New agents under development in children and neonates. *Curr Opin Infect Dis* 2005;18:484-489.
- ◆ Mohr J, Johnson M, Cooper T, et al: Current options in antifungal pharmacotherapy. *Pharmacotherapy* 2008;28:614-645.
- ◆ Product information, Astellas, 2008.

Added 3/2009



Dose & Administration

Cutaneous infections: Apply small amounts topically to affected areas 3 times daily.

Decolonization: Apply small amounts to anterior nares twice daily for 5 to 7 days.

Uses

Topical use for skin infections caused by *Staphylococcus aureus*, *S epidermidis*, *S saprophyticus*, and *Streptococcus pyogenes*. As part of multiple interventions for infection control during MRSA outbreaks in the NICU. Routine use for decolonization is not recommended.

Monitoring

Assess affected area for continued infection.

Adverse Effects/Precautions

Use only on the skin. No adverse effects reported from topical administration. Routine use may lead to selective bacterial resistance.

Pharmacology

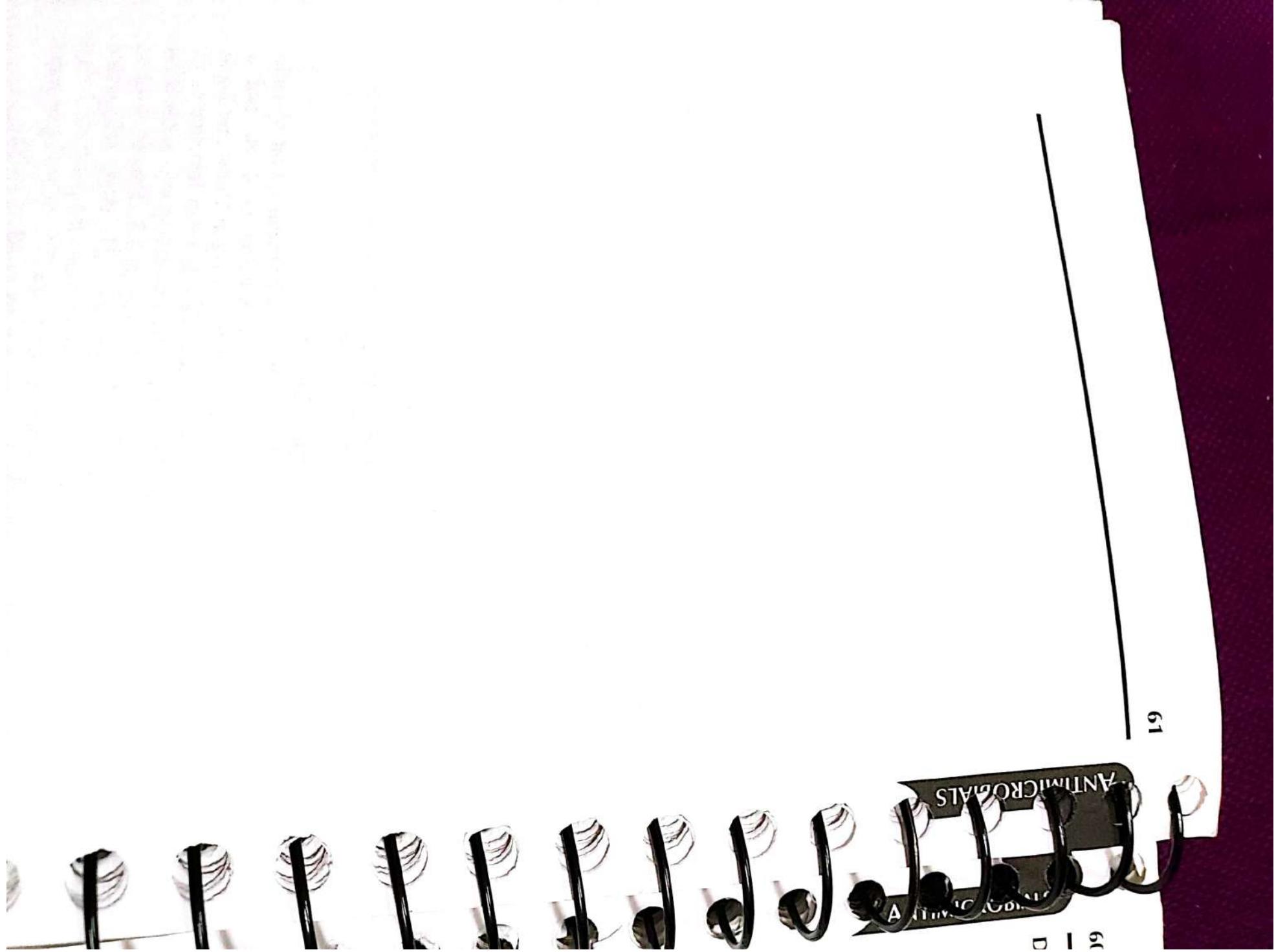
Topical antibacterial produced by fermentation of the organism *Pseudomonas fluorescens*. Inhibits protein synthesis by bonding to bacterial isoleucyl-transfer-RNA synthetase. Highly protein bound. Not absorbed into the systemic circulation after topical administration (older infants and children). Metabolized in the skin to an inactive compound and excreted.

Special Considerations/Preparation

Available in unit-dose packets and 15 and 30-g tubes as a 2% ointment and cream (20 mg/g).

Selected References

- ◆ American Academy of Pediatrics. Staphylococcal Infections. In: Pickering LK, Baker CJ, Long SS, McMillan JA, eds. *Red Book: 2006 Report of the Committee on Infectious Diseases*. 27th ed. Elk Grove Village, IL: American Academy of Pediatrics 2006: pp 608-610.
- ◆ Khoury J, Jones M, Grim A, et al: Eradication of methicillin-resistant *Staphylococcus aureus* from a neonatal intensive care unit by active surveillance and aggressive infection control measures. *Infect Control Hosp Epidemiol* 2005;26:616-621.
- ◆ Saiman L, Cronquist A, Wu F, et al: An outbreak of methicillin-resistant *Staphylococcus aureus* in a neonatal intensive care unit. *Infect Control Hosp Epidemiol* 2003;24:317-321.
- ◆ Zakrzewska-Bode A, Muytjens HL, Liem KD, Hoogkamp-Korstanje JAA: Mupirocin resistance in coagulase-negative staphylococci, after topical prophylaxis for the reduction of colonization of central venous catheters. *J Hosp Infect* 1995;31:189.
- ◆ Pappa KA: The clinical development of mupirocin. *J Am Acad Dermatol* 1990;22:873.
- ◆ Leyden JJ: Mupirocin: A new topical antibiotic. *Semin Dermatol* 1987;6:48.
- ◆ Davies EA, Emmerson AM, Hogg GM, et al: An outbreak of infection with a methicillin-resistant *Staphylococcus aureus* in a special care baby unit: Value of topical mupirocin and of traditional methods of infection control. *J Hosp Infect* 1987;10:120.
- ◆ Product Information, OrthoNeutrogena, 2006



Nafcillin

Dose & Administration

Usual dosage: 25 mg/kg per dose IV over 15 minutes.

Meningitis: 50 mg/kg per dose.

To use dosing chart, please refer to explanatory note on page 1.

Dosing Interval Chart

PMA (weeks)	PostNatal (days)	Interval (hours)
≤29	0 to 28 >28	12 8
30 to 36	0 to 14 >14	12 8
37 to 44	0 to 7 >7	12 8
≥45	ALL	6

Uses

Treatment of infections caused by penicillinase-producing staphylococci, particularly if evidence of renal dysfunction.

Monitoring

Periodic CBC. Observe IV site for signs of extravasation.

Adverse Effects/Precautions

Increase dosing interval in patients with hepatic dysfunction. Irritating to veins—watch for phlebitis. Cases of granulocytopenia have been reported.

Pharmacology

Inhibits synthesis of bacterial cell wall. Better penetration into CSF than methicillin. Excreted via hepatic clearance.

Special Considerations/Preparation

Available in 1 and 2-g vials. Reconstitute 1-g vial with 3.4 mL of sterile water for injection to provide a final volume of 4 mL and a concentration of 250 mg/mL. Also available in 1-g in 50-mL and 2-g in 100-mL frozen single-dose bags. Thaw bags at room temperature or under refrigeration. Do not force thaw by immersing into water baths or microwaving. pH of resulting solution 6 to 8.5. Thawed solution stable for 3 days at room temperature, 21 days refrigerator. Reconstituted solution stable for 3 days at room temperature, 7 days refrigerated. Osmolality was determined to be 709 mOsm/kg of water. For direct intravenous injection, dilute in 15 to 30 ml of NS.

Nafcillin

63

Solution Compatibility: D₅W, D₁₀W, and NS.

Terminal Injection Site Compatibility: Dex/AA solutions, fat emulsion. Acyclovir, aminophylline, atropine, chloramphenicol, cimetidine, dexamethasone, enalaprilat, esmolol, famotidine, fentanyl, fluconazole, heparin, lidocaine, morphine, nicardipine, potassium chloride, propofol, sodium bicarbonate, zidovudine.

Incompatibility: Amikacin, aztreonam, gentamicin, hydrocortisone succinate, insulin, methylprednisolone, midazolam, netilmicin, tobramycin, and vancomycin.

Selected References

- ◆ Prober CG, Stevenson DK, Benitz WE: The use of antibiotics in neonates weighing less than 1200 grams. *Pediatr Infect Dis J* 1990;9:111.
- ◆ Kitzing W, Nelson JD, Mohs E: Comparative toxicities of methicillin and nafcillin. *Am J Dis Child* 1981;135:52.
- ◆ Banner W, Gooch WM, Burkart G, Korones SB: Pharmacokinetics of nafcillin in infants with low birth weights. *Antimicrob Agents Chemother* 1980;17:691.
- ◆ Product Information, Sandoz, 2004

Compatibilities updated 3/2005
Text updated 3/1997



Dose & Administration

IV infusion by syringe pump over 30 minutes. Administer as a separate infusion from penicillin-containing compounds. IM injection is associated with variable absorption, especially in the very small infant.

To use dosing chart, please refer to explanatory note on page 1.

Dosing Chart

PMA (weeks)	Postnatal (days)	Dose (mg/kg)	Interval (hours)
$\leq 29^*$	0 to 7	5	48
	8 to 28	4	36
≥ 29	≥ 29	4	24
30 to 34	0 to 7	4.5	36
	≥ 8	4	24
≥ 35	ALL	4	24

* or significant asphyxia, PDA, or treatment with indomethacin

Uses

Treatment of infections caused by aerobic gram-negative bacilli (e.g. *Pseudomonas*, *Klebsiella*, *E coli*). Usually used in combination with a β -lactam antibiotic.

Monitoring

Measure serum concentrations when treating for more than 48 hours. Obtain peak concentration 30 minutes after end of infusion, and trough concentration just prior to the next dose. When treating patients with serious infections or significantly changing fluid or renal status consider measuring the serum concentration 24 hours after a dose, and use the chart below for the suggested dosing interval. Blood samples obtained to monitor serum drug concentrations should be spun and refrigerated or frozen as soon as possible.

Therapeutic serum concentrations:

Peak: 5 to 12 mcg/mL (or C_{max} /MIC ratio greater than 8:1)

Trough: 0.5 to 1 mcg/mL

Suggested Dosing Intervals

Level at 24 hours (mcg/mL)	Half-life (hours)	Suggested Dosing Interval (hours)
≤ 1	≈ 8	24
1.1 to 2.3	≈ 12	36
2.4 to 3.2	≈ 15	48
≥ 3.3		Measure level in 24 hours

Netilmicin

Adverse Effects/Precautions

Transient and reversible renal tubular dysfunction may occur, resulting in increased urinary losses of sodium, calcium, and magnesium. Vestibular and auditory ototoxicity. The addition of other nephrotoxic and/or ototoxic medications (e.g. furosemide, vancomycin) may increase these adverse effects. Increased neuromuscular blockade (i.e. neuromuscular weakness and respiratory failure) may occur when used with pancuronium or other neuromuscular blocking agents and in patients with hypermagnesemia.

Pharmacology

Dosing recommendations are based on: (1) Higher peak concentrations increase concentration-dependent bacterial killing; (2) There is a post-antibiotic effect on bacterial killing, especially when treating concurrently with a β -lactam antibiotic; (3) There may be less toxicity with less frequent dosing, due to less renal drug accumulation. Volume of distribution is increased and clearance is decreased in patients with PDA. Serum half-life is prolonged in premature and asphyxiated newborns. Inactivation of netilmicin by penicillin-containing compounds appears to be a time-, temperature-, and concentration-dependent process. This is probably clinically significant only when penicillin-containing compounds are mixed in IV solutions or when the blood is at room temperature for several hours before the assay is performed.

Special Considerations/Preparation

Available in a concentration of 100 mg/mL in 1.5 mL vials. A 10 mg/mL dilution may be made by adding 1 mL of this solution to 9 mL of sterile water for injection. Dilution is stable for 72 hours refrigerated. Do not freeze. **No longer available in the US.**

Solution Compatibility:

D₅W, D₁₀W, and NS.

Terminal Injection Site Compatibility: Dex/AA solutions, fat emulsion. Aminophylline, atropine, aztreonam, calcium gluconate, cefuroxime, clindamycin, dexamethasone, heparin (concentrations \leq 1 unit/mL), hydrocortisone succinate, iron dextran, isoproterenol, linezolid, metronidazole, neostigmine, norepinephrine, pancuronium bromide, potassium chloride, procainamide, remifentanil, sodium bicarbonate, and vitamin K₁.

Incompatibility: Amphotericin B, ampicillin, cefepime, furosemide, heparin (concentrations $>$ 1 unit/mL), methicillin, mezlocillin, nafcillin, oxacillin, penicillin G, propofol, and ticarcillin/clavulanate.

Selected References

- ◆ Contopoulos-Ioannidis DC, Giotsis ND, Ballatsa DV, Ioannidis JPA: Extended-interval aminoglycoside administration for children: a meta-analysis. *Pediatrics* 2004;114:e111-e118.
- ◆ Stolk LML, Degraeve PLJ, Nieman FHM, et al: Population pharmacokinetics and relationship between demographic and clinical variables and pharmacokinetics of gentamicin in neonates. *Ther Drug Monit* 2002;24:527-31.
- ◆ Avent ML, Kinney JS, Istre GR, Whitfield JM: Gentamicin and tobramycin in neonates: comparison of a new extended dosing regimen with a traditional multiple daily dosing regimen. *Am J Perinatol* 2002;19:413-19.
- ◆ Giapros VI, Andronikou S, Cholevas VI, Papadopoulou ZL: Renal function in premature infants during aminoglycoside therapy. *Pediatr Nephrol* 1995;9:163.
- ◆ Daly JS, Dodge RA, Glew RH, et al: Effect of time and temperature on inactivation of aminoglycosides by ampicillin at neonatal dosages. *J Perinatol* 1997;17:42-45.

References updated 3/2005



Dose & Administration

PO: 2 mg/kg single dose at 48 to 72 hours of age.
If the mother did not receive intrapartum single-dose nevirapine or dose received within 2 hours of delivery, administer 2 mg/kg as soon as possible after birth.

Uses

Used **only** in combination with zidovudine in the treatment of neonates born to HIV-infected women who have had no therapy during pregnancy (mother receives zidovudine plus a single 200-mg oral dose of nevirapine during labor). Dosing guidelines above are for prophylactic treatment of neonates born to HIV-infected women. Treatment of infected infants with combination antiretroviral therapy should be done in consultation with a pediatric infectious disease expert.

Monitoring

Specific monitoring unnecessary due to short treatment course.

Adverse Effects/Precuations

Limited data on toxicity—none reported in neonates.

Black Box Warning

According to the manufacturer's black box warning, severe, life-threatening, in some cases fatal, hepatotoxicity and skin reactions have been reported (in adults).

Pharmacology

Nevirapine is a non-nucleoside antiretroviral agent that inhibits HIV-1 replication by selectively interfering with viral reverse transcriptase without requiring intracellular metabolism. It also inactivates cell-free virions in the genital tract and breast milk. Synergistic antiviral activity occurs when administered with zidovudine. Nevirapine is rapidly absorbed after oral administration to pregnant women and is highly lipophilic, resulting in therapeutic concentrations being readily transferred across the placenta to the fetus. Serum half-life in the neonates is approximately 44 hours. With the maternal/newborn regimen described above, serum concentrations are above 100 mcg/L throughout the first week of life. Nevirapine is extensively metabolized by, and an inducer of, hepatic CYP3A4 and CYP2B6 isoenzymes. Concomitant administration of phenobarbital or phenytoin, CYP3A4 inducers, may affect plasma concentrations.

Special Considerations/Preparation

Available as an oral suspension in a concentration of 10 mg/mL. Store at room temperature. Shake suspension gently prior to administration.

Selected References

- ◆ Perinatal HIV Guidelines Working Group. Public Health Service Task Force Recommendations for Use of Antiretroviral Drugs in Pregnant HIV-1 Infected Women for Maternal Health and Interventions to Reduce Perinatal HIV-1 Transmission in the United States. July 8, 2008. Available at <http://aidsinfo.nih.gov/ContentFiles/PerinatalGL.pdf>.
- ◆ Mirochnick M, Dorenbau A, Blanchard S, et al: Predose infant nevirapine concentration with the two-dose intrapartum neonatal nevirapine regimen: association with timing of maternal intrapartum nevirapine dose. *JAIDS* 2003;33:153-56.
- ◆ Mirochnick M, Clarke DF, Dorenbau A: Nevirapine: pharmacokinetic considerations in children and pregnant women. *Drugs* 2000;39:281-293.
- ◆ Product Information, Boehringer Ingelheim, 2007
- Adverse Effects/Precautions updated 1/2009
- Dose & Administration and References updated 3/2008

Nystatin

Dose & Administration

Topical: Apply ointment or cream to affected area Q6 hours.

Continue treatment for 3 days after symptoms have subsided.

PO: 1 mL (preterm) to 2 mL (term) of 100,000-units/mL suspension divided and applied with swab to each side of mouth Q6 hours.

Continue treatment for 3 days after symptoms have subsided.

Prophylaxis: 1 mL of 100,000 units/mL suspension orally or instilled into stomach via oro/nasogastric tube 3 times per day.

Uses

Treatment of mucocutaneous candidal infections. Prophylaxis against invasive fungal infections in high risk VLBW infants.

Monitoring

Assess response to drug.

Adverse Effects/Precautions

Possible skin rash caused by vehicle in ointment/cream.

Pharmacology

Polyene antifungal similar in structure to amphotericin B. May be fungicidal or fungistatic. Binds to the fungal cell membrane causing disruption of the cell structure. Not absorbed well from the GI tract, skin, or mucous membranes.

Special Considerations/Preparation

Topical ointment/cream: 100,000 units/g in 15- and 30-g tubes. Ointment dissolved in polyethylene and mineral-oil-gel base.

Topical powder: 100,000 units/g in 15- and 30-g plastic squeeze bottles.

Oral suspension: 100,000 units/mL in 5-, 60-, and 480-mL bottles. Shake well before applying to mouth. Appears to work best when not mixed with formula. Contains <1% alcohol, saccharin, and 50% sucrose.

Selected References

- ◆ Ozturk MA, Gunes T, Koklu E, et al: Oral nystatin prophylaxis to prevent invasive candidiasis in neonatal intensive care unit. *Mycoses* 2006;49:484-492.
- ◆ Hoppe JE: Treatment of oropharyngeal candidiasis and candidal diaper dermatitis in neonates and infants: review and reappraisal. *Ped Inf Dis J* 1997;16:885-94.
- ◆ Faix RC, Kovarik SM, Shaw TR, Johnson RV: Mucocutaneous and invasive candidiasis among very low birth weight (<1500 grams) infants in intensive care nurseries: A prospective study. *Pediatrics* 1989;83:101.
- ◆ Roberts RJ: *Drug Therapy in Infants*. Philadelphia: WB Saunders Co, 1984, p 81.
- ◆ Munz D, Powell KR, Pai CH: Treatment of candidal diaper dermatitis: A double-blind placebo-controlled comparison of topical nystatin with topical plus oral nystatin. *J Pediatr* 1982;101:1022.
- ◆ Product Information, Actavis, 2006

Dose & Administration

Usual dosage: 25 mg/kg per dose IV over at least 10 minutes.

Meningitis: 50 mg/kg per dose.

To use dosing chart, please refer to explanatory note on page 1.

Dosing Interval Chart

PMA (weeks)	PostNatal (days)	Interval (hours)
≤ 29	0 to 28	12
	>28	8
30 to 36	0 to 14	12
	>14	8
37 to 44	0 to 7	12
	>7	8
≥ 45	ALL	6

Uses

Treatment of infections caused by penicillinase-producing staphylococci.

Monitoring

Periodic CBC and urinalysis. AST, ALT. Irritating to veins—watch for phlebitis. Observe IV site for signs of extravasation.

Adverse Effects/Precautions

Interstitial nephritis associated with hematuria, albuminuria, and casts in urine. Bone marrow depression. Elevated AST and ALT. Hypersensitivity in the form of a rash. Tolerant strains of staphylococci have been reported.

Pharmacology

Inhibits synthesis of bacterial cell wall. Rapidly excreted renally unchanged. Poor CSF penetration. Good penetration of pleural, pericardial, and synovial fluids.

Special Considerations/Preparation

Available as powder injection in 250-mg, 500-mg, 1-g, 2-g, and 10-g vials. Reconstitute 250 mg vial with 5 mL of sterile water for injection to make a concentration of 50 mg/mL. Reconstituted solution is stable for 4 days at room temperature, 7 days refrigerated. Dilute further using sterile water or NS to a concentration less than or equal to 40 mg/mL. Dilution stable for 4 days refrigerated.

Solution Compatibility: D₅W, D₁₀W, and NS.

Terminal Injection Site Compatibility: Dex/AA solutions, fat emulsion. Acyclovir, chloramphenicol, dopamine, famotidine, fluconazole, heparin, hydrocortisone succinate, milrinone, morphine, potassium chloride, and zidovudine.

Incompatibility: Amikacin, caffeine citrate, gentamicin, netilmicin, sodium bicarbonate, and tobramycin.

Oxacillin

Selected References

- ◆ Maraqa NF, Gomez MM, Rathore MH, Alvarez AM: Higher occurrence of hepatotoxicity and rash in patients treated with oxacillin, compared with those treated with nafcillin and other commonly used antimicrobials. *Clin Infect Dis* 2002;34:50-54.
- ◆ Prober CG, Stevenson DK, Benitz WE: The use of antibiotics in neonates weighing less than 1200 grams. *Pediatr Infect Dis J* 1990;9:111.
- ◆ Nahata MC, Debolt SL, Powell DA: Adverse effects of methicillin, nafcillin, and oxacillin in pediatric patients. *Dev Pharmacol Ther* 1982;4:117.
- ◆ Axline SG, Yaffe SJ, Simon HJ: Clinical pharmacology of antimicrobials in premature infants: II. Ampicillin, methicillin, oxacillin, neomycin, and colistin. *Pediatrics* 1967;39:97.
- ◆ Product Information, Sandoz, 2005

Compatibilities updated 3/2005

Text updated 3/1997

Dose & Administration

»Use only aqueous crystalline penicillin G for IV administration«

Meningitis: 75,000 to 100,000 units/kg per dose IV infusion over 30 minutes, or IM.

Bacteremia: 25,000 to 50,000 units/kg per dose IV infusion over 15 minutes, or IM.

Group B streptococcal infections: Some experts recommend using 200,000 units/kg per day for bacteremia and 450,000 units/kg per day for meningitis, in divided doses at more frequent intervals than those listed above. Consider adding aminoglycoside if tolerance is suspected or confirmed.

Gonococcal infection (only with proven penicillin-susceptible isolate): Use higher doses listed for meningitis and bacteremia.

Congenital syphilis: Aqueous crystalline penicillin G: 50,000 units/kg per dose IV over 15 minutes, given Q12 hours during the first 7 days of life, and Q8 hours thereafter, irrespective of gestational age; or Procaine penicillin G : 50,000 units/kg per dose IM, once daily.

Treat for 10 to 14 days.

Procaine and benzathine penicillin G are for IM administration only.

To use dosing chart, please refer to explanatory note on page 1.

Dosing Interval Chart

PMA (weeks)	PostNatal (days)	Interval (hours)
≤29	0 to 28	12
	>28	8
30 to 36	0 to 14	12
	>14	8
37 to 44	0 to 7	12
	>7	8
≥45	ALL	6,

Uses

Treatment of infections caused by susceptible organisms—congenital syphilis, gonococci, streptococci (non enterococcal).

Monitoring

Follow serum sodium and potassium when using high doses and in patients with renal failure. Observe IV site for signs of extravasation.

Adverse Effects/Precautions

Cardiac arrest has been reported in patients who received high doses infused rapidly. Significant CNS toxicity has been reported in adults with renal failure who developed CSF concentrations >10 mcg/mL. Bone marrow depression, granulocytopenia, and hepatitis are rare. Hypersensitivity has not been seen in neonates.

Black Box Warning According to the manufacturer's black box warning, inadvertent intravenous administration of penicillin G benzathine (to be given IM only) has been associated with cardiorespiratory arrest and death.

Pharmacology

Inhibits synthesis of bacterial cell wall. Excreted unchanged in the urine. CSF penetration is poor, except in inflamed meninges. Concentrates in joint fluid and urine.

continued...

Special Considerations/Preparation

Aqueous penicillin G is available as powder for injection in two salt forms: penicillin G potassium and penicillin G sodium. Penicillin G potassium contains 1.68 mEq (65.6 mg) potassium per 1 million units, and 0.3 mEq (6.8 mg) sodium per 1 million units. Penicillin G sodium contains 2 mEq (46 mg) sodium per 1 million units. Reconstitute the 5-million unit vial with 8 mL sterile water for injection to make a final concentration of 500,000 units/mL. Reconstituted solution good for 7 days refrigerated. A 100,000 unit/mL dilution may be made by adding 10 mL of reconstituted solution to 40 mL sterile water for injection. Dilution stable for 7 days refrigerated. Penicillin G sodium reconstituted solution stable for 3 days in refrigerator.

Penicillin G potassium is also available as a premixed frozen isosmotic solution containing 1, 2 or 3 million units in 50 mL.

Procaine and benzathine penicillin G for IM injection are available in multiple dosage strengths in vials and Tubex® syringes.

Note: Penicillin G is also known as benzylpenicillin - do not confuse with benzathine penicillin used for only for IM injections.

1 million units is the equivalent of 600 mg.

Solution Compatibility: D₅W, D₁₀W, and NS.

Terminal Injection Site Compatibility: Dex/AA solutions, fat emulsion. Acyclovir, amiodarone, caffeine citrate, calcium chloride, calcium gluconate, chloramphenicol, cimetidine, clindamycin, dopamine, enalaprilat, erythromycin lactobionate, esmolol, fluconazole, furosemide, heparin, hydrocortisone succinate, lidocaine, methicillin, metronidazole, morphine, nicardipine, pentobarbital, potassium chloride, prostaglandin E₁, ranitidine and sodium bicarbonate.

Incompatibility: Amikacin, aminophylline, amphotericin B, gentamicin, metoclopramide, netilmicin, and tobramycin.

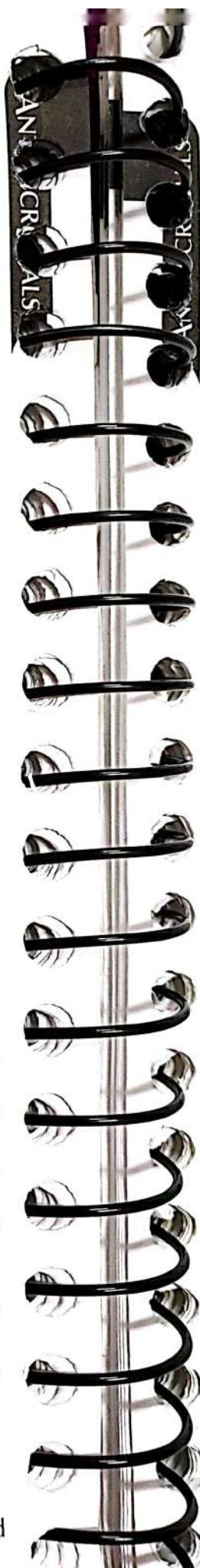
Selected References

- ◆ American Academy of Pediatrics. Syphilis. In: Pickering LK, Baker CJ, Long SS, McMillan JA, eds. *Red Book: 2006 Report of the Committee on Infectious Diseases*. 27th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2006: pp 637-638.
- ◆ Centers for Disease Control and Prevention: Sexually transmitted diseases treatment guidelines 2006. *MMWR* 2006;55(No. RR-11).
- ◆ Stoll BJ: Congenital syphilis: evaluation and management of neonates born to mothers with reactive serologic tests for syphilis. *Pediatr Infect Dis J* 1994;13:845.
- ◆ Prober CG, Stevenson DK, Benitz WE: The use of antibiotics in neonates weighing less than 1200 grams. *Pediatr Infect Dis J* 1990;9:111.
- ◆ Roberts RJ: *Drug Therapy in Infants*. Philadelphia: WB Saunders Co, 1984, p45.
- ◆ Pyati SP, Pildes RS, Jacobs NM, et al: Penicillin in infants weighing two kilograms or less with early onset group B streptococcal disease. *N Engl J Med* 1983;308:1383.
- ◆ McCracken GH Jr, Ginsburg C, Chrane DF, et al: Clinical pharmacology of penicillin in newborn infants. *J Pediatr* 1973;82:692.
- ◆ Product Information, Pfizer, 2005

Adverse Effects/Precautions updated 1/2009

References updated 3/2007

Dose & Administration, Preparations, and Compatibilities updated 3/2005



Dose & Administration

50 to 100 mg/kg per dose IV infusion by syringe pump over 30 minutes, or IM.

To use dosing chart, please refer to explanatory note on page 1.

Dosing Interval Chart

PMA (weeks)	PostNatal (days)	Interval (hours)
≤29	0 to 28 >28	12 8
30 to 36	0 to 14 >14	12 8
37 to 44	0 to 7 >7	12 8
≥45	ALL	6

Uses

Semisynthetic penicillin with increased activity against *Pseudomonas aeruginosa* and many strains of *Klebsiella*, *Serratia*, *E coli*, *Enterobacter*, *Citrobacter*, and *Proteus*. Also effective against group B *Streptococcus*.

Monitoring

Desired peak serum concentration is approximately 150 mcg/mL. Desired trough concentration ranges from 15 to 50 mcg/mL (available as bioassay). Peak serum concentration is lower with IM administration. Observe IV site for signs of extravasation.

Adverse Effects/Precautions

Eosinophilia. Hyperbilirubinemia. Elevations in ALT, AST, BUN, and serum creatinine.

Pharmacology

Piperacillin is a potent, broad-spectrum, semi-synthetic, ureidopenicillin possessing high activity against gram-negative bacteria. Inactivation by beta-lactamase-producing bacteria. Synergistic with aminoglycosides. Good penetration into bone; CSF penetration similar to that of other penicillins. Serum half-life depends on gestational age and postnatal age. Primarily excreted renally unchanged.

Piperacillin

Special Considerations/Preparation

Available as powder for injection in 2-g, 3-g, 4-g, and 40-g vials. Reconstitute 2-g vial with 10 mL of sterile water for injection to make a final concentration of 200 mg/mL. Reconstituted solution stable for 24 hours at room temperature, 2 days refrigerated. A 50 mg/mL dilution may be made by adding 2.5 mL of reconstituted solution to 7.5 mL sterile water for injection. Dilution stable for 2 days refrigerated.

IM Administration: Use 400 mg/mL concentration.

Solution Compatibility: D₅W, D₁₀W, and NS.

Terminal Injection Site Compatibility: Dex/AA solutions, fat emulsion. Acyclovir, aminophylline, aztreonam, clindamycin, enalaprilat, esmolol, famotidine, heparin, hydrocortisone succinate, linezolid, lorazepam, midazolam, milrinone, morphine, nicardipine, potassium chloride, propofol, ranitidine, remifentanil, and zidovudine.

Incompatibility: Amikacin, amiodarone, gentamicin, netilmicin, fluconazole, tobramycin, and vancomycin.

Selected References

- ◆ Kacet N, Roussel-Delvallez M, Gremillet C, et al: Pharmacokinetic study of piperacillin in newborns relating to gestational and postnatal age. *Pediatr Infect Dis J* 1992;11:365.
- ◆ Prober CG, Stevenson DK, Benitz WE: The use of antibiotics in neonates weighing less than 1200 grams. *Pediatr Infect Dis J* 1990;9:111.
- ◆ Reed MD, Myers CM, Yamashita TS, Blumer JL: Developmental pharmacology and therapeutics of piperacillin in gram-negative infections. *Dev Pharmacol Ther* 1986;9:102.
- ◆ Placzek M, Whitelaw A, Want S, et al: Piperacillin in early neonatal infection. *Arch Dis Child* 1983;58:1006-1009.
- ◆ Product Information, Abraxis Pharmaceutical Products, 2006

Updated 3/2008

Compatibilities updated 3/2005

Dose & Administration

50 to 100 mg/kg per dose (as piperacillin component) IV infusion by syringe pump over 30 minutes.

To use dosing chart, please refer to explanatory note on page 1.

Dosing Interval Chart

PMA (weeks)	PostNatal (days)	Interval (hours)
≤29	0 to 28 >28	12 8
30 to 36	0 to 14 >14	12 8
37 to 44	0 to 7 >7	12 8
≥45	ALL	8

Uses

Treatment of non-CNS infections, caused by susceptible beta-lactamase producing bacteria, including many strains of *E. coli*, *Enterobacter*, *Klebsiella*, *Haemophilus influenzae*, *Proteus mirabilis*, *Pseudomonas spp.*, and *Staph. aureus*. Also effective against group B *Streptococcus*.

Monitoring

Observe IV site for signs of extravasation.

Adverse Effects/Precautions

Eosinophilia. Hyperbilirubinemia. Elevations in ALT, AST, BUN, and serum creatinine.

Pharmacology

Zosyn® combines the extended-spectrum antibiotic piperacillin with the beta-lactamase inhibitor tazobactam in a 8:1 ratio. Piperacillin is primarily eliminated unchanged by renal mechanisms, whereas tazobactam undergoes significant hepatic metabolism. The mean half-life of piperacillin and tazobactam in neonates is approximately 1.5 hours. CNS penetration is modest (limited data). Sodium content is 2.35 mEq per gram of piperacillin.

Piperacillin-Tazobactam

Special Considerations/Preparation

Available as powder for injection (containing EDTA and sodium citrate) in 2.25-g, 3.375-g, and 4.5-g vials. Reconstitute 2.25-g vial with 10 mL of sterile water for injection to make a concentration of 200 mg/mL piperacillin. Reconstituted solution stable for 24 hours at room temperature, 48 hours refrigerated. pH 4.5 to 6.8. Each 2.25-g vial contains 2.79 mEq (64 mg) of sodium per gram of piperacillin.

Dilute reconstituted solution further to a final concentration of 50 mg/mL (some sources recommend 20 mg/mL) using compatible solution.

Solution Compatibility: D₅W, D₁₀W, NS and LR.

Terminal Injection Site Compatibility: Dex/AA solutions, fat emulsion. Aminophylline, aztreonam, bumetanide, calcium gluconate, cefepime, cimetidine, clindamycin, dexamethasone, dopamine, enalaprilat, esmolol, fluconazole, furosemide, heparin, hydrocortisone succinate, linezolid, lorazepam, metoclopramide, metronidazole, milrinone, morphine, potassium chloride, ranitidine, remifentanil, sodium bicarbonate, trimethoprim-sulfamethoxazole, and zidovudine.

Incompatibility: Acyclovir, amikacin, amiodarone, amphotericin B, azithromycin, dobutamine, famotidine, ganciclovir, gentamicin, netilmicin, tobramycin, and vancomycin.

Selected References

- ◆ Pillay T, Pillay DG, Adhikari M, Sturn AW: Piperacillin/tazobactam in the treatment of *Klebsiella pneumoniae* infections in neonates. *Am J Perinatol* 1998;15:47-51.
- ◆ Reed MD, Goldfarb J, Yamashita TS, Blumer JL: Single dose pharmacokinetics of piperacillin and tazobactam in infants and children. *Antimicrob Agents Chemother* 1994;38:2817-26.
- ◆ Schoonover L, Occhipinti D, Rodvold K, et al: Piperacillin/tazobactam: A new beta-lactam/beta-lactamase inhibitor combination. *Ann Pharmacother* 1995;29:501-14.
- ◆ Prober CG, Stevenson DK, Benitz WE: The use of antibiotics in neonates weighing less than 1200 grams. *Pediatr Infect Dis J* 1990;9:111.
- ◆ Product Information, Wyeth, 2007

Compatibilities updated 3/2008

Text updated 3/2008

Added 3/2003

Dose & Administration

7.5 mg/kg/dose Q12 hours by IV infusion over 60 minutes.
Administration via a central catheter is recommended.

Uses

Limited to treatment of infections caused by gram positive organisms resistant to other antibiotics, e.g. methicillin-resistant *Staph. aureus* and vancomycin-resistant *Enterococcus faecium* (not *E faecalis*).

Monitoring

Periodic measurement of serum bilirubin and transaminases. Assess peripheral IV site for signs of inflammation.

Adverse Effects/Precautions

Myalgias and arthralgias occur frequently in adults with hepatic or renal failure. Elevations in serum bilirubin and transaminases are common. Diarrhea and rash occur infrequently.

Pharmacology

No data are available for infants. Synercid® is a parenteral antimicrobial agent which consists of two streptogramin antibiotics (quinupristin and dalfopristin in a 30:70 ratio) that inhibit bacterial protein synthesis by binding to separate sites on the bacterial ribosome. Serum half-life of quinupristin in adults ranges from 1 to 3 hours, and of dalfopristin ranges from 5 to 9 hours. Seventy-five percent is excreted via the biliary route.

Special Considerations/Preparation

Synercid® is supplied as a lyophilized powder in single-dose, 10-mL vials containing 500 mg. Store refrigerated. Reconstitute under aseptic conditions by adding 5 mL of Sterile Water for Injection or D₅W. Before administration, dilute with D₅W to a concentration not exceeding 2 mg/mL. Diluted solution is stable for 5 hours at room temperature, or 54 hours if stored under refrigeration. **Do not freeze.**

Solution Compatibility: D₅W.

Solution Incompatibility: NS.

Terminal Injection Site Compatibility: Aztreonam, ciprofloxacin, fluconazole, metoclopramide, and potassium chloride.

Selected References

- ◆ Loeffler AM, Drew RH, Perfect JR, et al: Safety and efficacy of quinupristin/dalfopristin for treatment of invasive Gram-positive infections in pediatric patients. *Pediatr Infect Dis J* 2002;21:950-56.
- ◆ Gray JW, Darbyshire PJ, Beath SV, et al: Experience with quinupristin/dalfopristin in treating infections with vancomycin-resistant *Enterococcus faecium* in children. *Pediatr Infect Dis J* 2000;19:234-238.
- ◆ Lamb HM, Figgitt DP, Faulds D: Quinupristin/Dalfopristin: A review of its use in the management of serious gram-positive infections. *Drugs* 1999;58:1061-1097.
- ◆ Product Information, Monarch Pharmaceuticals, 2004.

Updated 3/2005



Dose & Administration

PO: 10 to 20 mg/kg per dose Q24 hours. May administer with feedings.

IV: 5 to 10 mg/kg per dose Q12 hours, given via syringe pump over 30 minutes.

Do not administer IM or SC.

Prophylaxis for high-risk contacts of invasive meningococcal disease: 5 mg/kg per dose PO Q12 hours, for 2 days.

Prophylaxis for high-risk contacts of invasive H influenzae type b disease: 10 mg/kg per dose PO Q24 hours, for 4 days.

Uses

Used in combination with vancomycin or aminoglycosides for treatment of persistent staphylococcal infections. Prophylaxis against infections caused by *N meningitidis* and *H influenzae* type b .

Monitoring

Monitor hepatic transaminases and bilirubin. Periodic CBC for thrombocytopenia. Observe IV site for signs of extravasation.

Adverse Effects/Precautions

Causes orange/red discoloration of body secretions (e.g. sweat, urine, tears, sputum). Extravasation may cause local irritation and inflammation. Rifampin is a potent inducer of several cytochrome P450 enzymes. If administered concomitantly, the following drugs may have decreased pharmacologic effects due to increased metabolism: aminophylline, amiodarone, ecimethidine, corticosteroids, digoxin, enalapril, fluconazole, midazolam, morphine, phenobarbital, phenytoin, propranolol, and zidovudine.

Pharmacology

Rifampin is a semisynthetic antibiotic with a wide spectrum of antibacterial activity against staphylococci, most streptococci, *H influenzae*, *Neisseria* sp., *Legionella*, *Listeria*, some *Bacteroides* species, *Mycobacterium tuberculosis*, and certain atypical mycobacterium. Enterococci and aerobic gram-negative bacilli are generally resistant. Not used as monotherapy because resistance may develop during therapy. Inhibits transcription of DNA to RNA by binding to the beta subunit of bacterial RNA-polymerase. Well absorbed orally. Rapidly deacetylated to desacetyl rifampin (active metabolite) and undergoes enterohepatic circulation. Nearly all of the rifampin excreted into the bile is deacetylated within 6 hours. Serum half-life ranges from 1 to 3 hours.

BIOLOGICALS

Special Considerations/Preparation

Available as a lyophilized powder for injection in 600-mg vials. Reconstitute with 10 mL of sterile water for injection to make a final concentration of 60 mg/mL. Reconstituted solution is stable for 24 hours at room temperature. Further dilution is required - maximum concentration for infusion is 6 mg/mL.

A 3 mg/mL dilution may be made by adding 0.5 mL of reconstituted solution to 9.5 mL of NS or D₅W. Dilution made with NS is stable for 24 hours at room temperature. Dilution made with D₅ W is stable for 4 hours at room temperature. Do not use if solution precipitates.

A neonatal suspension may be prepared by mixing 5 mL (300 mg) of the reconstituted IV solution with 25 mL of simple syrup to make a final concentration of 10 mg/mL. Shake well before use. Suspension is stable for 4 weeks at room temperature or refrigerated. Also available in 150- and 300-mg capsules. Preparation of oral suspension using capsules yields variable dosage bioavailability.

Solution Compatibility: D₅W and NS. No data available on Dex/AA or fat emulsion.

Terminal Injection Site Compatibility: No data available.

Selected References

- ◆ Shama A, Patole SK, Whitehall JS: Intravenous rifampicin in neonates with persistent staphylococcal bacteraemia. *Acta Paediatr* 2002;91:670-673.
- ◆ Fernandez M, Rench MA, Albanyan EA, Edwards MS: Failure of rifampin to eradicate group B streptococcal colonization in infants. *Pediatr Infect Dis J* 2001;20:371-376.
- ◆ Tan TQ, Mason EO, Ou C-N, et al: Use of intravenous rifampin in neonates with persistent staphylococcal bacteremia. *Antimicrob Agents Chemother* 1993;37:2401.
- ◆ Koup JR, William-Warren J, Viswanathan CT, et al: Pharmacokinetics of rifampin in children. II. Oral bioavailability. *Ther Drug Monit* 1986;8:17.
- ◆ Koup JR, William-Warren J, Weber A, et al: Pharmacokinetics of rifampin in children. I. Multiple dose intravenous infusion. *Ther Drug Monit* 1986;8:11.
- ◆ McCracken GH, Ginsburg CM, Zweighaft TC, et al: Pharmacokinetics of rifampin in infants and children: relevance to prophylaxis against Haemophilus influenzae type B disease. *Pediatrics* 1980;66:17
- ◆ Nahata MC, Morosco RS, Hipple TF: Effect of preparation method and storage on rifampin concentration in suspensions. *Ann Pharmacother* 1994;28:182.
- ◆ Product Information, Bedford, 2004

IV dose and References updated 3/2005.

Dose & Administration

75 to 100 mg/kg per dose IV infusion by syringe pump over 30 minutes.

To use dosing chart, please refer to explanatory note on page 1.

Dosing Interval Chart

PMA (weeks)	PostNatal (days)	Interval (hours)
≤ 29	0 to 28	12
	>28	8
30 to 36	0 to 14	12
	>14	8
37 to 44	0 to 7	12
	>7	8
≥ 45	ALL	6

Uses

Treatment of non-CNS infections, caused by susceptible β -lactamase producing bacteria, including many strains of *E. coli*, *Enterobacter*, *Klebsiella*, *Haemophilus influenzae*, *Proteus mirabilis*, *Pseudomonas spp.*, and *Staph. aureus*.

Monitoring

Serum concentrations are not routinely monitored. Assess renal function prior to therapy. Measure serum sodium concentrations and hepatic transaminases periodically. Observe IV site for signs of extravasation.

Adverse Effects/Precautions

Eosinophilia. Hyperbilirubinemia. Elevations in ALT, AST, BUN, and serum creatinine. Hypernatremia may be exacerbated in ELBW patients.

Pharmacology

Timentin® combines the extended-spectrum antibiotic ticarcillin with the β -lactamase inhibitor clavulanic acid in a 30:1 ratio. Ticarcillin is primarily eliminated unchanged by renal mechanisms, whereas clavulanate undergoes significant hepatic metabolism. As a result the mean half-life of ticarcillin in neonates is 4.2 hours compared to a mean half-life of 2 hours for clavulanate. CNS penetration is modest (limited data). Sodium content is 4.75 mEq per gram, therefore each dose will contain 0.35 to 0.48 mEq per kg body weight.

Ticarcillin/Clavulanate

Special Considerations/Preparation

Available as powder for injection in 3.1-g vials. Reconstitute vial by adding 13 mL of sterile water for injection. Dilute further with a compatible solution to a concentration between 10 and 100 mg/mL. Dilutions are stable for 24 hours at room temperature, 3 days refrigerated (D5W), and 7 days refrigerated (NS and LR). Frozen dilutions stable for 7 days for D5W and 30 days for NS and LR.

Solution Compatibility: D₅W, LR, and NS.

Terminal Injection Site Compatibility: Dex/AA solutions, fat emulsion. Acyclovir, aminophylline, aztreonam, cefepime, famotidine, fluconazole, heparin, insulin, milrinone, morphine, propofol, remifentanil, and theophylline.

Incompatibility: Amikacin, azithromycin, gentamicin, netilmicin, sodium bicarbonate, tobramycin, and vancomycin.

Selected References

- ◆ Rubino CM, Gal P, Ransom JL: A review of the pharmacokinetic and pharmacodynamic characteristics of β -lactam/ β -lactamase inhibitor combination antibiotics in premature infants. *Pediatr Infect Dis J* 1998;17:1200-1210.
- ◆ Reed MD: A reassessment of ticarcillin/clavulanic acid dose recommendations for infants, children, and adults. *Pediatr Infect Dis J* 1998;17:1195-1199.
- ◆ Product Information, GlaxoSmithKline, 2007

Compatibilities updated 3/2007

Added 3/2002



Dose & Administration

IV infusion by syringe pump over 30 minutes. Administer as a separate infusion from penicillin-containing compounds. IM injection is associated with variable absorption, especially in the very small infant.

To use dosing chart, please refer to explanatory note on page 1.

Dosing Chart

PMA (weeks)	Postnatal (days)	Dose (mg/kg)	Interval (hours)
$\leq 29^*$	0 to 7	5	48
	8 to 28	4	36
	≥ 29	4	24
30 to 34	0 to 7	4.5	36
	≥ 8	4	24
≥ 35	ALL	4	24

* or significant asphyxia, PDA, or treatment with indomethacin

Uses

Treatment of infections caused by aerobic gram-negative bacilli (e.g. *Pseudomonas*, *Klebsiella*, *E coli*). Usually used in combination with a β -lactam antibiotic.

Monitoring

Measure serum concentrations when treating for more than 48 hours. Obtain peak concentration 30 minutes after end of infusion, and trough concentration just prior to the next dose. When treating patients with serious infections or significantly changing fluid or renal status consider measuring the serum concentration 24 hours after a dose, and use the chart below for the suggested dosing interval. Blood samples obtained to monitor serum drug concentrations should be spun and refrigerated or frozen as soon as possible.

Therapeutic serum concentrations:

Peak: 5 to 12 mcg/mL (or C_{max} /MIC ratio greater than 8:1)

Trough: 0.5 to 1 mcg/mL

Suggested Dosing Intervals

Level at 24 hours (mcg/mL)	Half-life (hours)	Suggested Dosing Interval (hours)
≤ 1	≈ 8	24
1.1 to 2.3	≈ 12	36
2.4 to 3.2	≈ 15	48
≥ 3.3		Measure level in 24 hours

Tobramycin

Adverse Effects/Precautions

Black Box Warning According to the manufacturer's black box warning, aminoglycoside therapy has been associated with potential neurotoxicity, ototoxicity, and nephrotoxicity. Patients with impaired renal function, dehydration, and those who receive high dosage or prolonged therapy are at an increased risk of toxicity. Discontinue therapy or adjust dose if there is evidence of ototoxicity or nephrotoxicity. Aminoglycoside ototoxicity is usually irreversible.

Transient and reversible renal tubular dysfunction may occur, resulting in increased urinary losses of sodium, calcium, and magnesium. Vestibular and auditory ototoxicity may occur. The addition of other nephrotoxic and/or ototoxic medications (e.g. furosemide, vancomycin) may increase these adverse effects. Increased neuromuscular blockade (i.e. neuromuscular weakness and respiratory failure) may occur when used with pancuronium or other neuromuscular blocking agents and in patients with hypermagnesemia.

Pharmacology

Dosing recommendations are based on: (1) Higher peak concentrations increase concentration-dependent bacterial killing; (2) There is a post-antibiotic effect on bacterial killing, especially when treating concurrently with a β -lactam antibiotic; (3) There may be less toxicity with less frequent dosing, due to less renal drug accumulation. Volume of distribution is increased and clearance is decreased in patients with PDA. Serum half-life is prolonged in premature and asphyxiated newborns. Inactivation of tobramycin by penicillin-containing compounds appears to be a time-, temperature-, and concentration-dependent process. This is probably clinically significant only when penicillin-containing compounds are mixed in IV solutions or when the blood is at room temperature for several hours before the assay is performed.

Special Considerations/Preparation

Pediatric injectable solution available in a concentration of 10 mg/mL.

Solution Compatibility: D₅W, D₁₀W, and NS.

Terminal Injection Site Compatibility: Dex/AA solutions, fat emulsion. Acyclovir, aminophylline, amiodarone, aztreonam, calcium gluconate, cefoxitin, ceftazidime, ciprofloxacin, clindamycin, dopamine, enalaprilat, esmolol, fluconazole, furosemide, insulin, heparin (concentrations ≤ 1 unit/mL), linezolid, metronidazole, midazolam, milrinone, morphine, nicardipine, ranitidine, remifentanil, theophylline, and zidovudine.

Incompatibility: Amphotericin B, ampicillin, azithromycin, cefepime, imipenem/cilastatin, indomethacin, heparin (concentrations > 1 unit/mL), methicillin, mezlocillin, nafcillin, oxacillin, penicillin G, propofol, and ticarcillin/clavulanate.

Selected References

- ◆ Contopoulos-Ioannidis DG, Giotis ND, Baliatsa DV, Ioannidis JPA: Extended-interval aminoglycoside administration for children: a meta-analysis. *Pediatrics* 2004;114:e111-e118.
- ◆ Avent ML, Kinney JS, Istre GR, Whitfield JM: Gentamicin and tobramycin in neonates: comparison of a new extended dosing regimen with a traditional multiple daily dosing regimen. *Am J Perinatol* 2002;8:413-19.
- ◆ de Hoog M, Schoemaker RC, Mouton JW, van den Anker JN: Tobramycin population pharmacokinetics in neonates. *Clin Pharmacol Ther* 1997;62:392-399.
- ◆ Giapros VI, Andronikou S, Cholevas VI, Papadopoulou ZL: Renal function in premature infants during aminoglycoside therapy. *Pediatr Nephrol* 1995;9:163.
- ◆ Daly JS, Dodge RA, Glew RH, et al: Effect of time and temperature on inactivation of aminoglycosides by ampicillin at neonatal dosages. *J Perinatol* 1997;17:42-45.
- ◆ Williams BS, Ransom JL, Gal P, et al: Gentamicin pharmacokinetics in neonates with patent ductus arteriosus. *Crit Care Med* 1997;25:273-275.
- ◆ Product Information, Hospira, 2005

Adverse Effects/Precautions updated 1/2009

Dosing, Compatibilities, and References updated 3/2007



Dose & Administration

IV infusion by syringe pump over 60 minutes.

Meningitis: 15 mg/kg per dose

Bacteremia: 10 mg/kg per dose

To use dosing chart, please refer to explanatory note on page 1.

Dosing Interval Chart

PMA (weeks)	PostNatal (days)	Interval (hours)
≤29	0 to 14 ≥14	18 12
30 to 36	0 to 14 ≥14	12 8
37 to 44	0 to 7 ≥7	12 8
≥45	ALL	6

Uses

Drug of choice for serious infections caused by methicillin-resistant staphylococci (e.g. *S aureus* and *S epidermidis*) and penicillin-resistant pneumococci.

Monitoring

Serum trough concentrations should be followed in neonates because of changes in renal function related to maturation and severity of illness. Peak concentrations have not been clearly demonstrated to correlate with efficacy, but monitoring these has been recommended when treating meningitis.

Trough: 5 to 10 mcg/mL for most infections. Many experts recommend 15 to 20 mcg/mL when treating MRSA pneumonia, endocarditis, or bone/joint infections.

Peak: 30 to 40 mcg/mL when treating meningitis

(Draw 30 minutes after end of infusion.)

Assess renal function. Observe IV site for signs of extravasation and phlebitis.

Adverse Effects/Precautions

Nephrotoxicity and ototoxicity: Enhanced by aminoglycoside therapy.

Rash and hypotension (red man syndrome): Appears rapidly and resolves within minutes to hours. Lengthening infusion time usually eliminates risk for subsequent doses.

Neutropenia: Reported after prolonged administration (more than 3 weeks).

Phlebitis: May be minimized by slow infusion and dilution of the drug.

Pharmacology

Vancomycin is bactericidal for most gram-positive bacteria, but bacteriostatic for enterococci. It interferes with cell wall synthesis, inhibits RNA synthesis, and alters plasma membrane function. Killing activity is primarily a time-dependent process, not concentration-dependent. MICs for sensitive organisms are ≤ 1 mcg/mL. Diffusion into the lung and bone is variable. CSF concentrations in premature infants ranged from 26 to 68% of serum concentrations. Protein binding is as high as 50% in adults. Elimination is primarily by glomerular filtration, with a small amount of hepatic metabolism.

Special Considerations/Preparation

Available as powder for injection in 500-mg and 1-g vials. Reconstitute 500-mg vial with 10 mL sterile water for injection to make a final concentration of 50 mg/mL. Reconstituted solution stable for 14 days refrigerated. Dilute prior to administration using D5W or NS to a maximum concentration of 5 mg/mL.

Solution Compatibility: D₅W, D₁₀W, and NS.

Terminal Injection Site Compatibility: Dex/AA solutions, fat emulsion. Acyclovir, amikacin, ampicillin, aminophylline, amiodarone, aztreonam, caffeine citrate, calcium gluconate, cimetidine, enalaprilat, esmolol, famotidine, fluconazole, heparin (concentrations ≤ 1 unit/mL), hydrocortisone succinate, insulin, linezolid, lorazepam, meropenem, midazolam, milrinone, morphine, nicardipine, pancuronium bromide, potassium chloride, propofol, ranitidine, remifentanil, sodium bicarbonate, vecuronium, and zidovudine.

Incompatibility: Cefazolin, ceftazidime, cefepime, cefotaxime, cefoxitin, ceftriaxone, chloramphenicol, dexamethasone, heparin (concentrations > 1 unit/mL), methicillin, mezlocillin, nafcillin, pentobarbital, phenobarbital, piperacillin, piperacillin-tazobactam, ticarcillin, and ticarcillin/clavulanate.

Selected References

- ◆ Hidayat LK, Hsu DI, Quist R, et al: High-dose vancomycin therapy for methicillin-resistant *Staphylococcus aureus* infections. *Arch Intern Med* 2006;166:2138-2144.
- ◆ de Hoog M, Schoemaker RC, Mouton JW, van den Anker JN: Vancomycin population pharmacokinetics in neonates. *Clin Pharmacol Ther* 2000;67:360-367.
- ◆ Ahmed A: A critical evaluation of vancomycin for treatment of bacterial meningitis. *Pediatr Infect Dis J* 1997;16:895-903.
- ◆ Trissel LA, Gilbert DL, Martinez JF: Concentration dependency of vancomycin hydrochloride compatibility with beta-lactam antibiotics during simulated y-site administration. *Hosp Pharm* 1998;33:1515-1520.
- ◆ Reiter PD, Doron MW: Vancomycin cerebrospinal fluid concentrations after intravenous administration in premature infants. *J Perinatol* 1996;16:331-335.
- ◆ Schilling CG, Watson DM, McCoy HG, Uden DL: Stability and delivery of vancomycin hydrochloride when admixed in a total parenteral nutrition solution. *JPEN* 1989;13:63.
- ◆ Lacouture PG, Epstein MF, Mitchell AA: Vancomycin-associated shock and rash in newborn infants. *J Pediatr* 1987;111:615.
- ◆ Schaible DH, Rocci ML, Alpert GA, et al: Vancomycin pharmacokinetics in infants: Relationships to indices of maturation. *Pediatr Infect Dis* 1986;5:304.
- ◆ Product Information, Abraxis Pharmaceutical Products, 2006

Monitoring and References updated 3/2008
Compatibilities updated 3/2005



Dose & Administration

IV: 1.5 mg/kg per dose, given via infusion pump over 1 hour.

PO: 2 mg/kg per dose. **Do not administer IM.**

May administer with food, although manufacturer recommends administration 30 minutes before or 1 hour after a meal.

Begin treatment within 6 to 12 hours of birth, and continue for 6 weeks. Initiation of post-exposure prophylaxis after the age of 2 days is not likely to be effective. Subsequent treatment is based on antiretroviral drug resistance testing.

To use dosing chart, please refer to explanatory note on page 1.

Dosing Interval Chart

Gestational Age (weeks)	Postnatal Age (days)	Interval (hours)
≤ 29	0 to 28	12
	>28	8
30 to 34	0 to 14	12
	>14	8
≥ 35	ALL	6

Uses

Dosing guidelines above are for prophylactic treatment of neonates born to HIV-infected women. Treatment of infants with combination antiretroviral therapy should be done in consultation with a pediatric infectious disease expert.

Monitoring

CBC at the beginning of therapy, then every other week to assess for anemia, thrombocytopenia, and neutropenia.

Adverse Effects/Precautions

Anemia and neutropenia occur frequently, and are associated with serum concentrations greater than 3 micromol/L. Mild cases usually respond to a reduction in dose. Severe cases may require cessation of treatment and/or transfusion. Bone marrow toxicity may be increased by concomitant administration of acyclovir, ganciclovir, and TMP-SMX. Lactic acidemia is common in infants exposed to in utero highly active antiretroviral therapy. Concomitant treatment with fluconazole or methadone significantly reduces zidovudine metabolism - dosing interval should be prolonged.

Black Box Warning

According to the manufacturer's black box warning, zidovudine has been associated with hematologic toxicity, including neutropenia and severe anemia, particularly in patients with advanced HIV disease. Lactic acidosis and severe hepatomegaly with steatosis, including fatal cases, have been reported (in adults).

Zidovudine (ZDV, AZT)

Pharmacology

Zidovudine is a nucleoside analog that inhibits HIV replication by interfering with viral reverse transcriptase. It is converted intracellularly in several steps to a triphosphate derivative, metabolized via hepatic glucuronidation, then renally excreted. Protein binding is approximately 25%. Zidovudine distributes into cells by passive diffusion and is relatively lipophilic. The CSF: plasma ratio is 0.24. The relationship between serum concentration and clinical efficacy is unclear. The oral syrup is well-absorbed, but only 65% bioavailable due to significant first-pass metabolism. The serum half-life in term newborns is 3 hours, declining to 2 hours after 2 weeks of age. In preterm infants less than 33 weeks gestation, half-life during the first two weeks of life ranges from 5 to 10 hours, decreasing to 2 to 6 hours afterward.

Special Considerations/Preparation

Available as a syrup for oral use in a concentration of 10 mg/mL. The IV form is supplied in a concentration of 10 mg/mL in a 20 mL single-use vial. **Dilute before IV administration to a concentration not exceeding 4 mg/mL.** A dilution of 4 mg/mL may be prepared by adding 4 mL of the 10-mg/mL concentration to 6 mL D₅W. After dilution the drug is stable at room temperature for 24 hours. Both forms should be stored at room temperature and protected from light.

Solution Compatibility: D₅W and NS.

Terminal Injection Site Compatibility: Dex/AA solutions, fat emulsion. Acyclovir, amikacin, amphotericin B, aztreonam, cefepime, ceftazidime, ceftriaxone, cimetidine, clindamycin, dexamethasone, dobutamine, dopamine, erythromycin lactobionate, fluconazole, gentamicin, heparin, imipenem, linezolid, lorazepam, meropenem, metoclopramide, morphine, nafcillin, oxacillin, piperacillin, piperacillin-tazobactam, potassium chloride, ranitidine, remifentanil, tobramycin, trimethoprim-sulfamethoxazole, and vancomycin.

Incompatibility: Blood products and albumin solutions.

Selected References

- ◆ Havens PL, Mofenson LM, Committee on Pediatric AIDS: Evaluation and management of the infant exposed to HIV-1 in the United States. *Pediatrics* 2009;123:175-187.
- ◆ Perinatal HIV Guidelines Working Group. Public Health Service Task Force Recommendations for Use of Antiretroviral Drugs in Pregnant HIV-1 Infected Women for Maternal Health and Interventions to Reduce Perinatal HIV-1 Transmission in the United States. July 8, 2008. Available at <http://aidsinfo.nih.gov/ContentFiles/PerinatalGL.pdf>.
- ◆ Capparelli EV, Mirochnick MH, Danker WM: Pharmacokinetics and tolerance of zidovudine in preterm infants. *J Pediatr* 2003;142:47-52.
- ◆ Alimenti A, Burdge DR, Ogilvie GS, et al: Lactic acidemia in human immunodeficiency virus-uninfected infants exposed to antiretroviral therapy. *Pediatr Infect Dis J* 2003;22:782-8.
- ◆ Mirochnick M, Capparelli E, Conner J: Pharmacokinetics of zidovudine in infants: A population analysis across studies. *Clin Pharmacol Ther* 1999;66:16-24.
- ◆ Acosta EP, Page LM, Fletcher CV: Clinical pharmacokinetics of zidovudine. *Drugs* 1996;30:251.
- ◆ Connor EM, Sperling RS, Gelber R, et al: Reduction of maternal-infant transmission of human immunodeficiency virus type 1 with zidovudine treatment. *N Engl J Med* 1994;331:1173.
- ◆ Product Information, GlaxoSmithKline, 2006.

References updated 2/2009

Adverse Effects/Precautions updated 1/2009

© 2009 GlaxoSmithKline. All rights reserved.

Recommended Childhood Immunization Schedule United States, 2009

Vaccine▼	Age►	Birth	1 month	2 months	4 months	6 months	12 months	15 months	18 months
Hepatitis B ¹	HepB	HepB	HepB	See footnote 1					HepB
Rotavirus ²			Rota	Rota	Rota	Rota			
Diphtheria, Tetanus, Pertussis ³			DTaP	DTaP	DTaP	DTaP	DTaP		
<i>Haemophilus influenzae type b⁴</i>			Hib	Hib	Hib ⁴	Hib	Hib		
Pneumococcal ⁵			PCV	PCV	PCV	PCV	PCV		
Inactivated Poliovirus			IPV	IPV	IPV	IPV	IPV		
Influenza ⁶							Influenza (Yearly)		
Measles, Mumps, Rubella ⁷							MMR		
Varicella ⁸							Varicella		
Hepatitis A ⁹							HepA (2 doses)		

Range of recommended ages

Approved by the Advisory Committee on Immunization Practices www.cdc.gov/vaccines/recs/acip the American Academy of Pediatrics www.aap.org and the American Academy of Family Physicians www.aafp.org. When using licensed combination vaccines, providers should consult the respective ACIP statement for detailed recommendations.

1. Hepatitis B vaccine (HepB). (Minimum age: birth)

At birth:

- Administer monovalent HepB to all newborns before hospital discharge.
- If mother is hepatitis B surface antigen (HBsAg)-positive, administer HepB and 0.5 mL of hepatitis B immune globulin (HBIG) within 12 hours of birth.
- If mother's HBsAg status is unknown, administer HepB within 12 hours of birth. Determine the HBsAg status as soon as possible and if HBsAg-positive, administer HBIG (no later than age 1 week).
- If mother is HBsAg-negative, the birth dose can only be delayed with physician's order and mothers' negative HBsAg laboratory report documented in the infant's medical record.

After the birth dose:

- The HepB series should be completed with either monovalent HepB or a combination vaccine containing HepB. The second dose should be administered at age 1–2 months. The final dose should be administered at age \geq 24 weeks. Infants born to HBsAg-positive mothers should be tested for HBsAg and antibody to HBsAg after completion of at least 3 doses of the HepB series, at age 9–18 months (generally at the next well-child visit).
- **4-month dose:**
 - It is permissible to administer 4 doses of HepB when combination vaccines containing HepB are administered after the birth dose.

2. Rotavirus vaccine (Rota). (Minimum age: 6 weeks)

- Administer the first dose at age 6–14 weeks (maximum age: 14 weeks 6 days). Do not start the series for infants age 15 weeks or older.
- Administer the final dose in the series by age 8 months 0 days. Do not administer a dose later than age 8 months 0 days.
- If Rotarix® is given at ages 2 and 4 months, a dose at 6 months is not indicated.

3. Diphtheria and tetanus toxoids and acellular pertussis vaccine (DTaP).

(Minimum age: 6 weeks)

- The fourth dose may be administered as early as age 12 months, provided at least 6 months have elapsed since the third dose.
- Administer the final dose in the series at age 4–6 years.

4. Haemophilus influenzae type b conjugate vaccine (Hib). (Minimum age: 6 weeks)

- If PRP-OMP (PedvaxHIB® or ComVax® [HepB-Hib]) is administered at ages 2 and 4 months, a dose at age 6 months is not indicated.
- TriHIBit® (DTaP/Hib) combination products should not be used for doses at ages 2, 4 or 6 months but can be used as the final dose in children aged 12 months or older.

5. Pneumococcal vaccine. (Minimum age: 6 weeks for pneumococcal conjugate vaccine [PCV]; 2 years for pneumococcal polysaccharide vaccine [PPSV])

- PCV is recommended for all children aged younger than 5 years. Administer 1 dose of PCV to all healthy children aged 24–59 months who are not completely vaccinated for their age. Administer PPSV to children aged \geq 2 years with certain underlying medical conditions.
- **Influenza vaccine. (Minimum age: 6 months for trivalent inactivated influenza vaccine [TIV]; 2 years for live, attenuated influenza vaccine [LAIV])**
 - Administer annually to children aged 6 months through 18 years.
 - For healthy persons aged 2–49 years, either LAIV or TIV may be used.
 - Children receiving TIV should receive 0.25 mL if aged 6–35 months or 0.5 mL if aged \geq 3 years.
 - Children aged $<$ 9 years who are receiving influenza vaccine for the first time or were vaccinated for the first time last season but only received one dose should receive 2 doses separated by \geq 4 weeks.

7. Measles, mumps, and rubella vaccine (MMR). (Minimum age: 12 months)

8. Varicella vaccine. (Minimum age: 12 months)

9. Hepatitis A vaccine (HepA). (Minimum age: 12 months)

(Diphtheria and tetanus toxoids for pediatric use)**Dose & Administration**

0.5 mL IM in the anterolateral thigh. Immunize premature infants according to their postnatal age. Please refer to most recent AAP/ACIP immunization schedule.

When giving multiple vaccines, use a separate syringe for each and give at different sites. Care should be taken to draw back on the plunger of the syringe before injection to be certain the needle is not in a blood vessel.

Uses

Immunoprophylaxis against diphtheria and tetanus for infants who have a contraindication for pertussis vaccine.

Monitoring

Observe injection site for erythema, induration (common), palpable nodule (uncommon), or sterile abscess (rare). Fever (common) may be treated with acetaminophen. Other common, self-limited, systemic effects are drowsiness, fretfulness, and anorexia. Rare anaphylactic reactions (i.e. hives, swelling of the mouth, hypotension, breathing difficulty, and shock) have been reported.

Adverse Effects/Precautions

Infants with stable neurologic conditions, including well-controlled seizures, may be vaccinated. Infants who have had prior seizures are at increased risk for seizures following DT vaccination; acetaminophen should be used to prevent postvaccination fever.

Pharmacology

Diphtheria and tetanus toxoids are prepared by formaldehyde treatment of the respective toxins. DT vaccine is an aluminum-salt-adsorbed preparation.

Special Considerations/Preparation

DT vaccine (for pediatric use) is available as 0.5-mL single-dose vials. Store refrigerated. Do not freeze. Shake vial well before withdrawing each dose. Do not use if product contains clumps that cannot be resuspended with vigorous shaking. Normal appearance is a turbid whitish suspension.

Selected References

- ◆ American Academy of Pediatrics. Tetanus. In: Pickering LK, ed. *2006 Red Book: Report of the Committee on Infectious Diseases*. 27th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2006: pp 67-71.
- ◆ Advisory Committee on Immunization Practices: Recommendations of the ACIP. Most recent updates available on the National Immunization Program website: <http://www.cdc.gov/nip/publications/acip-list.htm>.
- ◆ Product Information, Sanofi Pasteur, 2005

References updated 3/2008

BIOLOGICALS

(Diphtheria and tetanus toxoids and acellular pertussis vaccine adsorbed)

Dose & Administration

0.5 mL IM in the anterolateral thigh. Shake vial vigorously before withdrawing each dose. Immunize premature infants according to their postnatal age. Please refer to the most recent AAP/ACIP immunization schedule.

When giving multiple vaccines, use a separate syringe for each and give at different sites. Care should be taken to draw back on the plunger of the syringe before injection to be certain the needle is not in a blood vessel.

Uses

Preferred immunoprophylaxis against diphtheria, tetanus, and pertussis.

Monitoring

Minor reactions, such as drowsiness, irritability, fever, anorexia, and pain/erythema/induration at the injection site are similar to those observed with DTwP vaccine, but are significantly less frequent. Moderate to severe reactions are also less frequent. Refer to Precautions section for more information.

Adverse Effects/Precautions

It is prudent to delay the initial dose of DTaP vaccine in infants with neurologic disorders until further observation and study have clarified their neurologic status and the effect of treatment. Those infants with stable neurologic conditions, including well-controlled seizures, may be vaccinated. Infants who have had prior seizures are at increased risk for seizures following DTP vaccination; acetaminophen should be used to prevent postvaccination fever.

Precautions to further DTaP vaccination (the benefits of administering DTaP may exceed risks in areas with a high incidence of pertussis; otherwise administer DT vaccine):

- 1) Temperature of $\geq 40.5^{\circ}\text{C}$ (105°F) within 48 hours with no other cause.
(Frequency approximately 1 per 3000 doses)
- 2) Hypotonic-hyporesponsive collapse or shock-like state within 48 hours.
(Frequency approximately 1 per 10,000 doses)
- 3) Inconsolable crying (≥ 3 hours) occurring within 48 hours.
(Frequency approximately 1 per 2000 doses)
- 4) Convulsions with or without fever occurring within 3 days.
(Frequency approximately 1 per 14,000 doses)

Contraindications to further DTaP vaccination: In children who develop encephalopathy within 7 days following any DTP vaccination, DT vaccine should be substituted for the remaining doses. In children who develop an immediate anaphylactic reaction, further immunization with any of the three antigens should be deferred.

Pharmacology

DTaP vaccines are aluminum-salt-adsorbed preparations. All acellular pertussis vaccines contain inactivated pertussis toxoid, but vary in the inclusion and concentration of four other pertussis antigens. Diphtheria and tetanus toxoids are prepared by formaldehyde treatment of the respective toxins. Daptacel®, Infanrix® and Tripedia® are thimerosal-free. Each dose of Daptacel® contains 15 Lf diphtheria toxoid, 5 Lf tetanus toxoid, 5 mcg fimbriae types 2 and 3, 5 mcg FHA, and 3 mcg pertactin, with 3.3 mg 2-phenoxyethanol as a preservative. Each dose of Infanrix® contains 25 Lf diphtheria toxoid, 10 Lf tetanus toxoid, 25 mcg inactivated toxin, 25 mcg FHA, and 8 mcg pertactin, with 2.5 mg 2-phenoxyethanol as a preservative. Each dose of Tripedia® contains 6.7 Lf diphtheria toxoid, 5 Lf tetanus toxoid, 23.4 mcg inactivated toxin, and 23.4 mcg FHA.

Special Considerations/Preparation

FDA-licensed DTaP vaccines as of March 2008: Infanrix® (GlaxoSmithKline), available in single-dose vials and single-dose prefilled syringes, Daptacel® (Sanofi Pasteur), available in single-dose vials and multi-dose vials, and Tripedia® (Sanofi Pasteur), available in single-dose vials. Store refrigerated at 2 °C to 8 °C (36 °F to 46 °F). **Do not freeze.** SHAKE VIAL WELL before withdrawing dose. Do not use if product contains clumps that cannot be resuspended with vigorous shaking. Normal appearance is a homogeneous (Tripedia® and Daptacel®) or turbid (Infanrix®) white suspension.

Selected References

- ◆ American Academy of Pediatrics. Pertussis. In: Pickering LK, Baker CJ, Long SS, McMillan JA, eds. *Red Book: 2006 Report of the Committee on Infectious Diseases*. 27th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2006: pp 505-513.
- ◆ American Academy of Pediatrics, Committee on Infectious Diseases: Acellular pertussis vaccine: recommendations for use as the initial series in infants and children. *Pediatrics* 1997;99:282.
- ◆ Advisory Committee on Immunization Practices: Recommendations of the ACIP. Most recent updates available on the National Immunization Program website: <http://www.cdc.gov/nip/publications/acip-list.htm>
- ◆ Product information, GlaxoSmithKline, 2007.
- ◆ Product information, Sanofi Pasteur, 2005, 2008.

References updated 3/2008

[Diphtheria and tetanus toxoids and acellular pertussis adsorbed, Hepatitis B (recombinant) and inactivated poliovirus vaccine combined]

Dose & Administration

0.5 mL IM in the anterolateral thigh. Shake vial vigorously before withdrawing dose. PEDIARIX® should not be administered to any infant before the age of 6 weeks. Only monovalent hepatitis B vaccine can be used for the birth dose.

Please refer to the most recent AAP/ACIP immunization schedule. It is recommended that premature infants should be immunized according to their postnatal age; however, inadequate seroconversion against hepatitis B may occur in chronically ill premature infants.

Uses

Immunoprophylaxis against diphtheria, tetanus, pertussis, hepatitis B, and polio. Using PEDIARIX® to complete the hepatitis B vaccination series in infants who were born of HBsAg-positive mothers and who received monovalent Hepatitis B vaccine (Recombinant) has not been studied.

Monitoring

Cardiorespiratory monitoring and pulse oximetry are recommended for premature infants who remain hospitalized at the time of vaccination.

Adverse Effects/Precautions

Fever is more common ($\approx 20\%$) after PEDIARIX® than with the individual component vaccines administered separately. Other local and systemic adverse events occur at similar rates. Apnea, bradycardia, and desaturation events are common in premature infants for 48 hours after vaccination.

Pharmacology

Each dose of PEDIARIX® contains the type and amount of diphtheria and tetanus toxoids and pertussis antigens as INFANRIX®, and hepatitis B virus antigens as Engerix-B®. The poliovirus component of DTaP-HepB-IPV contains the same strains and quantity of inactivated poliovirus Types 1, 2, and 3 as IPV from a different manufacturer (IPOL®, Sanofi Pasteur). The immunologic responses following 3 doses of DTaP-HepB-IPV were generally similar to those following 3 doses of the individual vaccines administered separately.

Special Considerations/Preparation

PEDIARIX® is supplied as a turbid white suspension in single dose (0.5 mL) vials, and in disposable prefilled Tip-Lock® syringes. Shake well prior to administration. Do not use if resuspension does not occur after vigorous shaking. Store refrigerated at 2° to 8°C (36°F to 46°F). **Do not freeze.** Discard if the vaccine has been frozen.

Selected References

- ◆ Advisory Committee on Immunization Practices: Recommendations of the ACIP. Most recent updates available on the National Immunization Program website: <http://www.cdc.gov/nip/publications/acip-list.htm>
- ◆ Centers for Disease Control and Prevention: FDA licensure of diphtheria and tetanus toxoids and acellular pertussis adsorbed, hepatitis B (recombinant), and poliovirus vaccine combined, (PEDIALRIX™) for use in infants. *MMWR* 2003;52(RR-10):202-203.
- ◆ Pfister RE, Aeschbach V, Niksic-Stuber V, et al: Safety of DTaP-based combined immunization in very-low-birth-weight premature infants: frequent but mostly benign cardiorespiratory events. *J Pediatr* 2004;145:58-66.
- ◆ Product information, GlaxoSmithKline Biologicals, 2007.

Monitoring updated 3/2005

Selected References

- ◆ Advisory Committee on Immunization Practices: Recommendations of the ACIP. Most recent updates available on the National Immunization Program website: <http://www.cdc.gov/nip/publications/acip-list.htm>
- ◆ Centers for Disease Control and Prevention: FDA licensure of diphtheria and tetanus toxoids and acellular pertussis adsorbed, hepatitis B (recombinant), and poliovirus vaccine combined, (PEDIALRIX™) for use in infants. *MMWR* 2003;52(RR-10):202-203.
- ◆ Pfister RE, Aeschbach V, Niksic-Stuber V, et al: Safety of DTaP-based combined immunization in very-low-birth-weight premature infants: frequent but mostly benign cardiorespiratory events. *J Pediatr* 2004;145:58-66.
- ◆ Product information, GlaxoSmithKline Biologicals, 2007.

Monitoring updated 3/2005

Dose & Administration

200 to 400 units/kg/dose, 3 to 5 times per week, for 2 to 6 weeks.

Total dose **per week** is 600 to 1400 units per kg.

Short course: 300 units/kg per dose daily for 10 days.

Administer subQ, or IV over at least 4 hours (even continuously in TPN).

Supplemental iron therapy should be initiated concurrently.

Uses

To stimulate erythropoiesis and decrease the need for erythrocyte transfusions in high-risk preterm infants. Those most likely to benefit are infants with birth weights < 800 g and phlebotomy losses > 30 mL/kg.

Monitoring

Weekly CBC to check for neutropenia and monitor RBC response.

Adverse Effects/Precautions

The only adverse effect in premature neonates is neutropenia, which occurs rarely and resolves with discontinuation of the drug.

Black Box Warning

According to the manufacturer's black box warning, (adult) patients with renal failure experienced greater risks for death and serious cardiovascular events when higher hemoglobin levels were achieved. It is recommended that (adult) patients with renal failure achieve and maintain hemoglobin levels of 10 to 12 g/dL. The relevance of this finding to the neonatal population is unknown.

Pharmacology

Epoetin alfa is a 165-amino acid glycoprotein manufactured by recombinant DNA technology that has the same biological effects as endogenous erythropoietin. It acts on mature erythroid progenitors, CFU-E, by binding to cell surface receptors and stimulating differentiation and cell division. Noticeable effects on hematocrit and reticulocyte counts occur within 2 weeks. Adequate iron and protein intake is necessary for epoetin to be effective (additional Vitamin E intake may be necessary as well). Subcutaneously administered drug appears to be pharmacodynamically as effective as IV, despite only 40% bioavailability. Half-life of r-HuEPO in preterm infants is approximately 12 hours. Doses reported in the literature are all stated as units/kg **per week**. Efficacy may be dose dependent in the range of 500 to 1500 units/kg per week (see meta-analysis by Garcia et al), but no differences were observed in the randomized trial by Maier et al.

Special Considerations/Preparation

Available in preservative-free, single-use, 1-mL vials containing 2000, 3000, 4000, 10,000, or 40,000 units formulated in an isotonic, sodium chloride/sodium citrate buffered solution with 2.5 mg human albumin.

Do not shake. Undiluted epoetin is stable in plastic syringes for 2 weeks. For IV infusion, dilute epoetin in 2 mL of solutions containing at least 0.05% protein and infuse over 4 hours. These dilutions are stable for 24 hours. Product support for use in neonates is handled by Ortho Biotech, Inc. (Procrit®). A multidose 2-mL vial is also available from both Ortho Biotech (Procrit®) and Amgen (Epogen®) containing 20,000 units in a 1% (10 mg/mL) benzyl alcohol solution with 2.5-mg albumin per mL.

Selected References

- ◆ Reiter PD, Rosenberg AA, Valuck R, Novak K: Effect of short-term erythropoietin therapy in anemic premature infants. *J Perinatol* 2005;25:125-129.
- ◆ Ohls R: Human recombinant erythropoietin in the prevention and treatment of anemia of prematurity. *Paediatr Drugs* 2002;4:111-121.
- ◆ Garcia MG, Hutson AD, Christensen RD: Effect of recombinant erythropoietin on "late" transfusions in the neonatal intensive care unit: A meta-analysis. *J Perinatol* 2002;22:108-111.
- ◆ Donato H, Vain N, Rendo P, et al: Effect of early versus late administration of human recombinant human erythropoietin on transfusion requirements in premature infants: Results of a randomized, placebo-controlled, multicenter trial. *Pediatrics* 2000;105:1066.
- ◆ Maier RF, Obladen M, Kattner E, et al: High- versus low-dose erythropoietin in extremely low birth weight infants. *J Pediatr* 1998;132:866-870.
- ◆ Ohls RK, Christensen RD: Stability of recombinant human epoetin alfa in commonly used neonatal intravenous solutions. *Ann Pharmacother* 1996;30:466.
- ◆ Shannon KM, Keith JF, Mentzer WC, et al: Recombinant human erythropoietin stimulates erythropoiesis and reduces erythrocyte transfusions in very low birth weight preterm infants. *Pediatrics* 1995;95:1.
- ◆ Ohls RK, Osborne KA, Christensen RD: Efficacy and cost analysis of treating very low birth weight infants with erythropoietin during their first two weeks of life: A randomized placebo controlled trial. *J Pediatr* 1995;126:421.
- ◆ Meyer MP, Meyer JH, Commerford A, et al: Recombinant erythropoietin in the treatment of the anemia of prematurity: Results of a double-blind, placebo-controlled study. *Pediatrics* 1994;93:918.
- ◆ Product Information, Amgen, 2008

Adverse Effects/Precautions updated 1/2009

Dose and References updated 3/2006

Dose & Administration

0.5 mL IM in the anterolateral thigh. Please refer to the most recent AAP/ACIP immunization schedule. It is recommended that premature infants should be immunized according to their postnatal age; however, inadequate seroconversion may occur in chronically ill premature infants.

For HbOC and PRP-T, second and third doses are given at 2-month intervals, followed by a fourth dose given at age 15 months.

For PRP-OMP, only the second dose is given after a 2-month interval; the third dose is given at age 15 months.

When giving multiple vaccines, use a separate syringe for each and give at different sites. Care should be taken to draw back on the plunger of the syringe before injection to be certain the needle is not in a blood vessel.

Uses

Immunoprophylaxis against invasive disease caused by *Haemophilus influenzae* type b.

Monitoring

Observe injection site for local reactions.

Adverse Effects/Precautions

Soreness at the injection site with local erythema, swelling, tenderness, and fever.

Pharmacology

Three conjugate vaccines are currently approved for use in infants older than 2 months of age. These vaccines are derived from *H influenzae* type b capsular polysaccharide, polyribosyribitol phosphate (PRP), which is linked to a T-cell-dependent protein antigen to enhance immunogenicity.

Special Considerations/Preparation

HibTITER® is a clear, colorless solution supplied in single-dose (preservative-free) vials. Discard if discolored or turbid. Store refrigerated at 2 °C to 8 °C (36 °F to 46 °F). **Do not freeze.**

ActHIB® is supplied as lyophilized powder. Store the lyophilized vaccine and diluent refrigerated at 2 °C to 8 °C (36 °F to 46 °F). **Do not freeze.** Reconstitute using only the 0.4% saline diluent provided in single-use 0.6-mL vials and use immediately. Reconstituted vaccine is a clear, colorless solution.

Liquid PedvaxHIB® is supplied in single-dose vials. It is a slightly opaque white suspension. Shake well before withdrawal and use. Store refrigerated at 2 °C to 8 °C (36 °F to 46 °F). **Do not freeze.**

Haemophilus b (Hib) Conjugate Vaccine

Products

Manufacturer	Abbreviation	Trade Name	Carrier Protein
Wyeth-Lederle Pharmaceuticals	HbOC	HibTITER®	CRM197 (a nontoxic mutant diphtheria toxin)
Sanofi Pasteur	PRP-T	ActHIB®	Tetanus toxoid
Merck & Co, Inc	PRP-OMP Liquid	PedvaxHIB®	OMP (an outer membrane protein complex of N meningitidis)

Selected References

- ◆ American Academy of Pediatrics. *Haemophilus Influenzae* Infections. In: Pickering LK, Baker CJ, Long SS, McMillan JA, eds. Red Book: 2006 Report of the Committee on Infectious Diseases. 27th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2006: pp 315-317.
- ◆ Advisory Committee on Immunization Practices: Recommendations of the ACIP. Most recent updates available on the National Immunization Program website: <http://www.cdc.gov/nip/publications/acip-list.htm>
- ◆ Washburn LK, O'Shea TM, Gillis DC, et al: Response to *Haemophilus influenzae* type b conjugate vaccine in chronically ill premature infants. *J Pediatr* 1993;123:791.
- ◆ Product information, Wyeth-Lederle Pharmaceuticals, 2007.
- ◆ Product information, Sanofi Pasteur, 2005.
- ◆ Product information, Merck & Co, 2004.

References Updated 3/2007

Dose & Administration

0.5 mL IM in the anterolateral thigh.

Term and preterm newborns born to HBsAg-positive mother: Give within 12 hours of birth.

Term and preterm newborns born to HBsAg status unknown mother with BW \geq 2000 g: Give as soon as it is determined that the mother is HBsAg-positive, within 7 days of birth.

Preterm newborns born to HBsAg status unknown mother with BW $<$ 2000 g: If mothers status unavailable, give within 12 hours of birth.

When given at the same time as the first dose of hepatitis B vaccine, use a separate syringe and a different site. Care should be taken to draw back on the plunger of the syringe before injection to be certain the needle is not in a blood vessel.

Uses

Passive immunization of newborns whose mothers have acute hepatitis B infection at the time of delivery, or who are HBsAg-positive. Infants born to mothers who are HBeAg-positive have the highest risk.

Monitoring

No specific monitoring required.

Adverse Effects/Precautions

Local pain and tenderness may occur at the injection site.

Do not administer IV because of the risk of serious systemic reactions. Serious complications of IM injections are rare. Universal precautions should be used with neonates born to HBsAg-positive mothers until they have been bathed carefully to remove maternal blood and secretions.

Pharmacology

Hepatitis B Immune Globulin (human) is a hyperimmune globulin solution prepared from pooled plasma of individuals with high titers of antibody to hepatitis B surface antigen (anti-HBsAg). All donors are HBsAg-negative and HIV-antibody negative. Nabi-HB™ (Nabi) and BayHep B™ (Bayer) are solvent detergent treated and thimerosal free hepatitis B immune globulin preparations.

Special Considerations/Preparation

Refrigerate. Supplied in 1-mL and 5-mL single-dose vials and 0.5-mL unit-dose syringes.

Selected References

- ◆ American Academy of Pediatrics. Hepatitis B. In: Pickering LK, Baker CJ, Long SS, McMillan JA, eds. *Red Book: 2006 Report of the Committee on Infectious Diseases*. 27th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2006: pp 341-347.
- ◆ Crumpacker CS: Hepatitis, in Remington JS, Klein JO (eds): *Infectious Diseases of the Fetus and Newborn Infant*, ed 5. Philadelphia: WB Saunders Co, 2001, pp 932-33.
- ◆ Product Information, Cangene, 2006

Updated 3/2008

References updated 3/2007



Dose & Administration

Engerix-B® 10 mcg (0.5 mL) or Recombivax HB® 5 mcg (0.5 mL) IM.

Maternal HBsAg-Positive: Administer first dose before 12 hours of age regardless of birth weight (administer HBIG also). Infants with BW < 2000 g should receive 3 additional vaccine doses, beginning at 1 to 2 months of age.

Maternal HBsAg Unknown: Administer first dose before 12 hours of age regardless of birth weight. If BW < 2000 g, administer HBIG if mother tests HBsAg positive or if mother's HBsAg result is not available within 12 hours of age. Administer HBIG to newborns with BW ≥ 2000 g within 7 days of birth if the mother tests HBsAg positive.

Maternal HBsAg Negative: Administer first dose shortly after birth, before hospital discharge. If BW < 2000 g and medically stable, administer first dose 1 to 30 days of chronologic age or at time of hospital discharge if before 30 days of chronologic age.

Please refer to the most recent AAP/ACIP immunization schedule for subsequent doses. Engerix-B® also has an alternative four-dose schedule: Birth, 1, 2, and 12 to 18 months of age.

Uses

Immunoprophylaxis against hepatitis B. Safe for use in infants born to HIV-positive mothers, although it may be less effective.

Monitoring

Testing for immunity 3 months after completion of the vaccination series is recommended for infants born to HBsAg-positive mothers and, perhaps, for premature infants who received an early first dose.

Adverse Effects/Precautions

The only common side effect is soreness at the injection site. Fever greater than 37.7 °C occurs in 1 to 6%.

Pharmacology

Recombinant hepatitis B vaccines are produced by *Saccharomyces cerevisiae* (common baker's yeast) that has been genetically modified to synthesize HBsAg. Both vaccines are inactivated (noninfective) products that contain HBsAg protein adsorbed to aluminum hydroxide, and may be interchanged with comparable efficacy.

Special Considerations/Preparation

Recombivax HB® for infant use is supplied in 0.5 mL single-dose vials and single-dose prefilled syringes containing 5 mcg. Engerix-B® is supplied in 0.5 mL single-dose vials and 0.5 mL single-dose prefilled disposable syringes containing 10 mcg per 0.5 mL. Preservative free. The vaccine should be used as supplied; do not dilute. **Shake well before withdrawal and use.** Store refrigerated at 2 °C to 8 °C (36 °F to 46 °F). **Do not freeze**-destroys potency.

Hepatitis B Vaccine (Recombinant)

Selected References

- ◆ American Academy of Pediatrics. Hepatitis B. In: Pickering LK, Baker CJ, Long SS, McMillan JA, eds. *Red Book: 2006 Report of the Committee on Infectious Diseases*. 27th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2006: pp 341-347.
- ◆ Centers for Disease Control and Prevention: A comprehensive immunization strategy to eliminate transmission of hepatitis B virus in the United States. Recommendations of the Advisory Committee on Immunization Practices (ACIP) part 1: immunization of infants, children and adolescents. *MMWR Recomm Rep* 2005;54 (RR-16):1-23.
- ◆ Saari TN, Committee on Infectious Diseases: Immunization of preterm and low birth weight infants. *Pediatrics* 2003;112:193-98.
- ◆ Product Information, Merck and Company, 2007
- ◆ Product Information, GlaxoSmithKline, 2006

Updated 3/2008

References updated 3/2007

Dose & Administration

0.5 mL IM in the anterolateral thigh.

Please refer to the most recent AAP/ACIP immunization schedule. It is recommended that premature infants should be immunized according to their postnatal age; some data, however, suggest delaying the first dose in chronically ill premature infants due to inadequate seroconversion against *H influenzae*.

When giving multiple vaccines, use a separate syringe for each and give at different sites. Care should be taken to draw back on the plunger of the syringe before injection to be certain the needle is not in a blood vessel.

Uses

COMVAX® is indicated for vaccination against invasive disease caused by *Haemophilus influenzae* type b and against infection caused by all known subtypes of hepatitis B virus in infants 6 weeks to 15 months of age born to HBsAg-negative mothers. COMVAX® should not be used in infants younger than 6 weeks of age.

Monitoring

Observe injection site for local reactions.

Adverse Effects/Precautions

Local pain and tenderness may occur at the injection site.

Pharmacology

COMVAX® (preservative-free) combines the antigenic components of Recombivax HB® and PedvaxHIB®. Each 0.5 mL dose contains 5 mcg HBsAg and 7.5 mcg *Haemophilus b* -PRP.

Special Considerations/Preparation

Supplied in 0.5-mL single-dose vial. Store refrigerated. **Do not freeze.**

Selected References

- ◆ American Academy of Pediatrics. Hepatitis B. In: Pickering LK, Baker CJ, Long SS, McMillan JA, eds. Red Book: 2006 Report of the Committee on Infectious Diseases. 27th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2006: pp 341-343.
- ◆ Product information, Merck & Co, 2004.

References updated 3/2007



Dose & Administration

Usual dosage: 500 to 750 mg/kg per dose over 2 to 6 hours.

For neonatal alloimmune thrombocytopenia, doses have ranged from 400 mg/kg to 1 gram/kg.

Most studies have used a single dose, although additional doses have been given at 24 hour intervals.

See "Special Considerations/Preparation" for product-specific information.

Uses

Adjuvant treatment of fulminant neonatal sepsis, hemolytic jaundice, and neonatal alloimmune thrombocytopenia.

Monitoring

Frequent monitoring of heart rate and blood pressure. Check IV site for signs of phlebitis.

Adverse Effects/Precautions

Rare cases of hypoglycemia, transient tachycardia, and hypotension that resolved after stopping the infusion have been reported. No short-term or long-term adverse effects have been reported in neonates. Animal studies have demonstrated reticuloendothelial system blockade when higher doses (>1 g/kg) have been used. All donor units are nonreactive to HBsAg and HIV. The manufacturing process of these products now includes a solvent/detergent treatment to inactivate hepatitis C and other membrane-enveloped viruses.

Black Box Warning

According to the manufacturer's black box warning, immune globulin intravenous (IGIV) products have been reported to be associated with renal dysfunction, acute renal failure, osmotic nephrosis, and death. Use caution in patients predisposed to acute renal failure and administer at the minimum concentration available and the minimum rate of infusion practicable in such patients. Higher rates of renal failure were associated with IGIV products containing sucrose.

Pharmacology

IVIG is a plasma-derived, concentrated form of IgG antibodies present in the donor population. Significant lot-to-lot variation of specific antibodies may occur with all products. No significant differences in clinical outcomes using the different products have been seen. All preparations are reported to contain more than 92% IgG monomers and a normal distribution of IgG subclasses. Total IgG titers in treated, septic neonates remain elevated for approximately 10 days.

Special Considerations/Preparation

Reconstitute lyophilized products with supplied diluent. All products are preservative-free. Shelf life varies, but is at least 2 years when stored properly.

Intravenous Immune Globulin (Human)

IVIG Preparations

Brand	Form	Storage	Preparation*
Gamunex 10% (Talecris)	10, 25, 50, 100, and 200 mL vials	Refrigerate	Allow to come to room temperature
Flebogamma 5% (Grifols)	10, 50, 100, and 200 mL vials 50 mg/mL, 5% solution	Room temperature	Rotate gently. Preservative-free.
Octagam (Octapharma)	1, 2.5, 5, and 10 g vials 5% solution	Room temperature	5% solution. Do not shake.
Carimune NF (ZLB Behring)	1, 3, 6, and 12 g lyophilized vials	Room temperature	Preservative-free.
Polygam®, S/D (American Red Cross)	2.5, 5, and 10 g lyophilized vials 5% glucose, pH 6.8	Room temperature	5% and 10% solution. Preservative-free.
Panglobulin NF (American Red Cross)	1, 3, 6, and 12 g lyophilized vials	Room temperature	Preservative-free.
Gammagard S/D (Baxter)	0.5, 2.5, 5, and 10 g lyophilized vials	Room temperature	5% and 10% solution
Gammagard Liquid 10% (Baxter)	1, 2.5, 5, 10, and 20 g liquid vials	Refrigerate or Room temperature	10% solution

* Reconstitute lyophilized products with supplied diluent. All products are preservative free. Shelf life varies, but is at least 2 years, when stored properly.

Solution Compatibility: D₅W, D₁₅W, and Dex/AA.

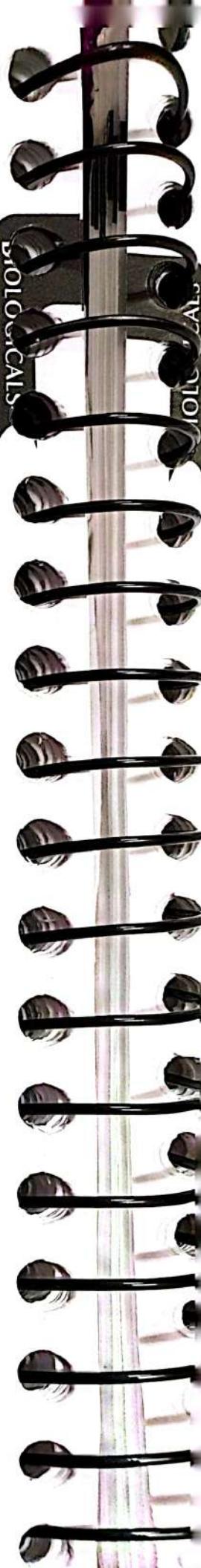
Terminal Injection Site Compatibility: Fluconazole.

Selected References

- ◆ Kreymann KG, de Heer G, Nierhaus A, Kluge S: Use of polyclonal immunoglobulins as adjunctive therapy for sepsis or septic shock. *Crit Care Med* 2007;35:2677-2685.
- ◆ Sandberg K, Fasth A, Berger A, et al: Preterm infants with low immunoglobulin G levels have increased risk for neonatal sepsis but do not benefit from prophylactic immunoglobulin G. *J Pediatr* 2000;137:623-628.
- ◆ Jenson HB, Pollock BH: Meta-analyses of the effectiveness of intravenous immune globulin for prevention and treatment of neonatal sepsis. *Pediatrics* 1997;99(2):e2.
- ◆ Blanchette VS, Rand ML: Platelet disorders in newborn infants: diagnosis and management. *Semin Perinatol* 1997;21:53-62.
- ◆ Weismann LE, Stoll BJ, Kueser TJ: Intravenous immunoglobulin therapy for early-onset sepsis in premature neonates. *J Pediatr* 1992;121:434.
- ◆ Christensen RD, Brown MS, Hall DC, et al: Effect on neutrophil kinetics and serum opsonic capacity of intravenous administration of immune globulin to neonates with clinical signs of early-onset sepsis. *J Pediatr* 1991;118:606.
- ◆ Gottstein R, Cooke RWI: Systematic review of intravenous immunoglobulin in haemolytic disease of the newborn. *Arch Dis Child Fetal Neonatal Ed* 2003;88:F6-F10.
- ◆ Tanyer G, Suklar Z, Dallar Y, et al: Multiple dose IVIG treatment of neonatal immune hemolytic jaundice. *J Trop Pediatr* 2001;47:50-53.

Adverse Effects/Precautions updated 1/2009

Preparation Chart and References updated 3/2008



Dose & Administration

15 mg/kg per dose IM, preferably in the anterolateral aspect of the thigh.
Repeat monthly during RSV season.

Uses

Immunoprophylaxis against severe RSV lower respiratory tract infections in high risk infants:

- ◆ up to 24 months of age, hemodynamically significant acyanotic and cyanotic congenital heart disease,
- ◆ less than 24 months of age, chronic lung disease of prematurity (CLD) who have required medical therapy for CLD within 6 months before the start of the RSV season,
- ◆ up to 12 months of age, born at 28 weeks gestation or earlier,
- ◆ up to 6 months of age, born at 29 to 32 weeks gestation,
- ◆ less than 6 months of age, born between 32 to 35 weeks gestation with at least 2 additional risk factors.

Risk factors include child care attendance, school-aged siblings, exposure to environmental air pollutants, congenital abnormalities of the airways, or severe neuromuscular disease.

Once an infant qualifies for initiation of prophylaxis, it should continue throughout the RSV season. Palivizumab is not effective for treatment of established RSV disease.

Monitoring

Observe injection site for induration and swelling.

Adverse Effects/Precautions

In clinical trials, upper respiratory infection, otitis media, fever, and rhinitis occurred slightly more frequently in palivizumab recipients. Cyanosis and arrhythmia were also seen slightly more frequently in patients with CHD. There are rare reports (<1 per 100,000 patients) of anaphylaxis, and hypersensitivity reactions have been reported. Do not administer to patients with a history of a prior severe reaction.

Pharmacology

Synagis® is a humanized monoclonal antibody produced by recombinant DNA technology. This composite of human (95%) and murine (5%) antibody sequences inhibits RSV replication. The mean half-life of Synagis® is approximately 20 days. Adequate antibody titers are maintained in most infants for one month following a 15-mg/kg dose. Due to a faster metabolic rate, some hospitalized VLBW infants (<500 g) may not maintain optimal RSV titers for the entire initial month until after the second dose. Palivizumab does not interfere with the response to other vaccines and as such, they can be administered concurrently.

Special Considerations/Preparation

Synagis® is supplied as 50-mg and 100-mg single-dose vials in ready-to-use, **NO RECONSTITUTION required**, liquid solution. Do not add any diluent to the liquid solution and use one dose per vial. Do not re-enter vial after initial withdrawal and discard any unused portions. Administer as soon as possible after withdrawal from the vial. **Do not FREEZE or SHAKE.** The liquid solution should be stored **refrigerated between 2 to 8°C (36 to 46°F)**. Synagis® contains no preservatives, thiomersol, or other mercury salts.

Selected References

- ◆ American Academy of Pediatrics. Respiratory Syncytial Virus (RSV) Infections. In: Pickering LK, Baker CJ, Long SS, McMillan JA, eds. *Red Book: 2006 Report of the Committee on Infectious Diseases*. 27th ed. Elk Grove Village, IL: American Academy of Pediatrics 2006:560-566.
- ◆ Meissner HC, Long SS, Committee on Infectious Diseases and Committee on Fetus and Newborn: Revised indications for the use of palivizumab and respiratory syncytial virus immune globulin intravenous for the prevention of respiratory syncytial virus infections. Policy Statement and Technical Report. *Pediatrics* 2003;122:1442-46 and 1447-52.
- ◆ Romero JR: Palivizumab prophylaxis of respiratory syncytial virus disease from 1998 to 2002: results from four years of palivizumab usage. *Pediatr Infect Dis J* 2003;22:S46-54.
- ◆ The Impact-RSV Study Group: Palivizumab, a humanized respiratory syncytial virus monoclonal antibody, reduces hospitalization from respiratory syncytial virus infection in high-risk infants. *Pediatrics* 1998;102:531-537.
- ◆ Groothuis JR: Safety and tolerance of palivizumab administration in a large northern hemisphere trial. *Pediatr Infect Dis J* 2001;20:628-629.
- ◆ Wu S-Y, Bonaparte J, Pyati S: Palivizumab use in very premature infants in the neonatal intensive care unit. *Pediatrics* 2004;114:e554-e556.
- ◆ Product Information, MedImmune, 2007.

References updated 3/2007

Product information updated 3/2008

Dose & Administration

0.5 mL IM in the anterolateral thigh. Please refer to the most recent AAP/ACIP immunization schedule. Shake vial vigorously before withdrawing dose.

Do not mix with other vaccines.

When giving multiple vaccines, use a separate syringe for each and give at different sites. Care should be taken to draw back on the plunger of the syringe before injection to be certain the needle is not in a blood vessel.

Uses

Immunoprophylaxis against invasive disease caused by *S. pneumoniae*.

Monitoring

Observe injection site for erythema, induration (common), palpable nodule (uncommon), or sterile abscess (rare). Fever (common) may be treated with acetaminophen. Other common, self-limiting, systemic effects are drowsiness, fretfulness, and anorexia.

Adverse Effects/Precautions

Hypersensitivity to any component of the vaccine, including diphtheria toxoid, is a contraindication to the vaccine.

Pharmacology

Prevnr® is a sterile solution of saccharides of the capsular antigens of *Streptococcus pneumoniae* serotypes 4, 6B, 9V, 14, 18C, 19F, and 23F individually conjugated to diphtheria CRM₁₉₇ protein. The seven serotypes account for over 80% of invasive pneumococcal disease in children in the United States. Eighty percent of penicillin-nonsusceptible strains in the United States are one of these 7 serotypes. Each dose contains 0.125 mg aluminum as aluminum phosphate adjuvant.

Special Considerations/Preparation

Prevnr® is supplied in 0.5-mL single-dose vials and single-dose syringes. After being shaken vigorously, it should appear as a homogeneous white suspension. The vaccine should not be used if it cannot be resuspended. Store refrigerated at 2 °C to 8 °C (36 °F to 46 °F). **Do not freeze.**

Selected References

- ◆ American Academy of Pediatrics. Pneumococcal Infections. In: Pickering LK, Baker CJ, Long SS, McMillan JA, eds. *Red Book: 2006 Report of the Committee on Infectious Diseases*. 27th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2006: pp 532-534.
- ◆ Advisory Committee on Immunization Practices: Recommendations of the ACIP. Most recent updates available on the National Immunization Program website: <http://www.cdc.gov/nip/publications/acip-list.htm>
- ◆ American Academy of Pediatrics, Committee on Infectious Diseases: Recommendations for the prevention of pneumococcal infections, including the use of pneumococcal conjugate vaccine (Prevnr®), pneumococcal polysaccharide vaccine, and antibiotic prophylaxis. *Pediatrics* 2000;106:362-366.
- ◆ Shinefield H, Black S, Ray P, et al: Efficacy, immunogenicity and safety of heptavalent pneumococcal conjugate vaccine in low birth weight and preterm infants. *Pediatr Infect Dis J* 2002;21:182-186.
- ◆ Product information, Wyeth Pharmaceuticals, 2007.

References update 3/2008

Poliovirus Vaccine Enhanced-Inactivated

Dose & Administration

0.5 mL injected **subcutaneously** in the midlateral thigh or IM in the anterolateral thigh. Immunize premature infants according to their postnatal age. Please refer to the most recent immunization schedule.

When giving multiple vaccines, use a separate syringe for each and give at different sites. Care should be taken to draw back on the plunger of the syringe before injection to be certain the needle is not in a blood vessel.

Uses

Inactivated poliovirus vaccine is now the only poliovirus vaccine available in the United States. Indications in other countries include hospitalized infants, and infants with contraindications for OPV (e.g. immunodeficiency, HIV-positive, those with immunodeficient contacts).

Monitoring

No specific monitoring required.

Adverse Effects/Precautions

Occasional reactions include erythema and tenderness at the injection site. Trace components may infrequently cause allergic reactions.

Pharmacology

Sterile suspension of types 1, 2, and 3 poliovirus inactivated with formaldehyde. The vaccine produced using a microcarrier culture technique of monkey kidney cells has enhanced potency. Contains traces of streptomycin, neomycin, and polymyxin B.

Special Considerations/Preparation

IPOL® (Sanofi Pasteur) is a clear, colorless suspension, available in 0.5 mL single-dose syringes and multidose vial. Do not use if the vaccine is turbid or discolored. Refrigerate at 2 °C to 8 °C (36 °F to 46 °F). **Do not freeze.**

Selected References

- ◆ American Academy of Pediatrics. Poliovirus Infections. In: Pickering LK, Baker CJ, Long SS, McMillan JA, eds. *Red Book: 2006 Report of the Committee on Infectious Diseases*. 27th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2006: pp 544-545.
- ◆ Advisory Committee on Immunization Practices: Recommendations of the ACIP. Most recent updates available on the National Immunization Program website: <http://www.cdc.gov/nip/publications/acip-list.htm>
- ◆ American Academy of Pediatrics, Committee on Infectious Diseases: Poliomyelitis prevention: recommendations for use of inactivated poliovirus vaccine and live oral poliovirus vaccine. *Pediatrics* 1997;99:300.
- ◆ Product information, Sanofi Pasteur, 2005

References updated 3/2007

Dose & Administration

1 mL per dose.

FOR ORAL USE ONLY. NOT FOR INJECTION.

The Rotarix® vaccine is a 2-dose series with at least 4 weeks between each dose. The recommended vaccination schedule is 2 months of age (minimum age 6 weeks and maximum age 14 weeks 6 days) and 4 months of age (maximum age 8 months). Please refer to the most recent AAP/ACIP immunization recommendations.

To administer the vaccine: 1) Connect transfer adapter onto vial of lyophilized vaccine. 2) Shake the oral applicator containing the liquid diluent (white, turbid suspension). 3) Connect the oral applicator to the transfer adapter. 4) Push plunger of oral applicator to transfer diluent into vial (suspension will appear white and turbid). 5) Withdraw the entire mixture back into the oral applicator. 6) Twist and remove the oral applicator from the transfer adapter. 7) With infant seated in a reclining position, administer orally the entire contents of the oral applicator (on the inside of the cheek). Refer to package insert for illustrations.

If the infant spits out or regurgitates most of the vaccine dose, a single replacement dose may be considered at the same visit. There are no restrictions on the infant's liquid consumption (including breastmilk) before or after vaccination.

Uses

Immunoprophylaxis against rotavirus gastroenteritis caused by G1 and non-G1 types (G3, G4, and G9).

Adverse Effects/Precautions

Vaccination not recommended in infants with a history of uncorrected congenital malformation of the gastrointestinal tract that would predispose the infant for intussusception. Infants with severe latex allergy (anaphylaxis) should not receive Rotarix® (oral applicator contains latex rubber). In a safety study (n=63,225 infants), no increased risk of intussusception was observed in infants receiving Rotarix® when compared with placebo. There were 6 cases of intussusception reported in the Rotarix® infants versus 7 cases in the placebo infants within 31 days after any dose.

Pharmacology

Rotarix® is a human-derived rotavirus vaccine from the 89-12 strain, which belongs to G1P[8] type. The lyophilized vaccine contains amino acids, dextran, Dulbecco's Modified Eagle Medium, sorbitol, and sucrose. The liquid diluent contains calcium carbonate (to protect the vaccine during passage through the stomach and prevent inactivation), sterile water, and xanthan.

Fecal shedding after vaccination was reported in approximately 26% of vaccinated infants, in two studies. Peak excretion occurred around day 7 after the first dose. Transmission of virus was not evaluated, and the potential for transmission of vaccine virus is not known.

Approximately 80% of Rotarix® recipients will be seroconverted one to two months after a 2-dose series.

Special Considerations/Preparation

Rotarix® is supplied as a vial of lyophilized vaccine, a prefilled oral applicator of liquid diluent (1 mL) with a plunger stopper, and a transfer adapter for reconstitution. The vaccine contains no preservatives. Oral applicator contains latex rubber. Lyophilized vials should be refrigerated and protected from light, and the diluent can be stored at room temperature.

Do not freeze, and discard vaccine if frozen.

Reconstituted vaccine may be stored refrigerated or at room temperature, and vaccine should be administered within 24 hours of reconstitution. Discard if not used within 24 hours.

Selected References

- ◆ Advisory Committee on Immunization Practices. Vaccines For Children Program. Vaccines To Prevent Rotavirus Gastroenteritis. Resolution adopted and effective June 25, 2008. Available at: <http://www.cdc.gov/vaccines/programs/vfc/downloads/resolutions/0608rotavirus.pdf>.
- ◆ Vesikari T, Karvonen A, Prymula R, et al: Efficacy of human rotavirus vaccine against rotavirus gastroenteritis during the first 2 years of life in European infants: randomised, double-blind controlled study. *Lancet* 2007;370:1757-1763.
- ◆ Ruiz-Palacios GM, Perez-Schael I, Velazquez FR, et al: Safety and efficacy of an attenuated vaccine against severe rotavirus gastroenteritis. *N Engl J Med* 2006;354:11-22.
- ◆ Product Information, GlaxoSmithKline, 2008.

Dose & Administration and Special Considerations/Preparation updated 1/2009

Added 7/2008

Dose & Administration

2 mL per dose.

FOR ORAL USE ONLY. NOT FOR INJECTION.

The RotaTeq® vaccine is a 3-dose series with at least 4 weeks between each dose. The recommended vaccination schedule is 2 months of age (minimum age 6 weeks and maximum age 14 weeks 6 days), 4 months of age, and 6 months of age (maximum age 8 months). Please refer to the most recent AAP/ACIP immunization schedule.

To administer the vaccine: 1) Tear open the pouch and remove the dosing tube. 2) Clear the fluid from the dispensing tip by holding tube vertically and tapping cap. 3) Puncture the dispensing tip by screwing cap *clockwise* until it becomes tight, then remove the cap by turning it *countrerclockwise*. 4) Administer dose by gently squeezing liquid into infant's mouth toward the inner cheek until dosing tube is empty.

If for any reason an incomplete dose is administered (e.g., infant spits or regurgitates the vaccine), a replacement dose is NOT recommended, since this was not studied in the clinical trials.

Uses

Immunoprophylaxis against rotavirus gastroenteritis caused by serotypes G1, G2, G3, and G4.

Adverse Effects/Precautions

Data from the phase III efficacy trials ($n = 71725$) did not suggest an increased risk of intussusception relative to placebo. However, the Food and Drug Administration (FDA) notified health care providers and consumers on February 13, 2007 about 28 post-marketing reports of intussusception following administration of RotaTeq®. According to the FDA, approximately 3.5 million doses of RotaTeq® were distributed in the United States as of February 1, 2007. Intussusception can occur spontaneously in the absence of vaccination and its cause is usually unknown. Of the 28 reported cases of intussusception, it is not known how many, if any, were vaccine-related. However, the number of intussusception cases reported to date after RotaTeq® administration does not exceed the number expected based on background rates of 18-43 per 100,000 per year for an unvaccinated population of children ages 6 to 35 weeks.

RotaTeq® or placebo was administered to 2,070 pre-term infants (25 to 36 weeks gestational age, median 34 weeks) according to their age in weeks since birth. Safety and efficacy were similar as for full term infants.

Pharmacology

RotaTeq® is a bovine-based pentavalent vaccine containing 5 live reassortant rotaviruses. The rotavirus parent strains of the reassortants were isolated from human and bovine hosts. Four reassortant rotaviruses express 1 of the outer capsid proteins (G1, G2, G3, or G4) from the human rotavirus parent strain and the attachment protein (P7[5]) from the bovine rotavirus parent strain. The fifth reassortant virus expresses the attachment protein (P1A[8]) from the human rotavirus parent strain and the outer capsid protein G6 from the bovine rotavirus parent strain. The reassortants are suspended in a buffered stabilizer solution. Each vaccine dose contains sucrose, sodium citrate, sodium phosphate monobasic monohydrate, sodium hydroxide, polysorbate 80, cell-culture media, and trace amounts of fetal bovine serum. There are no preservatives or thimerosal.

Fecal shedding of vaccine virus occurred in 32 (8.9%) of 360 subjects after dose 1, 0 (0%) of 249 subjects after dose 2, and 1 (0.3%) of 385 subjects after dose 3. In phase III studies, shedding was observed as early as 1 day and as late as 15 days after a dose. The potential for transmission of vaccine virus was not assessed through epidemiologic studies.

RotaTeq® can be coadministered with other childhood vaccines. It has 98% efficacy for prevention of severe illness and 74% for prevention of rotavirus-induced diarrheal episodes.

Special Considerations/Preparation

RotaTeq® is supplied as a suspension for oral use in individually pouched single-dose tubes. Each dosage tube contains 2 mL. It is a pale yellow clear liquid that may have a pink tint. Store and transport refrigerated. Protect from light. Administer as soon as possible after being removed from refrigeration. Discard in approved biological waste containers.

Selected References

- ◆ Advisory Committee on Immunization Practices. Vaccines For Children Program. Vaccines To Prevent Rotavirus Gastroenteritis. Resolution adopted and effective June 25, 2008. Available at: <http://www.cdc.gov/vaccines/programs/vfc/downloads/resolutions/0608rotavirus.pdf>.
- ◆ American Academy of Pediatrics, Committee on Infectious Diseases. Prevention of rotavirus disease: guidelines for use of rotavirus vaccine. *Pediatrics* 2007;119:171181.
- ◆ Centers for Disease Control and Prevention. Postmarketing monitoring of intussusception after RotaTeq® vaccination - United States, February 1, 2006–February 15, 2007. *MMWR* 2007; 56(10):218-222.
- ◆ Parashar UD, Alexander JP, Glass RI; Advisory Committee on Immunization Practices (ACIP), Centers for Disease Control and Prevention (CDC). Prevention of rotavirus gastroenteritis among infants and children: recommendations of the Advisory Committee on Immunization Practices. *MMWR Recomm Rep.* 2006;55(RR-12):113.
- ◆ Product information, Merck & Co., 2007.

Added 3/2007

CARDIOVASCULAR DRUGS

Dose & Administration

Starting dose: 50 mcg/kg rapid IV push (1 to 2 seconds). Increase dose in 50 mcg/kg increments Q2 minutes until return of sinus rhythm. Usual maximum dose: 250 mcg/kg. Infuse as close to IV site as possible. Flush IV with saline immediately. Intraosseous administration has also been reported to be successful.

Uses

Acute treatment of sustained paroxysmal supraventricular tachycardia. It may also be useful in establishing the cause of the SVT.

Monitoring

Continuous EKG and blood pressure monitoring.

Adverse Effects/Precautions

Flushing, dyspnea, and irritability occur frequently, but usually resolve within 1 minute. Transient (duration <1 minute) arrhythmias may occur between termination of SVT and onset of normal sinus rhythm. Apnea has been reported in one preterm infant. Recurrence of SVT occurs in approximately 30% of treated patients. Aminophylline/Theophylline and caffeine diminish adenosine's effect by competitive antagonism.

Pharmacology

Adenosine is the pharmacologically active metabolite of ATP. It acts by depressing sinus node automaticity and A-V node conduction.

It does **not** have negative inotropic effects. Response should occur within 2 minutes of the dose. Estimated serum half-life is 10 seconds.

Special Considerations/Preparation

Supplied in 2 mL vials containing 6 mg adenosine dissolved in NS. Contains no preservative. Store at room temperature. **Do not refrigerate**; crystallization will occur. Solution must be clear at the time of use.

Dilutions can be made with NS for doses <0.2 mL (600 mcg). Use 1 mL (3000 mcg) with 9 mL NS to make a solution with a final concentration of 300 mcg/mL.

Solution Compatibility: D5W and NS**Selected References**

- ◆ Paret G, Steinmetz D, Kuint J et al: Adenosine for the treatment of paroxysmal supraventricular tachycardia in fullterm and preterm newborn infants. *Am J Perinatol* 1996;13:343-46.
- ◆ Friedman FD: Intraosseous adenosine for the termination of supraventricular tachycardia in an infant. *Ann Emerg Med* 1996;28:356-58.
- ◆ Crosson JE, Etheridge SP, Milstein S et al: Therapeutic and diagnostic utility of adenosine during tachycardia evaluation in children. *Am J Cardiol* 1994;74:155-60.
- ◆ Till J, Shinebourne EA, Rigby ML, et al: Efficacy and safety of adenosine in the treatment of supraventricular tachycardia in infants and children. *Br Heart J* 1989;62:204.
- ◆ Overholt ED, Rhuban KS, Gutgesell HP, et al: Usefulness of adenosine for arrhythmias in infants and children. *Am J Cardiol* 1988;61:336.
- ◆ Product Information, Astellas, 2005

Updated 3/98

Compatibilities updated 3/2005



Dose & Administration

Initial dose: 0.05 to 0.1 mcg/kg per minute by continuous IV infusion. Titrate to infant's response—oxygenation *versus* adverse effects.

Maintenance dose: May be as low as 0.01 mcg/kg per minute. Higher initial doses are usually no more effective and have a high incidence of adverse effects. May also be given via UAC positioned near ductus arteriosus.

Sample Dilution and Infusion Rate: Mix 1 ampule (500 mcg) in 49 mL of compatible solution (e.g., D5W) yielding a concentration of 10 mcg/mL. Infuse at a rate of 0.6 mL/kg per hour to provide a dose of 0.1 mcg/kg per minute.

10ng/kg/min.

Uses

To promote dilation of ductus arteriosus in infants with congenital heart disease dependent on ductal shunting for oxygenation/perfusion.

Monitoring

Closely monitor respiratory and cardiovascular status. Assess for improvement in oxygenation. Closely monitor infant's temperature. Ensure reliable IV access: duration of effect is short.

Adverse Effects/Precautions**Black Box Warning**

According to the manufacturer's black box warning, apnea has been reported in 10% to 12% of neonates with congenital heart defects treated with alprostadil. Apnea is seen most often in neonates weighing less than 2 kg at birth, and usually appears during the first hour of drug infusion.

Be prepared to intubate/resuscitate.

Common (6% to 15%): Apnea (consider treating with aminophylline), hypotension, fever, leukocytosis, cutaneous flushing, and bradycardia. Hypokalemia reported with long-term therapy (> 20 days), especially with doses > 0.05 mcg/kg/minute. Gastric outlet obstruction and reversible cortical proliferation of the long bones after prolonged treatment (> 120 hours).

Uncommon (1% to 5%): Seizures, hypoventilation, tachycardia, cardiac arrest, edema, sepsis, diarrhea, and disseminated intravascular coagulation.

Rare (<1%): Urticaria, bronchospasm, hemorrhage, hypoglycemia, and hypocalcemia.

Musculoskeletal changes: Widened fontanelles, pretibial and soft tissue swelling, and swelling of the extremities may occur after 9 days of therapy. Cortical hyperostosis and periostitis may occur with long-term (>3 months) therapy. These changes resolve over weeks after discontinuation of therapy.

Alprostadil (Prostaglandin E₁)

Pharmacology

Alprostadil causes vasodilation of **all** arterioles. Inhibition of platelet aggregation. Stimulation of uterine and intestinal smooth muscle. Maximal drug effect usually seen within 30 minutes in cyanotic lesion; may take several hours in acyanotic lesions.

Special Considerations/Preparation

Supplied in 1 mL (500 mcg) ampules that must be refrigerated. **Dilute before administration to a concentration $\leq 20 \text{ mcg/mL}$.** Prepare fresh infusion solutions every 24 hours. Osmolality of undiluted (500 mcg/mL) is 23,250 mOsm/kg. Extravasation may cause tissue sloughing and necrosis.

Sample Dilution and Infusion Rate: Mix 1 ampule (500 mcg) in 49 mL of compatible solution (e.g. D₅W) yielding a concentration of 10 mcg/mL. Infuse at a rate of 0.6 mL/kg per hour to provide a dose of 0.1 mcg/kg per minute.

Solution Compatibility: D₅W and NS. No data are currently available on Dex/AA.

Terminal Injection Site Compatibility: Aminophylline, atropine, caffeine citrate, calcium chloride, cefazolin, cimetidine, clindamycin, dexamethasone, digoxin, dopamine, epinephrine, furosemide, gentamicin, glycopyrrolate, heparin, hydralazine, hydrocortisone succinate, isoproterenol, lidocaine, metoclopramide, metronidazole, midazolam, morphine, nitroglycerin, nitroprusside, pancuronium, phenobarbital, potassium chloride, penicillin G, and ranitidine.

Selected References

- ◆ Meckler GD, Lowe C: To intubate or not to intubate? Transporting infants on prostaglandin E₁. *Pediatrics* 2009;123:e25-e30.
- ◆ Talosi G, Katona M, Turi S: Side-effects of long-term prostaglandin E₁ treatment in neonates. *Pediatr Int* 2007;49:335-340.
- ◆ Lim DS, Kulik TJ, Kim DW: Aminophylline for the prevention of apnea during prostaglandin E₁ infusion. *Pediatrics* 2003;112:e27-e29.
- ◆ Arav-Boger R, Baggett HC, Spevak PJ, Willoughby RE: Leukocytosis caused by prostaglandin E₁ in neonates. *J Pediatr* 2001;138:263-265.
- ◆ Kaufman MB, El-Chaar GM: Bone and tissue changes following prostaglandin therapy in neonates. *Ann Pharmacother* 1996;30:269.
- ◆ Peled N, Dagan O, Babyn P, et al: Gastric-outlet obstruction induced by prostaglandin therapy in neonates. *N Engl J Med* 1992;327:505.
- ◆ Gannaway WI, et al: Chemical stability of alprostadil (PGE-1) in combination with common injectable medications (abstract #P-152E). *American Society of Hospital Pharmacists Midyear Clinical Meeting Abstracts* 1989;24:75A.
- ◆ Roberts RJ: *Drug Therapy in Infants*. Philadelphia: WB Saunders Co, 1984, p 250.
- ◆ Lewis AB, Freed MD, Heymann MA, et al: Side effects of therapy with prostaglandin E₁ in infants with congenital heart disease. *Circulation* 1981;64:893.
- ◆ Heymann MA: Pharmacologic use of prostaglandin E₁ in infants with congenital heart disease. *Am Heart J* 1981;101:837.
- ◆ Product Information, Pfizer, 2002

Adverse effects and References updated 1/2009
Compatibilities updated 3/2005

Dose & Administration

Restoration of function to central venous catheter: Instill into dysfunctional catheter at a concentration of 1 mg/mL. Use 110% of the internal lumen volume of the catheter, not to exceed 2 mg in 2 mL. If catheter function is not restored in 120 minutes after 1 dose, a second dose may be instilled.

Dissolution of intravascular thrombi: 200 mcg/kg per hour (0.2 mg/kg per hour). Duration of therapy is 6 to 48 hours. If administering directly into the thrombus, dose may be increased after 6 hours to a maximum of 500 mcg/kg per hour. If localized bleeding occurs, stop infusion for 1 hour and restart using 100 mcg/kg per hour. Discontinue heparin several hours prior to initiation of therapy.

Note: Reports in the literature are a collection of cases gathered over several years. Some authors used loading doses, others did not. Infused doses ranged from 20 to 500 mcg/kg per hour. Complications were most often linked with higher doses and longer duration of therapy. Call 1-800-NOCLOTS for case reporting and treatment guidance.

Uses

Dissolution of intravascular thrombi of recent onset that are either intraarterial or life-threatening. Adjuvant treatment of infective endocarditis vegetations.

Monitoring

Follow coagulation studies (PT, aPTT, fibrinogen, fibrin split products) prior to therapy and at least daily during treatment. Maintain fibrinogen levels greater than 100 mg/dL and platelets $> 50,000/\text{mm}^3$. Echocardiography to assess clot lysis at least every 12 hours (Q6 hours optimal). Cranial ultrasound to assess for hemorrhage prior to therapy.

Adverse Effects/Precautions

Intracranial hemorrhage may occur, especially in premature infants treated for prolonged periods. Bleeding from venipuncture sites occurs in approximately half of treated patients. The risk of complications increases at doses above 450 mcg/kg per hour.

Pharmacology

Alteplase binds strongly and specifically to fibrin in a thrombus and converts the entrapped plasminogen to plasmin. This initiates local fibrinolysis with limited systemic proteolysis. Alteplase has a shorter half-life than streptokinase and does not cause anaphylactic reactions. It is cleared rapidly from the plasma, primarily via the liver.

Alteplase

Special Considerations/Preparation

Activase® is supplied as lyophilized powder in 50 mg and 100 mg vials. Reconstitute 50 mg vial by adding 50 mL sterile water for injection (do not use bacteriostatic water for injection) for a concentration of 1 mg/mL. Can be further diluted with NS or D₅W to a concentration of 0.5 mg/mL if necessary. Use reconstituted solution within 8 hours of mixing when stored refrigerated or at room temperature.

Cathflo® Activase® is supplied as lyophilized powder in 2 mg vials. Reconstitute by adding 2.2 mL sterile water for injection to a final concentration of 1 mg/mL. Do not use bacteriostatic water for injection. Mix by gently swirling until the contents are completely dissolved. DO NOT SHAKE. Use reconstituted solution within 8 hours of mixing. Reconstituted solution may be stored refrigerated or at room temperature.

Solution Compatibility: NS, and D₅W

Terminal Injection Site Compatibility: Lidocaine, morphine, nitroglycerin, and propranolol.

Incompatibility: Dobutamine, dopamine, and heparin.

Selected References

- ◆ Manco-Johnson M, Nuss R: Neonatal thrombotic disorders. *NeoReviews* 2000;1:e201.
- ◆ Hartmann J, Hussein A, Trowitzsch E, et al: Treatment of neonatal thrombus formation with recombinant tissue plasminogen activator: six years experience and review of the literature. *Arch Dis Child Fetal Neonatal Ed* 2001;85:F18-F22.
- ◆ Marks KA, Zucker N, Kapelushnik J, et al: Infective endocarditis successfully treated in extremely low birth weight infants with recombinant tissue plasminogen activator. *Pediatrics* 2002;109:153-158.
- ◆ Weiner GM, Castle VP, DiPietro MA, Faix RG: Successful treatment of neonatal arterial thromboses with recombinant tissue plasminogen activator. *J Pediatr* 1998;133:133-136.
- ◆ Product Information, Genentech, Inc., 2005.

Dose, Administration updated 3/2005

Preparation updated 3/2008

Compatibilities updated 3/2005

Dose & Administration

IV Loading dose: 5 mg/kg IV infusion given over 30 to 60 minutes, preferably in a central vein.

Maintenance infusion: 7 to 15 mcg/kg per minute (10 to 20 mg/kg per 24 hours). Begin at 7 mcg/kg per minute and titrate by monitoring effects. For infusions lasting longer than 1 hour, amiodarone IV concentrations should not exceed 2 mg/mL unless using a central line.

Consider switching to oral therapy within 24 to 48 hours.

PO: 5 to 10 mg/kg per dose Q12 hours.

Uses

Treatment of life-threatening or drug-resistant refractory supraventricular (SVT), ventricular tachyarrhythmias (VT), and postoperative junctional ectopic tachycardia (JET) - see Adverse Effects.

Monitoring

Continuous EKG and blood pressure (for IV). Follow AST and ALT. Monitor T₃, T₄, and TSH. Observe IV site for extravasation.

Adverse Effects/Precautions

Short term toxicity: Bradycardia and hypotension (possibly associated with rapid rates of infusion). In a study of pediatric patients (n=61), ages 30 days to 15 years, hypotension and bradycardia were reported in 36% and 20% of patients, respectively. AV block was reported in 15% of patients. Polymorphic ventricular tachycardia may occur. Irritating to the peripheral vessels (concentrations > 2 mg/mL). Administration through central vein preferred.

Long term toxicity: Hyperthyroidism (due to inhibition of T₄ to T₃) and hypothyroidism (due to high concentration of inorganic iodine). Generic formulation contains 2% benzyl alcohol (20 mg/mL). Hepatitis and cholestatic hepatitis (rare). Photosensitivity (10%), nausea and vomiting (10%), optic neuritis (4% to 9%), and pulmonary fibrosis (4% to 9%) have been reported with prolonged oral use in adults.

Black Box Warning

According to the manufacturer's black box warning, a potentially fatal toxicity associated with amiodarone is hypersensitivity pneumonitis or interstitial/alveolar pneumonitis (reported in adults). Liver injury is common but usually mild. Amiodarone may exacerbate an existing arrhythmia.

Pharmacology

Class III antiarrhythmic agent that is an iodinated benzofuran compound. Electrophysiologic activity is accomplished by prolonging the duration of the action potential and increasing the effective refractory period. Increases cardiac blood flow and decreases cardiac work and myocardial oxygen consumption. Highly protein bound (95%) in adults. Extensively metabolized to an active metabolite by the cytochrome CYP3A4 isoenzyme system (limited in preterm infants). Drug-drug interaction potentially occur when given in combination with drugs that inhibit cytochrome CYP3A4: phenytoin, fosphenytoin, clarithromycin, erythromycin, azole antifungals (e.g. fluconazole, ketoconazole, itraconazole), protease inhibitors (e.g. indinavir, ritonavir), class IA and class III antiarrhythmics (e.g. quinidine, procainamide, sotalol) and cimetidine (amiodarone levels increase). Amiodarone prevents the elimination of digoxin resulting in high digoxin levels. Half-life reported to be 26 to 107 days in adults. No data in preterm infants. Accumulates in tissues; serum levels can be detected for months. Contains 37.3% iodine by weight. Adheres to PVC tubing: low infusion rates in neonates may lead to reduced drug delivery during continuous infusions. Oral absorption is variable with approximately 50% bioavailability.

Special Considerations/Preparation

IV: The preferred formulation is Nexterone®, available as 50 mg/mL concentration in 5, 10, and 20 mL vials, as well as a 5 mL prefilled syringe. Nexterone® does not contain benzyl alcohol or polysorbate 80, and therefore does not carry a warning regarding benzyl alcohol and fatal gasping syndrome in neonates. There are also no limitations regarding compatibility and stability with plastics and isotonic infusion fluids. Store at room temperature and protect from light.

Generic amiodarone is also available as 50 mg/mL concentration in 5, 10, and 20 mL vials. Contains 2% (20 mg/mL) of benzyl alcohol and 10% (100 mg/mL) polysorbate (Tween) 80 as a preservative. Store at room temperature and protect from light.

PO: Supplied in 200 mg tablets. An oral suspension with a final concentration of 5 mg/mL may be made as follows: crush a 200 mg tablet, slowly mix in 20 mL of 1% methylcellulose, then add in 20 mL of simple syrup to make a total volume of 40 mL. Stable for six weeks at room temperature and three months refrigerated when stored in glass or plastic.

Solution Compatibility: D₅W, and NS at concentrations of 1 to 6 mg/mL.

Solution Incompatibility: No data available for Dex/AA solutions.

Terminal Injection Site Compatibility: (Data for old formulation): Amikacin, amphotericin B, atropine, calcium chloride, calcium gluconate, ciprofloxacin, ceftizoxime, ceftriaxone, cefuroxime, clindamycin, dobutamine, dopamine, epinephrine, famotidine, fentanyl, fluconazole, furosemide, esmolol, erythromycin, gentamicin, insulin, isoproterenol, lidocaine, lorazepam, metronidazole, midazolam, milrinone, morphine, nitroglycerin, norepinephrine, penicillin G, phenolamine, potassium chloride, procainamide, tobramycin, vancomycin, and vecuronium.

Incompatibility: (Data for old formulation): Aminophylline, ampicillin, ceftazidime, cefazolin, digoxin, heparin, imipenem-cilastatin, mezlocillin, micafungin, piperacillin, piperacillin-tazobactam, sodium bicarbonate, and sodium nitroprusside.

No data available for Dex/AA solutions.

Selected References

- ◆ Etheridge SP, Craig JE, Compton SJ. Amiodarone is safe and highly effective therapy for supraventricular tachycardia in infants. *Am Heart J* 2001;141:105-110.
- ◆ Yap SC, Hoomtje T, Sreeram N: Polymorphic ventricular tachycardia after use of intravenous amiodarone for postoperative junctional ectopic tachycardia. *Internat J Cardiol* 2000;76:245-247.
- ◆ Drago F, Mazza A, Guccione P, et al: Amiodarone used alone or in combination with propranolol: A very effective therapy for tachyarrhythmias in infants and children. *Pediatr Cardiol* 1998;19:445-449.
- ◆ Gandy J, Wonko N, Kantoch MJ, et al: Risks of intravenous amiodarone in neonates. *Can J Cardiol* 1998;14:855-858.
- ◆ Bowers PN, Fields J, Schwartz D, et al: Amiodarone induced pulmonary fibrosis in infancy. *PACE* 1998;21:1665-1667.
- ◆ Nahata MC, Morosco RS, Hippel TF: Stability of amiodarone in extemporaneously oral suspension prepared from commonly available vehicles. *J Pediatr Pharm Pract* 1999;4:186-189.
- ◆ Pramar YV: Chemical stability of amiodarone hydrocortisone in intravenous fluids. *Int J Pharm Comp* 1997;1:347-348.
- ◆ Perry JC, Fenrich AL, Hulse JE, et al: Pediatric use of intravenous amiodarone: Efficacy and safety in critically ill patients from a multicenter protocol. *J Am Coll Cardiol* 1996;27:1246-1250.
- ◆ Soult JA, Munoz M, Lopez JD, et al: Efficacy and safety of intravenous amiodarone for short-term treatment of paroxysmal supraventricular tachycardia in children. *Pediatr Cardiol* 1995;16:16-19.
- ◆ Figa FH, Gow RW, Hamilton RM, et al: Clinical efficacy and safety of intravenous amiodarone in infants and children. *Am J Cardiol* 1994;74:573-577.
- ◆ Product Information, Abraxis, 2006
- ◆ Product Information, Prism Pharmaceuticals, 2008

Adverse Effects/Precautions, Special Considerations, Compatibilities, and References updated 1/2009

Added 3/2001

CARDIOVASCULAR

Dose & Administration

IV: 0.01 to 0.03 mg/kg per dose IV over 1 minute, or IM.

Dose can be repeated Q10 to 15 minutes to achieve desired effect, with a maximum total dose of 0.04 mg/kg.

ET: 0.01 to 0.03 mg/kg per dose immediately followed by 1 mL NS.

PO: Begin with 0.02 mg/kg per dose given Q4 to 6 hours. May increase gradually to 0.09 mg/kg per dose.

Uses

Reversal of severe sinus bradycardia, particularly when parasympathetic influences on the heart (digoxin, beta-blocker drugs, hyperactive carotid sinus reflex) predominate. Also used to reduce the muscarinic effects of neostigmine when reversing neuromuscular blockade.

Monitoring

Heart rate.

Adverse Effects/Precautions

Cardiac arrhythmias can occur, particularly during the first 2 minutes following IV administration; usually a simple A-V dissociation, more often caused by smaller rather than larger doses. Fever, especially in brain-damaged infants. Abdominal distention with decreased bowel activity. Esophageal reflux. Mydriasis and cycloplegia.

Pharmacology

Anticholinergic. Increases heart rate by decreasing the effects of the parasympathetic system while increasing the effects of the sympathetic system. Peak tachycardia is 12 to 16 minutes after dose is given. Relaxes bronchial smooth muscle, thus reducing airway resistance and increasing dead space by 30%. Motor activity in the stomach and small and large intestines is reduced. Esophageal sphincter tone is reduced. Salivary secretion is inhibited. Duration of action is 6 hours. Primarily excreted renally unchanged.

Special Considerations/Preparation

Supplied in multiple concentrations (0.05-, 0.1-, 0.4-, and 1-mg/mL) for injection. Give IV dosage form PO. Prepare IV or PO dilution by mixing 1 mL of injectable atropine (0.4 mg/mL) in 7 mL of sterile water for injection to yield final concentration of 0.05 mg/mL. Stable for 28 days refrigerated.

Solution Compatibility: D₅W, D₁₀W, and NS.

Terminal Injection Site Compatibility: Dex/AA. Amiodarone, cimetidine, dobutamine, famotidine, fentanyl, furosemide, glycopyrrolate, heparin, hydrocortisone succinate, meropenem, metoclopramide, midazolam, milrinone, morphine, nafcillin, netilmicin, pentobarbital, potassium chloride, propofol, prostaglandin E₁, ranitidine, and sodium bicarbonate.

Incompatibility: Phenytoin, trimethoprim sulfamethoxazole.

Selected References

- ◆ Miller BR, Friesen RH: Oral atropine premedication in infants attenuates cardiovascular depression during Halothane anesthesia. *Anesth Analg* 1988;67:180.
- ◆ Roberts RJ: *Drug Therapy in Infants*. Philadelphia: WB Saunders Co, 1984, p 284.
- ◆ Adams RG, Verma P, Jackson AJ, Miller RL: Plasma pharmacokinetics of intravenously administered atropine in normal human subjects. *J Clin Pharmacol* 1982;22:477.
- ◆ Kattwinkel J, Fanaroff AA, Klaus M: Bradycardia in preterm infants: Indications and hazards of atropine therapy. *Pediatrics* 1976;58:494.
- ◆ Unna KR, Glaser K, Lipton E, Patterson PR: Dosage of drugs in infants and children: I. Atropine. *Pediatrics* 1950;6:197.
- ◆ Product Information, Hospira, 2004

Text updated 3/2008

Incompatibilities updated 3/2008

CARDIOVASCULAR

Dose & Administration

Initial dose: 0.01 to 0.05 mg/kg per dose PO Q8 to 12 hours.

Adjust dose and interval based on response. Administer 1 hour before feeding.

Uses

Treatment of moderate to severe hypertension. Afterload reduction in patients with congestive heart failure.

Monitoring

Frequent assessment of blood pressure, particularly after the first dose. Periodic assessment of renal function and serum potassium.

Adverse Effects/Precautions

Neonates are more sensitive to the effects of captopril than are older infants and children. Significant decreases in cerebral and renal blood flow have occurred in premature infants with chronic hypertension who received higher doses (0.15 to 0.30 mg/kg per dose) than those recommended above. These episodes occurred unpredictably during chronic therapy, and some were associated with neurologic (seizures, apnea, lethargy) and renal (oliguria) complications. **The use of captopril is contraindicated in** patients with bilateral renovascular disease or with unilateral renal artery stenosis in a solitary kidney, as the loss of adequate renal perfusion could precipitate acute renal failure. Hyperkalemia occurs primarily in patients receiving potassium-sparing diuretics or potassium supplements.

Pharmacology

Captopril is an angiotensin-converting enzyme (ACE) inhibitor that blocks the conversion of angiotensin I to angiotensin II, a potent vasoconstrictor. It thereby decreases plasma and tissue concentrations of angiotensin II and aldosterone, and increases plasma and tissue renin activity. Captopril also prevents the breakdown of bradykinin, a potent vasodilator. Vascular resistance is reduced without reflex tachycardia. Beneficial effects are thought to be caused by a combination of afterload reduction and long-term inhibition of salt and water retention. Bioavailability is good in neonates, although food will decrease absorption. Onset of action is 15 minutes after a dose, with peak effects seen in 30 to 90 minutes. Duration of action is usually 2 to 6 hours, but may be significantly longer (>24 hours).

Special Considerations/Preparation

Captopril oral suspension can be made by dissolving 6.25 mg (one-half of a scored 12.5 mg tablet) in 10 mL of sterile water, adding 1000 mg of sodium ascorbate for injection (4 mL of 250 mg/mL solution) to decrease oxidation, then adding sufficient water to make a final volume of 200 mL. The final concentration is 0.03 mg/mL captopril and 5 mg/mL sodium ascorbate. Solution is stable for 14 days at room temperature, 56 days refrigerated. Some undissolved excipients will remain visible.

Selected References

- ◆ Nahata MC, Morosco RS, Hippel TF: Stability of captopril in liquid containing ascorbic acid or sodium ascorbate. *Am J Hosp Pharm* 1994;1707-1708.
- ◆ Perlman JM, Volpe JJ: Neurologic complications of captopril treatment of neonatal hypertension. *Pediatrics* 1989;83:47.
- ◆ O'Dea RF, Mirkin BL, Alward CT: Treatment of neonatal hypertension with captopril. *J Pediatr* 1988;113:403.

Added 1/94

References updated 3/2007

Dose & Administration

Loading doses: ("Digitalization") are generally used only when treating arrhythmias and acute congestive heart failure. Give over 24 hours as 3 divided doses. Administer IV slow push over 5 to 10 minutes.

Oral doses should be 25% greater than IV doses. Do not administer IM.

Note: These beginning doses are based primarily on studies that measured echocardiographic changes and EKG signs of toxicity and take into account renal maturation. We recommend titrating dosage based on clinical response. Decrease dose proportional to the reduction in creatinine clearance.

Total Loading Dose

PMA weeks	IV mcg/kg	PO mcg/kg
≤29	15	20
30 to 36	20	25
37 to 48	30	40
≥49	40	50
Divide into 3 doses over 24 hours		

Maintenance Doses

PMA weeks	IV mcg/kg	PO mcg/kg	Interval hours
≤29	4	5	24
30 to 36	5	6	24
37 to 48	4	5	12
≥49	5	6	12
Titrate based on clinical response			

Uses

Treatment of heart failure caused by diminished myocardial contractility. Treatment of SVT, atrial flutter, and atrial fibrillation.

Monitoring

Follow heart rate and rhythm closely. Periodic EKGs to assess both desired effects and signs of toxicity. Follow closely (especially in patients receiving diuretics or amphotericin B) for decreased serum potassium and magnesium, or increased calcium and magnesium, all of which predispose to digoxin toxicity. Assess renal function. Be aware of drug interactions. May follow serum drug concentrations if assay is available that excludes endogenous digoxin-like substances. Therapeutic serum concentration is 1 to 2 ng/mL.

Adverse Effects/Precautions

Toxic Cardiac Effects:

- PR interval prolongation
- Sinus bradycardia or SA block
- Atrial or nodal ectopic beats
- Ventricular arrhythmias

Nontoxic Cardiac Effects:

- QTc interval shortening
- ST segment sagging
- T-wave amplitude dampening
- Heart rate slowing

Other Effects: Feeding intolerance, vomiting, diarrhea, and lethargy.

Treatment of Life-Threatening Digoxin Toxicity:

Digibind® Digoxin Immune Fab, IV over 30 minutes through 0.22 micron filter.

$$\text{Dose (# of vials)} = \frac{(\text{weight [kg]}) \times (\text{serum digoxin concentration})}{100}$$

Each vial of digibind contains 38 mg (enough to bind 0.5 mg Digoxin).

continued...

Pharmacology

Digitalis glycoside with positive inotropic and negative chronotropic actions. Increases myocardial catecholamine levels (low doses) and inhibits sarcolemmal sodium-potassium-ATPase (higher doses) to enhance contractility by increasing systolic intracellular calcium-ion concentrations. Indirectly increases vagal activity, thereby slowing S-A node firing and A-V node conduction. Other effects include peripheral, splanchnic, and perhaps, pulmonary vasoconstriction, and reduced CSF production. Serum concentration peaks 30 to 90 minutes after an oral dose, with myocardial peak occurring in 4 to 6 hours. Large volume of distribution that increases with age during infancy. Rapid absorption of oral dose from small intestine; reduced by antacids and rapid transit times. 20% protein bound. Probably not significantly metabolized. Glomerular filtration and tubular secretion account for most of the total body clearance of digoxin, although significant nonrenal elimination has been proposed.

Special Considerations/Preparation

Pediatric dosage forms: Injectable (100 mcg/mL) and elixir (50 mcg/mL).

Store at room temperature and protect from light.

Dilute injectable as follows:

- 1) Draw up digoxin into syringe.
- 2) Inject desired amount of drug into second syringe containing a fourfold or greater volume of solution-compatible diluent. Use diluted product immediately.

Drug Interactions: Amiodarone, indomethacin, spironolactone, quinidine, and verapamil decrease digoxin clearance. Cisapride and metoclopramide decrease digoxin absorption. Spironolactone interferes with radioimmunoassay. Erythromycin may increase digoxin absorption.

Solution Compatibility: (only when diluted fourfold or greater): D₅W, D₁₀W, NS, and sterile water for injection.

Terminal Injection Site Compatibility: Dex/AA solutions, fat emulsion. Cimetidine, ciprofloxacin, famotidine, furosemide, heparin, hydrocortisone succinate, insulin, lidocaine, linezolid, meropenem, midazolam, milrinone, morphine, potassium chloride, propofol, prostaglandin E₁, ranitidine, and remifentanil.

Incompatibility: Amiodarone, dobutamine and fluconazole.

Selected References

- ◆ Smith TW: Digitalis: Mechanisms of action and clinical use. *N Engl J Med* 1988;318:358.
- ◆ Roberts RJ: *Drug Therapy in Infants*. Philadelphia: WB Saunders Co, 1984, p 138.
- ◆ Johnson GL, Desai NS, Pauly TH, Cunningham MD: Complications associated with digoxin in low-birth-weight infants. *Pediatrics* 1982;69:463.
- ◆ Nyberg L, Wettrell G: Pharmacokinetics and dosage of digoxin in neonates and infants. *Eur J Clin Pharmacol* 1980;18:69.
- ◆ Pinsky WW, Jacobsen JR, Gillette PC, et al: Dosage of digoxin in premature infants. *J Pediatr* 1979;96:639.
- ◆ Product Information, GlaxoSmithKline, 2002

Special Considerations updated 3/2002

Compatibilities updated 3/2005

References updated 3/2004

Dose & Administration

2 to 25 mcg/kg per minute continuous IV infusion. Begin at a low dose and titrate by monitoring effects. Use a large vein for IV.

Solution Preparation Calculations

To calculate the AMOUNT of drug needed per defined final fluid volume:

Desired final concentration (mg/mL) x defined final fluid volume (mL) = AMOUNT of drug to add to final infusion solution (mg).

To calculate the VOLUME of drug needed per defined final fluid volume:

$$\frac{\text{*AMOUNT of drug to add (mg)}}{\text{drug (vial) concentration (mg/mL)}} = \text{VOLUME of drug to add (mL)}$$

Example (for Dobutamine): Mix 30 mL of 800 mcg/mL solution using dobutamine concentration of 12.5 mg/mL.

$$800 \text{ mcg/mL} = 0.8 \text{ mg/mL}$$

$$0.8 \text{ mg/mL} \times 30 \text{ mL} = 24 \text{ mg dobutamine}$$

$$\frac{\text{*24 mg}}{\text{12.5 mg/mL}} = 1.9 \text{ mL of dobutamine}$$

Add 1.9 mL of dobutamine (12.5 mg/mL) to 28.1 mL of compatible solution (eg, D₅W) to yield 30 mL of infusion solution with a concentration of 800 mcg/mL.

Dobutamine Titration Chart

Concentration (mcg/mL)	Dose (mcg/kg/min)	IV Rate (mL/kg/hour)
500	2.5	0.3
	5	0.6
	7.5	0.9
	10	1.2
800	2.5	0.19
	5	0.38
	7.5	0.56
	10	0.75
1000	2.5	0.15
	5	0.3
	7.5	0.45
	10	0.6
1600	2.5	0.094
	5	0.19
	7.5	0.28
	10	0.38
2000	2.5	0.075
	5	0.15
	7.5	0.23
	10	0.3
3200	2.5	0.047
	5	0.094
	7.5	0.14
	10	0.19
4000	2.5	0.038
	5	0.075
	7.5	0.11
	10	0.15

continued...

Uses

Treatment of hypoperfusion and hypotension, especially if related to myocardial dysfunction.

Monitoring

Continuous heart rate and intra-arterial blood pressure monitoring preferable. Observe IV site for signs of extravasation.

Adverse Effects/Precautions

May cause hypotension if patient is hypovolemic. Volume loading is recommended before starting dobutamine therapy. Tachycardia occurs at high dosage. Arrhythmias, hypertension, and cutaneous vasodilation. Increases myocardial oxygen consumption. Tissue ischemia occurs with infiltration.

Pharmacology

Synthetic catecholamine with primarily β_1 -adrenergic activity. Inotropic vasopressor. Increases myocardial contractility, cardiac index, oxygen delivery, and oxygen consumption. Decreases systemic and pulmonary vascular resistance (adults). Dobutamine has a more prominent effect on cardiac output than dopamine but less of an effect on blood pressure. Onset of action is 1 to 2 minutes after IV administration, with peak effect in 10 minutes. Must be administered by continuous IV infusion because of rapid metabolism of drug. Serum half-life is several minutes. Metabolized in the liver by sulfoconjugation to an inactive compound. There is wide interpatient variability in plasma clearance due to differences in metabolism and renal excretion.

Special Considerations/Preparation

Supplied as 250 mg per 20 mL vial (12.5 mg/mL). Diluted solutions for infusion should be used within 24 hours.

There are no specific data regarding the compatibility of dobutamine and fat emulsions. Dobutamine is most stable in solutions with a pH at or below 5. In alkaline solutions, the catechol moieties are oxidized, cyclized, and polymerized to colored materials. All fat emulsions have pH ranges from 6 to 9. Caution is urged when co-infusing dobutamine and fat emulsion together; dobutamine may degrade over time in this alkaline pH resulting in lower than expected clinical effects.

Solution Compatibility: D₅W, D₅NS, D₁₀W, LR, and NS.

Terminal Injection Site Compatibility: Dex/AA solutions. Amiodarone, atropine, aztreonam, caffeine citrate, calcium chloride, calcium gluconate, ciprofloxacin, dopamine, enalaprilat, epinephrine, famotidine, fentanyl, fluconazole, flumazenil, heparin, hydralazine, insulin, isoproterenol, lidocaine, linezolid, lorazepam, magnesium sulfate, meropenem, midazolam, milrinone, morphine, nicaldipine, nitroglycerin, nitroprusside, pancuronium bromide, phentolamine, potassium chloride, procainamide, propofol, propranolol, phytonadione, ranitidine, remifentanil, vecuronium, and zidovudine.

Incompatibility: Acyclovir, alteplase, aminophylline, cefepime, bumetanide, diazepam, digoxin, furosemide, indomethacin, micafungin, phenytoin, piperacillin-tazobactam, and sodium bicarbonate.

continued...

Selected References

- ◆ Noori S, Friedlich P, Seri I: The use of dobutamine in the treatment of neonatal cardiovascular compromise. *NeoReviews* 2004;5:e22-e26.
- ◆ Berg RA, Donnerstein RL, Padbury JF: Dobutamine infusion in stable, critically ill children: pharmacokinetics and hemodynamic actions. *Crit Care Med* 1993;21:678-86.
- ◆ Martinez AM, Padbury JF, Thio S: Dobutamine pharmacokinetics and cardiovascular responses in critically ill neonates. *Pediatrics* 1992;89:47.
- ◆ Leier CV, Unverferth DV: Dobutamine. *Ann Intern Med* 1983;99:490.
- ◆ Perkin RM, Levin DL, Webb R, et al: Dobutamine: A hemodynamic evaluation in children with shock. *J Pediatr* 1982;100:977.
- ◆ Product Information, Bedford, 2005

Special Considerations updated 3/2008

References and Compatibilities updated 3/2007

CARDIOVASCULAR

Dose & Administration

2 to 20 mcg/kg per minute continuous IV infusion. Begin at a low dose and titrate by monitoring effects. Use a large vein for IV.

Solution Preparation Calculations

To calculate the AMOUNT of drug needed per defined final fluid volume:

Desired final concentration (mg/mL) x defined final fluid volume (mL) = AMOUNT of drug to add to final infusion solution (mg).

To calculate the VOLUME of drug needed per defined final fluid volume:

$$\frac{\text{*AMOUNT of drug to add (mg)}}{\text{drug (vial) concentration (mg/mL)}} = \text{VOLUME of drug to add (mL)}$$

Example (for Dopamine): Mix 30 mL of 800 mcg/mL solution using dopamine concentration of 40 mg/mL.

$$800 \text{ mcg/mL} = 0.8 \text{ mg/mL}$$

$$0.8 \text{ mg/mL} \times 30 \text{ mL} = 24 \text{ mg dopamine}$$

$$\frac{\text{*24 mg}}{\text{40 mg/mL}} = 0.6 \text{ mL of dopamine}$$

Add 0.6 mL of dopamine (40 mg/mL) to 29.4 mL of compatible solution (eg, D₅W) to yield 30 mL of infusion solution with a concentration of 800 mcg/mL.

Dopamine Titration Chart

Concentration (mcg/mL)	Dose (mcg/kg/min)	IV Rate (mL/kg/hour)
500	2.5	0.3
	5	0.6
	7.5	0.9
	10	1.2
800	2.5	0.19
	5	0.38
	7.5	0.56
	10	0.75
1000	2.5	0.15
	5	0.3
	7.5	0.45
	10	0.6
1600	2.5	0.094
	5	0.19
	7.5	0.28
	10	0.38
2000	2.5	0.075
	5	0.15
	7.5	0.23
	10	0.3
3200	2.5	0.047
	5	0.094
	7.5	0.14
	10	0.19

continued...

Uses

Treatment of hypotension.

Monitoring

Continuous heart rate and intra-arterial blood pressure monitoring is preferable. Assess urine output and peripheral perfusion frequently. Observe IV site closely for blanching and infiltration.

Adverse Effects/Precautions

Tachycardia and arrhythmias. May increase pulmonary artery pressure. Reversible suppression of prolactin and thyrotropin secretion.

Black Box Warning Tissue sloughing may occur with IV infiltration. According to the manufacturer's black box warning, to prevent sloughing and necrosis in areas of extravasation, the area should be infiltrated as soon as possible with a saline solution containing phentolamine mesylate.

Suggested treatment: Inject a 0.5 mg/mL solution of phentolamine into the affected area. The usual amount needed is 1 to 5 mL, depending on the size of the infiltrate.

Pharmacology

Catecholamine. Metabolized rapidly. Serum half-life is 2 to 5 minutes, but clearance is quite variable.

Dopamine increases blood pressure primarily by increasing systemic vascular resistance via α -adrenergic effects. Effects on cardiac output vary with gestational age and baseline stroke volume. Selective renal vasodilation associated with increases in urine output has been noted in preterm neonates at doses of 2 to 5 mcg/kg/minute. No changes in mesenteric or cerebral blood flow were observed. Mechanism of action in neonates is controversial. Relative effects of dopamine at different doses are uncertain because of developmental differences in 1) endogenous norepinephrine stores, 2) α -adrenergic, β -adrenergic, and dopaminergic receptor functions, and 3) the ability of the neonatal heart to increase stroke volume. Responses tend to be individualized. Use higher doses with caution in patients with persistent pulmonary hypertension of the newborn.

Special Considerations/Preparation

Available in 40-mg/mL, 80-mg/mL, and 160-mg/mL vials for injection and premixed bags in concentrations of 800-, 1600-, and 3200-mcg/mL. Diluted solutions stable for 24 hours. **Admixtures exhibiting a color change should not be used.**

There are no specific data regarding the compatibility of dopamine and fat emulsions. Dopamine is most stable in solutions with a pH at or below 5. In alkaline solutions, the catechol moieties are oxidized, cyclized, and polymerized to colored materials. All fat emulsions have pH ranges from 6 to 9. Caution is urged when co-infusing dopamine and fat emulsion together; dopamine may degrade over time in this alkaline pH resulting in lower than expected clinical effects.

Solution Compatibility: D₅W, D₅NS, D₁₀W, LR, and NS.

Terminal Injection Site Compatibility: Dex/AA solutions. Aminophylline, amiodarone, ampicillin, aztreonam, caffeine citrate, calcium chloride, chloramphenicol, dobutamine, enalaprilat, epinephrine, esmolol, famotidine, fentanyl, fluconazole, flumazenil, gentamicin, heparin, hydrocortisone succinate, lidocaine, linezolid, lorazepam, meropenem, metronidazole, micafungin, midazolam, milrinone, morphine, nicardipine, nitroglycerin, nitroprusside, oxacillin, pancuronium bromide, penicillin G, piperacillin-tazobactam, potassium chloride, propofol, prostaglandin E₁, ranitidine, tobramycin, vecuronium, and zidovudine.

Incompatibility: Acyclovir, alteplase, amphotericin B, cefepime, furosemide, indomethacin, insulin, and sodium bicarbonate.

Selected References

- ◆ Valverde E, Pellicer A, Madero R, et al: Dopamine versus epinephrine for cardiovascular support in low birth weight infants: analysis of systemic effects and neonatal clinical outcomes. *Pediatrics* 2006;117:e1213-e1222.
- ◆ Lynch SK, Lemley KV, Polak MJ: The effect of dopamine on glomerular filtration rate in normotensive, oliguric premature neonates. *Pediatr Nephrol* 2003;18:649-652.
- ◆ Seri I, Abbasi S, Wood DC, Gerdes JS: Regional hemodynamic effects of dopamine in the sick preterm neonate. *J Pediatr* 1998;133:728-734.
- ◆ Seri I: Cardiovascular, renal, and endocrine actions of dopamine in neonates and children. *J Pediatr* 1995;126:333.
- ◆ Filippi L, Pezzati M, Cecchi A, et al: Dopamine infusion and anterior pituitary gland function in very low birth weight infants. *Biol Neonate* 2006;89:274-280.
- ◆ Van den Berghe G, de Zegher F, Lauwers P: Dopamine suppresses pituitary function in infants and children. *Crit Care Med* 1994;22:1747.
- ◆ Roze JC, Tohier C, Maingueneau C, et al: Response to dobutamine and dopamine in the hypotensive very preterm infant. *Arch Dis Child* 1993;69:59-63.
- ◆ Padbury JF, Agata Y, Baylen BG, et al: Dopamine pharmacokinetics in critically ill newborn infants. *J Pediatr* 1987;110:293.
- ◆ DiSessa TG, Leitner M, Ti CC, et al: The cardiovascular effects of dopamine in the severely asphyxiated neonate. *J Pediatr* 1981;99:772.
- ◆ Product Information, American Regent, 2001

Adverse Effects/Precautions updated 1/2009

Special Considerations and References updated 3/2008

Compatibilities updated 3/2007

Dose & Administration

Begin with 40 mcg/kg per dose (0.04 mg/kg per dose) given PO Q24 hours. Usual maximum dose 150 mcg/kg per dose (0.15 mg/kg per dose), as frequently as Q6 hours. Titrate subsequent doses and interval based on amount and duration of response. Dosage may need to be increased every few days.

Uses

Treatment of moderate to severe hypertension. Afterload reduction in patients with congestive heart failure.

Monitoring

Frequent assessment of blood pressure, particularly after the first dose. Periodic assessment of renal function and serum potassium.

Adverse Effects/Precautions

Use with extreme caution in patients with impaired renal function: oliguria and increased serum creatinine occur frequently. Hypotension occurs primarily in patients who are volume-depleted. Hyperkalemia occurs primarily in patients receiving potassium-sparing diuretics or potassium supplements. Cough has been reported frequently in adults.

Pharmacology

Enalapril is a prodrug that is hydrolyzed in the liver to form the active angiotensin-converting enzyme (ACE) inhibitor enalaprilat, which blocks the conversion of angiotensin I to angiotensin II, a potent vasoconstrictor. It thereby decreases plasma and tissue concentrations of angiotensin II and aldosterone, and increases plasma and tissue renin activity. Enalaprilat also prevents the breakdown of bradykinin, a potent vasodilator. Vascular resistance is reduced without reflex tachycardia. Beneficial effects are thought to be caused by a combination of afterload reduction and long-term inhibition of salt and water retention. Bioavailability of oral dosage form is uncertain in neonates, but is significantly less than the 60% reported in adults. Onset of action after oral dose is 1 to 2 hours. Duration of action is quite variable in neonates, ranging from 8 to 24 hours.

Special Considerations/Preparation

Supplied in 2.5-mg, 5-mg, 10-mg, and 20-mg tablets. Enalapril maleate oral suspension can be prepared by crushing a 2.5 mg tablet and adding to 25 mL of isotonic citrate buffer, yielding a final concentration of 100 mcg/mL (0.1 mg/mL). Suspension is stable for 30 days refrigerated.

Selected References

- ◆ Schilder JLAM, Van den Anker JN: Use of enalapril in neonatal hypertension. *Acta Paediatr* 1995;84:1426.
- ◆ Nahata MC, Morosco RS, Hippel TF: Stability of enalapril maleate in three extemporaneously prepared oral liquids. *Am J Health Syst Pharm* 1998;55:1155-1157.
- ◆ Mason T, Polak MJ, Pyles L, et al: Treatment of neonatal renovascular hypertension with intravenous enalapril. *Am J Perinatol* 1992;9:254.
- ◆ Rasoulpour M, Marinelli KA: Systemic hypertension. *Clin Perinatol* 1992;19:121.
- ◆ Wells TG, Bunchman TE, Kearns GL: Treatment of neonatal hypertension with enalaprilat. *J Pediatr* 1990;117:665.
- ◆ Frenneaux M, Stewart RAH, Newman CMH, Hallidie-Smith KA: Enalapril for severe heart failure in infancy. *Arch Dis Child* 1989;64:219.
- ◆ Product Information, Ivax Pharmaceuticals, Inc., 2003

Text updated 3/97

References updated 3/2007

Dose & Administration

Begin with 10 mcg/kg per dose (0.01 mg/kg per dose) IV over 5 minutes Q24 hours. Titrate subsequent doses and interval based on amount and duration of response. Dosage may need to be increased every few days.

Uses

Treatment of moderate to severe hypertension. Afterload reduction in patients with congestive heart failure.

Monitoring

Frequent assessment of blood pressure, particularly after the first dose. Periodic assessment of renal function and serum potassium.

Adverse Effects/Precautions

Use with extreme caution in patients with impaired renal function: oliguria and increased serum creatinine occur frequently. Hypotension occurs primarily in patients who are volume-depleted. Hyperkalemia occurs primarily in patients receiving potassium-sparing diuretics or potassium supplements. Cough has been reported frequently in adults.

Pharmacology

Enalaprilat is an ACE inhibitor which blocks the production of the potent vasoconstrictor angiotensin II. It thereby decreases plasma and tissue concentrations of angiotensin II and aldosterone, and increases plasma and tissue renin activity. Enalaprilat also prevents the breakdown of bradykinin, a potent vasodilator. Vascular resistance is reduced without reflex tachycardia. Beneficial effects are thought to be caused by a combination of afterload reduction and long-term inhibition of salt and water retention. Duration of action is quite variable in neonates, ranging from 8 to 24 hours.

Special Considerations/Preparation

Enalaprilat is supplied as a 1.25 mg/mL solution for injection in 1 mL and 2 mL vials. Benzyl alcohol content is 9 mg/mL. To make a dilution for IV use, take 1 mL (1.25 mg) of solution and add 49 mL NS to make a final concentration of 25 mcg/mL (0.025 mg/mL). Dilution stable for 24 hours.

Solution Compatibility: D₅W, D₅NS, and NS.

Terminal Injection Site Compatibility: Fat emulsion. Amikacin, aminophylline, ampicillin, aztreonam, calcium gluconate, cefazolin, ceftazidime, chloramphenicol, cimetidine, clindamycin, dobutamine, dopamine, erythromycin lactobionate, esmolol, famotidine, fentanyl, gentamicin, heparin, hydrocortisone succinate, lidocaine, linezolid, magnesium sulfate, meropenem, metronidazole, morphine, nafcillin, nicardipine, nitroprusside, penicillin G, phenobarbital, piperacillin, piperacillin-tazobactam, potassium chloride, propofol, ranitidine, remifentanil, tobramycin, trimethoprim-sulfamethoxazole, and vancomycin.

Incompatibility: Amphotericin B, cefepime, and phenytoin.

continued

Selected References

- ◆ Schilder JLAM, Van den Anker JN: Use of enalapril in neonatal hypertension. *Acta Paediatr* 1995;84:1426.
- ◆ Mason T, Polak MJ, Pyles L, et al: Treatment of neonatal renovascular hypertension with intravenous enalapril. *Am J Perinatol* 1992;9:254.
- ◆ Rasoulpour M, Marinelli KA: Systemic hypertension. *Clin Perinatol* 1992;19:121.
- ◆ Wells TG, Bunchman TE, Kearns GL: Treatment of neonatal hypertension with enalaprilat. *J Pediatr* 1990;117:665.
- ◆ Frenneaux M, Stewart RAH, Newman CMH, Hallidie-Smith KA: Enalapril for severe heart failure in infancy. *Arch Dis Child* 1989;64:219.
- ◆ Product Information, Hospira, 2006

Text updated 3/2008

Compatibilities updated 3/2005

(Low Molecular Weight Heparin)**Dose & Administration****Initial treatment of thrombosis:**

Term infants: 1.7 mg/kg per dose subQ every 12 hours.

Preterm infants: 2 mg/kg per dose subQ every 12 hours.

Adjust dosage to maintain anti-factor X_a level between 0.5 and 1.0 units/mL. It will usually take several days to attain levels in the target range.

Dosage requirements to maintain target anti-factor X_a levels in preterm infants are quite variable, ranging from 0.8 to 3 mg/kg every 12 hours. Infants older than 3 months of age: 1 mg/kg per dose subQ every 12 hours.

Call 1-800-NOCLOTS for case reporting and treatment guidance.

Low-risk prophylaxis: 0.75 mg/kg per dose subQ every 12 hours.

Infants older than 3 months of age: 0.5 mg/kg per dose subQ every 12 hours.

Adjust dosage to maintain anti-factor X_a level between 0.1 and 0.4 units/mL.

Administration may be aided by using a small plastic indwelling subcutaneous catheter (Insuflon®, Hypoguard USA). Adverse events related to these catheters are much more frequent in ELBW infants.

Uses

Anticoagulation. Advantages over standard unfractionated heparin:

(1) may be given subcutaneously, (2) more predictable pharmacokinetics, (3) dosing every 8 to 12 hours, (4) less frequent bleeding complications.

Monitoring

Measure anti-factor X_a concentrations 4 hours after a dose (See above for desired range). Preterm infants are likely to require several dosage adjustments to achieve the target levels. After attaining target levels, dosage adjustments will be necessary once or twice a month, perhaps more often in preterm infants and infants with hepatic or renal dysfunction. Assess for signs of bleeding and thrombosis.

Adverse Effects/Precautions

Major bleeding may occur even with anti-factor X_a levels in the therapeutic range. The overall incidence is approximately 4%. Reported complications include major bleeding or hematoma at the administration site, compartment syndrome, intracranial hemorrhage, and gastrointestinal hemorrhage.

Pharmacology

Enoxaparin is a low-molecular weight heparin that has considerably less activity against thrombin than does standard heparin. Efficacy in neonates is decreased due to low antithrombin plasma concentrations. It is also much less likely to interfere with platelet function or cause osteoporosis. It activates antithrombin III, which progressively inactivates both thrombin and factor X_a , key proteolytic enzymes in the formation of fibrinogen and activation of prothrombin. Bioavailability is almost 100% after subcutaneous administration, with peak activity 2.5 to 4 hours later. The apparent half-life of anti- X_a activity is 4 to 5 hours. Clearance in neonates is more rapid than in older infants, children or adults.

continued

Special Considerations/Preparation

Available as 100 mg/mL concentration as 30 mg/0.3 mL, 40 mg/0.4 mL, 60 mg/0.6 mL, 80 mg/0.8 mL, 100 mg/mL in preservative-free prefilled syringes. Multidose vial available in 100 mg/mL concentration with 15 mg benzyl alcohol per 1 mL as a preservative.

Solution Compatibility: NS and sterile water.

Selected References

- ◆ Malowany JI, Monagle P, Knoppert DC, et al: Enoxaparin for neonatal thrombosis: a call for a higher dose in neonates. *Thrombosis Research* 2008; in press.
- ◆ Malowany JI, Knoppert DC, Chan AKC, et al: Enoxaparin use in the neonatal intensive care unit: experience over 8 years. *Pharmacotherapy* 2007;27:1263-1271.
- ◆ Streif W, Goebel G, Chan AKC, Massicotte MP: Use of low molecular mass heparin (enoxaparin) in newborn infants: a prospective cohort study of 62 newborn infants. *Arch Dis Child Fetal Neonatal Ed* 2003;88:F365-F370.
- ◆ Fareed J, Hoppensteadt D, Walenga J, et al: Pharmacodynamic and pharmacokinetic properties of enoxaparin. *Clin Pharmacokinet* 2003;42:1043-57.
- ◆ Edstrom CS, Christensen RD: Evaluation and treatment of thrombosis in the neonatal intensive care unit. *Clin Perinatol* 2000;27:623-41.
- ◆ Dunaway KK, Gal P, Ransom JL: Use of enoxaparin in a preterm infant. *Ann Pharmacother* 2000;34:1410-3.
- ◆ Klinger G, Hellmann J, Daneman A: Severe aortic thrombosis in the neonate - successful treatment with low-molecular-weight heparin: Two case reports and review of the literature. *Am J Perinatol* 2000;17:151-8.
- ◆ Product Information, Sanofi-Aventis, 2007

Dose, Administration, Adverse Effects, Special Considerations, and References updated 3/2008

Dose & Administration

Resuscitation and severe bradycardia: 0.1 to 0.3 mL/kg 1:10,000 concentration; equal to 0.01 to 0.03 mg/kg (10 to 30 mcg/kg). IV push, or IC.

May be given ET using higher doses, up to 0.1 mg/kg (100 mcg/kg), immediately followed by 1 mL NS. Do **not** administer these higher doses of epinephrine intravenously.

IV continuous infusion: Start at 0.1 mcg/kg per minute and adjust to desired response, to a maximum of 1 mcg/kg per minute.

If possible, correct acidosis before administration of epinephrine to enhance the effectiveness of the drug.

Solution Preparation Calculations

To calculate the AMOUNT of drug needed per defined final fluid volume:

Desired final concentration (mg/mL) x defined final fluid volume (mL) = AMOUNT of drug to add to final infusion solution (mg).

To calculate the VOLUME of drug needed per defined final fluid volume:

$$\frac{\text{*AMOUNT of drug to add (mg)}}{\text{drug (vial) concentration (mg/mL)}} = \text{VOLUME of drug to add (mL)}$$

Example (for Epinephrine): Mix 50 mL of 20 mcg/mL solution using epinephrine concentration of 1 mg/mL.

$$20 \text{ mcg/mL} = 0.02 \text{ mg/mL}$$

$$0.02 \text{ mg/mL} \times 50 \text{ mL} = 1 \text{ mg epinephrine}$$

$$\frac{\text{*1 mg}}{\text{1 mg/mL}} = 1 \text{ mL of epinephrine}$$

Add 1 mL of epinephrine (1:1000) to 49 mL of compatible solution (eg, D₅W) to yield 50 mL of infusion solution with a concentration of 20 mcg/mL.

Maximum concentration 64 mcg/mL.

Epinephrine (Adrenaline)

Epinephrine Titration Chart

Concentration (mcg/mL)	Dose (mcg/kg/min)	IV Rate (mL/kg/hour)
10	0.05	0.3
	0.1	0.6
	0.5	3
	1	6
20	0.05	0.15
	0.1	0.3
	0.5	1.5
	1	3
30	0.05	0.1
	0.1	0.2
	0.5	1
	1	2
40	0.05	0.075
	0.1	0.15
	0.5	0.75
	1	1.5
50	0.05	0.06
	0.1	0.12
	0.5	0.6
	1	1.2
60	0.05	0.05
	0.1	0.1
	0.5	0.5
	1	1

Uses

Acute cardiovascular collapse. Short-term use for treatment of systemic hypotension. Despite the widespread use of epinephrine/adrenaline during resuscitation, no placebo-controlled studies have evaluated either the tracheal or intravenous administration of epinephrine at any stage during cardiac arrest in human neonates. Nonetheless, it is reasonable to continue to use epinephrine when adequate ventilation and chest compressions have failed to increase the heart rate to >60 beats per minute.

Monitoring

Monitor heart rate and blood pressure continuously. Observe IV site for signs of infiltration.

Adverse Effects/Precautions

Compared to dopamine, continuous infusions at doses yielding similar changes in blood pressure are more likely to cause hyperglycemia, tachycardia, and elevations in serum lactate. Cardiac arrhythmias (PVCs and ventricular tachycardia) are also more likely. Renal vascular ischemia may occur at higher doses. Bolus doses are associated with severe hypertension and intracranial hemorrhage. Increased myocardial oxygen requirements.

IV infiltration may cause tissue ischemia and necrosis. Suggested treatment: Inject a 1 mg/mL solution of phentolamine into the affected area. The usual amount needed is 1 to 5 mL, depending on the size of the infiltrate.

continued...

Pharmacology

Epinephrine (adrenaline) is the major hormone secreted by the adrenal medulla. It is a potent stimulator of both alpha and beta adrenergic receptors, with complex effects on body organ systems. Low doses are associated with systemic and pulmonary vasodilation. Higher doses increase blood pressure by direct myocardial stimulation, increases in heart rate, and vasoconstriction. Myocardial oxygen consumption is increased. Blood flow to skeletal muscle, brain, liver, and myocardium is increased. However, blood flow to the kidney is decreased due to increased vascular resistance.

Special Considerations/Preparation

Always use as a 1:10,000 concentration (0.1 mg/mL) for individual doses.

Use 1:1000 (1 mg/mL) concentration to prepare continuous infusion solution.

Protect from light.

Solution Compatibility: D₅W, D₁₀W, and NS.

Terminal Injection Site Compatibility: Dex/AA. Amikacin, amiodarone, ampicillin, caffeine citrate, calcium chloride, calcium gluconate, cimetidine, dobutamine, dopamine, famotidine, fentanyl, furosemide, heparin, hydrocortisone succinate, lorazepam, midazolam, milrinone, morphine, nicardipine, nitroglycerin, nitroprusside, pancuronium bromide, potassium chloride, propofol, prostaglandin E₁, ranitidine, remifentanil, vecuronium, and vitamin K₁.

Incompatibility: Aminophylline, hyaluronidase, micafungin, and sodium bicarbonate.

Selected References

- ◆ International Liaison Committee on Resuscitation: The International Liaison Committee on Resuscitation (ILCOR) consensus on science with treatment recommendations for pediatric and neonatal patients: neonatal resuscitation. *Pediatrics* 2006;117:e978-e988. URL: <http://www.pediatrics.org/cgi/content/full/117/5/e978>.
- ◆ Barber CA, Wyckoff MH: Use and efficacy of endotracheal versus intravenous epinephrine during neonatal cardiopulmonary resuscitation in the delivery room. *Pediatrics* 2006;118:1028-1034.
- ◆ Valverde E, Pellicer A, Madero R, et al: Dopamine versus epinephrine for cardiovascular support in low birth weight infants: analysis of systemic effects and neonatal clinical outcomes. *Pediatrics* 2006;117(6):e1213-22. URL: <http://www.pediatrics.org/cgi/content/full/117/6/e1213>.
- ◆ Pellicer A, Valverde E, Elorza MD, et al: Cardiovascular support for low birth weight infants and cerebral hemodynamics: a randomized, blinded clinical trial. *Pediatrics* 2005; 115: 1501-1512.
- ◆ Burchfield DJ: Medication use in neonatal resuscitation. *Clin Perinatol* 1999;26:683-691.

Updated 3/2008

Compatibilities updated 3/2005



Dose & Administration

Starting IV doses:

Supraventricular tachycardia (SVT): 100 mcg/kg per minute continuous infusion. Increase in increments of 50 to 100 mcg/kg per minute every 5 minutes until control of the ventricular rate is achieved.

Acute management of postoperative hypertension: 50 mcg/kg per minute continuous infusion. Increase in increments of 25 to 50 mcg/kg per minute every 5 minutes until desired blood pressure is achieved.

Usual maximum dosage: 200 mcg/kg per minute.

Doses greater than 300 mcg/kg per minute are likely to cause hypotension.

Uses

Short term treatment of postoperative hypertension, supraventricular tachycardia (SVT), and ventricular tachycardia (VT).

Monitoring

Continuous EKG monitoring during acute treatment of arrhythmias. Measure systemic blood pressure and heart rate frequently.

Adverse Effects/Precautions

May cause hypotension in high doses. Adverse effects reversible with discontinuation of drug. Monitor IV site closely for vein irritation and phlebitis, especially at high concentrations (> 10 mg/mL).

Pharmacology

Esmolol is a potent cardio-selective beta-blocking agent with a uniquely short half-life (2.8 to 4.5 minutes) and a brief (10 to 15 minute) duration of action. There appears to be no correlation between age and pharmacodynamic response or pharmacokinetic profile. Esmolol is cleared primarily by red blood cell esterases. Renal or hepatic failure does not effect elimination.

Special Considerations/Preparation

Esmolol is supplied in preservative-free 10 mL (10 mg/mL) and a 5-mL (20 mg/mL) ready-to-use vials and 2500 mg/250 mL and 2000 mg/100 mL ready to use premixed bags. The pH is approximately 3.5-5.5. Osmolarity is 312 mOsm/L. Store at room temperature.

Solution Compatibility: D₅W, LR, and NS.

Terminal Injection Site Compatibility: Amikacin, aminophylline, atracurium, calcium chloride, cefazolin, ceftazidime, chloramphenicol, cimetidine, clindamycin, digoxin, dopamine, enalaprilat, erythromycin lactobionate, famoditine, fentanyl, gentamicin, heparin, hydrocortisone, insulin, lidocaine, linezolid, magnesium sulfate, metronidazole, micafungin, midazolam, morphine, nafcillin, nicardipine, nitroglycerin, norepinephrine, pancuronium, penicillin G, phenytoin, piperacillin, potassium chloride, propofol, ranitidine, remifentanil, sodium nitroprusside, tobramycin, trimethoprim-sulfamethoxazole, vancomycin, and vecuronium.

Incompatibility: Amphotericin B, diazepam, furosemide, and procainamide.

Selected References

- ◆ Wiest DB, Garner SS, Uber WE, et al: Esmolol for the management of pediatric hypertension after cardiac operations. *J Thoracic Cardiov Surg* 1998;115:890-897.
- ◆ Cuneo B, Zales VR, Blahunka PC, et al: Pharmacodynamics and pharmacokinetics of esmolol, a short-acting β -blocking agent, in children. *Pediatr Cardiol* 1994;15:296-301.
- ◆ Trippel MD, Wiest DB, Gillette PC: Cardiovascular and antiarrhythmic effects of esmolol in children. *J Pediatr* 1991;119:142-147.
- ◆ Wiest DB, Trippel MD, Gillette PC, et al: Pharmacokinetics of esmolol in children. *Clin Pharmacol Ther* 1991;49:618-623.
- ◆ Product Information, Baxter, 2007.

Added 3/2006

Dose and Compatibilities updated 3/2007

Dose & Administration

Begin at 2 mg/kg per dose Q12 hours PO. Adjust dose based on response and serum concentrations to a maximum of 4 mg/kg per dose Q12 hours. Correct preexisting hypokalemia or hyperkalemia before administration. Optimal effect may take 2 to 3 days of therapy to achieve, and steady-state plasma levels may not be reached until 3 to 5 days at a given dosage in patients with normal renal and hepatic function. Therefore, do not increase dosage more frequently than approximately once every 4 days.

Uses

Treatment of supraventricular arrhythmias not responsive to conventional therapies. Contraindicated in patients with structurally abnormal hearts.

Monitoring

Continuous EKG during initiation of therapy, as this is the most common time to see drug-induced arrhythmias. Follow trough serum concentrations closely at initiation, 3 to 5 days after any dose change, and with any significant change in clinical status or diet. Therapeutic trough levels are 200 to 800 nanograms/mL.

Adverse Effects/Precautions

Flecainide can cause new or worsened arrhythmias, including AV block, bradycardia, ventricular tachycardia, torsades de pointes. There is also a negative inotropic effect. Dizziness, blurred vision, and headache have been reported in children.

Pharmacology

Flecainide is a Class I-C antiarrhythmic that produces a dose-related decrease in intracardiac conduction in all parts of the heart, thereby increasing PR, QRS and QT intervals. Effects upon atrioventricular (AV) nodal conduction time and intra-atrial conduction times are less pronounced than those on the ventricle. Peak serum concentrations occur 2 to 3 hours after an oral dose. Infant formula and milk products interfere with drug absorption. Plasma protein binding is about 40% in adults and is independent of plasma drug level. Children under 1 year of age have elimination half-life values of 11 to 12 hours. Elimination half-life in newborns after maternal administration is as long as 29 hours.

Special Considerations/Preparation

Supplied in 50-mg, 100-mg, and 150-mg tablets. An oral suspension with a final concentration of 5 mg/mL can be made as follows: crush 6 (six) 100-mg tablets, slowly mix in 20 mL of a 1:1 mixture of Ora-Sweet® and Ora-Plus®, or cherry syrup (cherry syrup concentrate diluted 1:4 with simple syrup) to form a uniform paste, then add to this mixture enough vehicle to make a final volume of 120 mL. Shake well and protect from light. Stable for 45 days refrigerated and at room temperature when stored in amber glass or plastic.

Selected References

- ◆ O'Sullivan JJ, Gardiner HM, Wren C: Digoxin or flecainide for prophylaxis of supraventricular tachycardia in infants? *J Am Coll Cardiol* 1995;26:991-994.
- ◆ Luedtke SA, Kuhn RJ, McCaffrey FM: Pharmacologic management of supraventricular tachycardia in children. *Ann Pharmacother* 1997;31:1227-43.
- ◆ Perry JC, Garson A: Flecainide acetate for treatment of tachyarrhythmias in children: Review of world literature on efficacy, safety, and dosing. *Am Heart J* 1992;124:1614-21.
- ◆ Wiest DB, Garner SS, Pagacz LR, et al: Stability of flecainide acetate in an extemporaneously compounded oral suspension. *Am J Hosp Pharm* 1992;49:1467-70.

Added 3/2003

Dose & Administration

Maintaining patency of peripheral and central vascular catheters:
0.5 to 1 unit/mL of IV fluid.

Treatment of thrombosis: 75 units/kg bolus, followed by 28 units/kg per hour continuous infusion. Four hours after initiating therapy, measure aPTT, then adjust dose to achieve an aPTT that corresponds to an anti-factor X_a level of 0.3 to 0.7 (this is usually equivalent to an aPTT of 60 to 85 seconds). Treatment should be limited to 10 to 14 days.

Make certain correct concentration is used.

Uses

See above. Only continuous infusions (rather than intermittent flushes) have been demonstrated to maintain catheter patency. Treatment of renal vein thromboses is limited to those that are bilateral or extend into the IVC. Although data are limited, enoxaparin may be preferable to heparin for treatment of thromboses.

Call 1-800-NOCLOTS for case reporting and treatment guidance.

Monitoring

Follow platelet counts every 2 to 3 days. When treating thromboses, maintain a prolonged aPTT in a range corresponding to an anti-factor X_a level of 0.3 to 0.7 units/mL. Assess for signs of bleeding and thrombosis.

Adverse Effects/Precautions

Data are insufficient to make specific recommendations regarding anticoagulation therapy. Heparin-induced thrombocytopenia (HIT) has been reported to occur in approximately 1% of newborns exposed to heparin. Heparin-associated antiplatelet antibodies were found in half of the newborns who were both thrombocytopenic and heparin-exposed. Although the thrombocytopenia resolved spontaneously in most patients upon stopping the heparin, a high incidence of ultrasonographic-documented aortic thrombosis was seen. Contraindicated in infants with evidence of intracranial or GI bleeding or thrombocytopenia (below 50,000/mm³). Long term use of therapeutic doses of heparin can lead to osteoporosis.

Confirm heparin vial concentration prior to administration of the drug. Fatal hemorrhages have occurred in pediatric patients when the incorrect heparin concentration was administered.

Pharmacology

Activates antithrombin III, which progressively inactivates both thrombin and factor X_a, key proteolytic enzymes in the formation of fibrinogen and activation of prothrombin. Efficacy in neonates is decreased due to low antithrombin plasma concentrations. Metabolized by liver. Renal excretion should occur within 6 hours, but may be delayed. Clearance in neonates is more rapid than in children or adults. Half-life is dose-dependent, but averages 1 to 3 hours.

Special Considerations/Preparation

Keep protamine sulfate on hand to manage hemorrhage (see Protamine monograph for appropriate dosing).

Heparin available in 10 units/mL (for IV reservoirs); 100 units/mL; 1000 units/mL (for central catheters); 5000 units/mL, and 10,000 units/mL.

Solution Compatibility: D₅W, D₁₀W, and NS.

Terminal Injection Site Compatibility: Dex/AA solutions, fat emulsion. Acyclovir, aminophylline, amphotericin B, ampicillin, atropine, aztreonam, caffeine citrate, calcium gluconate, cefazolin, ceftazidime, cefepime, cefotaxime, cefoxitin, ceftriaxone, chloramphenicol, cimetidine, clindamycin, dexamethasone, digoxin, dobutamine, dopamine, enalaprilat, epinephrine, erythromycin lactobionate, esmolol, famotidine, fentanyl, fluconazole, flumazenil, furosemide, hydralazine, hydrocortisone succinate, insulin, isoproterenol, lidocaine, linezolid, lorazepam, meropenem, methicillin, metoclopramide, metronidazole, mezlocillin, micafungin, midazolam, milrinone, morphine, nafcillin, naloxone, netilmicin, neostigmine, nitroglycerin, oxacillin, pancuronium bromide, penicillin G, phenobarbital, phytonadione, piperacillin, piperacillin-tazobactam, potassium chloride, procainamide, propofol, propranolol, prostaglandin E₁, ranitidine, remifentanil, sodium bicarbonate, sodium nitroprusside, ticarcillin/clavulanate, trimethoprim-sulfamethoxazole, vecuronium, and zidovudine.

Incompatibility: Alteplase, amikacin, amiodarone, ciprofloxacin, diazepam, gentamicin, hyaluronidase, methadone, phenytoin, tobramycin, and vancomycin.

Selected References

- ◆ Monagle P, Chan A, Massicotte P, et al: Antithrombotic therapy in children: the seventh ACCP conference on antithrombotic and thrombolytic therapy. *Chest* 2004;126:645-687.
- ◆ Schmugge M, Risch L, Huber AR, et al: Heparin-induced thrombocytopenia-associated thrombosis in pediatric intensive care patients. *Pediatrics* 2002;109(1). URL:<http://www.pediatrics.org/cgi/content/full/109/1/e10>.
- ◆ Edstrom CS, Christensen RD: Evaluation and treatment of thrombosis in the neonatal intensive care unit. *Clin Perinatol* 2000;27:623-41.
- ◆ Chang GY, Leuder FL, DiMichele DM, et al: Heparin and the risk of intraventricular hemorrhage in premature infants. *J Pediatr* 1997;131:362-66.
- ◆ Paisley MK, Stamper M, Brown J, et al: The use of heparin and normal saline flushes in neonatal intravenous catheters. *Pediatr Nurs* 1997;23:521-27.
- ◆ Kotter RW: Heparin vs saline for intermittent intravenous device maintenance in neonates. *Neonat Network* 1996;15:43-47.
- ◆ Moclair A, Bates I: The efficacy of heparin in maintaining peripheral infusions in neonates. *Eur J Pediatr* 1995;154:567-70.
- ◆ Spadone D, Clark F, James E, et al: Heparin-induced thrombocytopenia in the newborn. *J Vasc Surg* 1992;15:306.
- ◆ Product Information, Abraxis, 2008

Adverse Effects/Precautions updated 1/2009

Text and References updated 3/2008

Compatibilities updated 3/2007

Dose & Administration

IV: Begin with 0.1 to 0.5 mg/kg per dose Q6 to 8 hours. Dose may be gradually increased as required for blood pressure control to a maximum of 2 mg/kg per dose Q6 hours.

PO: 0.25 to 1 mg/kg per dose Q6 to 8 hours, or approximately twice the required IV dose. Administer with food to enhance absorption.

Note: Use with a beta-blocking agent is often recommended to enhance the antihypertensive effect and decrease the magnitude of the reflex tachycardia. This is expected to reduce hydralazine IV dosage requirements to less than 0.15 mg/kg per dose.

Uses

Treatment of mild to moderate neonatal hypertension by vasodilation. Afterload reduction in patients with congestive heart failure.

Monitoring

Frequent assessment of blood pressure and heart rate. Guaiac stools. Periodic CBC during long-term use.

Adverse Effects/Precautions

Diarrhea, emesis, and temporary agranulocytosis have been reported in neonates. Tachycardia, postural hypotension, headache, nausea, and a lupus-like syndrome occur in 10% to 20% of adults. Uncommon reactions in adults include GI irritation and bleeding, drug fever, rash, conjunctivitis, and bone marrow suppression.

Pharmacology

Causes direct relaxation of smooth muscle in the arteriolar resistance vessels. Major hemodynamic effects: Decrease in systemic vascular resistance and a resultant increase in cardiac output. Increases renal, coronary, cerebral, and splanchnic blood flow. When administered orally, hydralazine has low bioavailability because of extensive first-pass metabolism by the liver and intestines. The rate of enzymatic metabolism is genetically determined by the acetylator phenotype—slow acetylators have higher plasma concentrations and a higher incidence of adverse effects.

Special Considerations/Preparation

Hydralazine hydrochloride injection for IV use (20 mg/mL) is available in 1 mL vial. A 1 mg/mL dilution may be made by diluting 0.5 mL of the 20 mg/mL concentrate with 9.5 mL of preservative-free normal saline for injection. Dilution is stable for 24 hours.

Oral tablet strengths include 10-, 25-, 50-, and 100-mg. Oral formulations using simple syrups containing dextrose, fructose, or sucrose are unstable. To prepare an oral suspension, crush a 50 mg tablet and dissolve in 4 mL of 5% mannitol, then add 46 mL of sterile water to make a final concentration of 1 mg/mL. Protect from light. Stable for 7 days refrigerated.

Solution Compatibility: NS.

Terminal Injection Site Compatibility: Dex/AA. Dobutamine, heparin, hydrocortisone succinate, potassium chloride, and prostaglandin E₁.

Incompatibility: Aminophylline, ampicillin, diazoxide, furosemide, and phenobarbital.

Selected References

- ◆ Artman M, Graham TP Jr: Guidelines for vasodilator therapy of congestive heart failure in infants and children. *Am Heart J* 1987;113:995.
- ◆ Gupta VD, Stewart KR, Bethea C: Stability of hydralazine hydrochloride in aqueous vehicles. *J Clin Hosp Pharm* 1986;11:215.
- ◆ Beekman RH, Rocchini AP, Rosenthal A: Hemodynamic effects of hydralazine in infants with a large ventricular septal defect. *Circulation* 1982;65:523.
- ◆ Fried R, Steinherz LJ, Levin AR, et al: Use of hydralazine for intractable cardiac failure in childhood. *J Pediatr* 1980;97:1009.
- ◆ Product Information, American Regent, 2003

Text updated 3/96

Compatibilities updated 3/2008

Dose & Administration

First dose: 10 mg/kg.

Second and third doses: 5 mg/kg.

Administer IV by syringe pump over 15 minutes at 24 hour intervals.

Uses

Closure of Patent Ductus Arteriosus. Not indicated for IVH prophylaxis.

Monitoring

Assess for ductal closure. Monitor urine output. Assess for signs of bleeding.

Adverse Effects/Precautions

NeoProfen® is contraindicated in preterm neonates with 1) infection, 2) active bleeding, 3) thrombocytopenia or coagulation defects, 4) NEC, 5) significant renal dysfunction, and 6) congenital heart disease with ductal-dependent systemic blood flow. Decreased urine output is less severe and occurs less frequently than with indomethacin. Although the available (and few) data suggest that the displacement of bilirubin from albumin is minimal with an ibuprofen dosing regimen of 10-, 5-, 5-mg/kg (q24hr), a more significant increase in unbound bilirubin can be expected in those infants with a high unconjugated bilirubin/albumin ratio and those in whom high ibuprofen concentrations are achieved. There is one recent case report of pulmonary hypertension in a 32 week gestation infant in Italy who received ibuprofen lysine (not NeoProfen) for treatment of PDA. Several studies have demonstrated an increased risk of oxygen dependency at 28 days postnatal age, but not 36 weeks PMA. Ibuprofen, like other nonsteroidal anti-inflammatory drugs, can inhibit platelet aggregation.

Pharmacology

NeoProfen® is a lysine salt solution of racemic ibuprofen, an inhibitor of prostaglandin synthesis. In adults (no data in neonates) metabolism is primarily via hydroxylation by hepatic CYP 2C9 and 2C8, with renal elimination of unchanged drug (10-15%) and metabolites. The mean half-life in premature neonates is approximately 43 hours, with large interpatient variability. Clearance increases rapidly with postnatal age and PDA closure.

Special Considerations/Preparation

Supplied as a 10 mg/mL sterile solution for injection in 2 mL single use vials. Should be diluted prior to administration in an appropriate volume of dextrose or saline. Contains no preservatives and is not buffered. Administer within 30 minutes of preparation. The pH is adjusted to 7. Store at room temperature. **Protect from light.**

Solution Compatibility: NS, 0.45% NS, D5W, D10W, and LR.

Terminal Injection Site Compatibility: No data available.

Selected References

- ◆ Aranda JV, Clyman R, Cox B, et al: A randomized, double-blind, placebo-controlled trial on intravenous ibuprofen L-lysine for the early closure of nonsymptomatic patent ductus arteriosus within 72 hours of birth in extremely low-birth-weight infants. *Am J Perinatol* 2009;26:235-45.
- ◆ Ambat MT, Ostrea EM Jr, Aranda JV: Effect of ibuprofen L-lysinate on bilirubin binding to albumin as measured by saturation index and horseradish peroxidase assays. *J Perinatol* 2008;28:287-90.
- ◆ Capparelli EV, et al. Population pharmacokinetics of ibuprofen L-lysine during early treatment of patent ductus arteriosus in premature infants. Abstract 2863.253, Pediatric Academic Societies Annual Meeting, 2006.
- ◆ Ohlsson A, Walia R, Shah S. Ibuprofen for the treatment of patent ductus arteriosus in preterm and/or low birth weight infants. The Cochrane Database of Systematic Reviews 2005, Issue 4. Art. No.: CD003481. DOI: 10.1002/14651858.CD003481.pub2.
- ◆ Thomas RL, Parker GC, Van Overmeire B, Aranda JV. A meta-analysis of ibuprofen versus indomethacin for closure of patent ductus arteriosus. *Eur J Pediatr* 2005;164:135-140.
- ◆ Desfrere L, Zohar S, Morville P, et al. Dose-finding study of ibuprofen in patent ductus arteriosus using the continual reassessment method. *J Clin Pharm Ther* 2005;30:121-132.
- ◆ Van Overmeire B, Touw D, Schepens PJC, et al. Ibuprofen pharmacokinetics in preterm infants with patent ductus arteriosus. *Clin Pharmacol Ther* 2001;70:336-343.
- ◆ Bellini C, Campone F, Serra G. Pulmonary hypertension following L-lysine ibuprofen therapy in a preterm infant with patent ductus arteriosus. *CMAJ* 2006;174:1843-44.
- ◆ Product Information, Ovation, 2007

Adverse Effects, Compatibilities and References updated 3/2007

Dose & Administration

IV infusion by syringe pump over at least 30 minutes to minimize adverse effects on cerebral, GI, and renal blood flow velocities. Usually three doses per course, maximum two courses. Give at 12- to 24-hour intervals with close monitoring of urine output. If anuria or severe oliguria occurs, subsequent doses should be delayed. Longer treatment courses may be used: 0.2 mg/kg Q24 hours for a total of 5 to 7 days.

Prevention of IVH: 0.1 mg/kg Q24 hours for 3 doses, beginning at 6 to 12 hours of age.

PDA Closure Dose (mg/kg)

Age at 1st dose	1st	2nd	3rd
< 48 h	0.2	0.1	0.1
2 to 7 d	0.2	0.2	0.2
> 7 d	0.2	0.25	0.25

Uses

Closure of ductus arteriosus. Prevention of intraventricular hemorrhage.

Monitoring

Monitor urine output, serum electrolytes, glucose, creatinine and BUN, and platelet counts. Assess murmur, pulse pressure. Assess for GI bleeding by guaiac-ing stools and gastric aspirate. Observe for prolonged bleeding from puncture sites.

Adverse Effects/Precautions

If oliguria occurs, observe for hyponatremia and hypokalemia, and consider prolonging the dosing interval of renally excreted drugs (e.g. gentamicin). Consider withholding feedings. Hypoglycemia is common, usually preventable by increasing the glucose infusion rate by 2 mg/kg per minute. Causes platelet dysfunction. Contraindicated in active bleeding, significant thrombocytopenia or coagulation defects, necrotizing enterocolitis, and/or significantly impaired renal function. Rapid (<5-minute) infusions are associated with reductions in organ blood flow. Gastrointestinal perforations occur frequently if used concurrently with corticosteroids.

Pharmacology

Inhibitor of prostaglandin synthesis. Decreases cerebral, renal and GI blood flow. Metabolized in the liver to inactive compounds and excreted in the urine and feces. Serum half-life is approximately 30 hours, with a range of 15 to 50 hours, partially dependent on postnatal age. In most studies, the response of the ductus and adverse effects of indomethacin are only weakly correlated with plasma concentration.

Special Considerations/Preparation

Supplied as a lyophilized powder in 1-mg single dose vials.

Indomethacin sodium trihydrate salt is not buffered, and is insoluble in solutions with pH <6; the manufacturer therefore recommends against continuous infusion in typical IV solutions. Reconstitute using 1 to 2 mL of preservative-free NS or sterile water for injection. Reconstituted indomethacin is stable in polypropylene syringes and glass vials for 12 days when stored at room temperature or refrigerated. Observe for precipitation.

Solution Compatibility: Sterile water for injection.

(No visual precipitation in 24 hours): D_{2.5}W, D₅W, and NS.

Terminal Injection Site Compatibility: Furosemide, insulin, nitroprusside, potassium chloride, and sodium bicarbonate.

Incompatibility: D_{7.5}W, D₁₀W, Dex/AA. Calcium gluconate, cimetidine, dobutamine, dopamine, gentamicin, and, tobramycin.

Selected References

- ◆ Fowlie PW, Davis PG: Prophylactic indomethacin for preterm infants: a systematic review and meta-analysis. *Arch Dis Child Fetal Neonatal Ed* 2003;88:F464-66.
- ◆ Itabashi K, Ohno T, Nishida H: Indomethacin responsiveness of patent ductus arteriosus and renal abnormalities in preterm infants treated with indomethacin. *J Pediatr* 2003;143:203-7.
- ◆ Clyman RI: Recommendations for the postnatal use of indomethacin: an analysis of four separate treatment strategies. *J Pediatr* 1996;128:601.
- ◆ Hammerman C, Aramburu MJ: Prolonged indomethacin therapy for the prevention of recurrences of patent ductus arteriosus. *J Pediatr* 1990;117:771.
- ◆ Hosono S, Ohono T, Kimoto H: Preventative management of hypoglycemia in very low-birthweight infants following indomethacin therapy for patent ductus arteriosus. *Pediatr Internat* 2001;43:465-468.
- ◆ Coombs RC, Morgan MEI, Durbin GM, et al: Gut blood flow velocities in the newborn: Effects of patent ductus arteriosus and parenteral indomethacin. *Arch Dis Child* 1990;65:1067.
- ◆ Colditz P, Murphy D, Rolfe P, Wilkinson AR: Effect of infusion rate of indomethacin on cerebrovascular responses in preterm infants. *Arch Dis Child* 1989;64:8.
- ◆ Walker SE, Gray S, Schmidt B: Stability of reconstituted indomethacin sodium trihydrate in original vials and polypropylene syringes. *Am J Health-Syst Pharm* 1998;15:154.
- ◆ Ishisaka DY, Van Vleet J, Marquardt E: Visual compatibility of indomethacin sodium trihydrate with drugs given to neonates by continuous infusion. *Am J Hosp Pharm* 1991;48:2442.
- ◆ Gersony WM, Peckham GJ, Ellison RC, et al: Effects of indomethacin in premature infants with patent ductus arteriosus: Results of a national collaborative study. *J Pediatr* 1983;102:895.
- ◆ Brash AR, Hickey DE, Graham TP, et al: Pharmacokinetics of indomethacin in the neonate: Relation of plasma indomethacin levels to response of the ductus arteriosus. *N Engl J Med* 1981;305:67.
- ◆ Yaffe SJ, Friedmann WF, Rogers D, et al: The disposition of indomethacin in preterm babies. *J Pediatr* 1980;97:1001.
- ◆ Schmidt B, Davis P, Muddeman D, et al: Long-term effects of indomethacin prophylaxis in extremely-low-birth-weight infants. *N Engl J Med* 2001; 344:1966-1972.
- ◆ Ment LR, Oh W, Ehrenkranz RA, et al: Low-dose indomethacin and prevention of intraventricular hemorrhage: A multicenter randomized trial. *Pediatrics* 1994;93:543.
- ◆ Product Information, Ovation Pharmaceuticals, 2006

References updated 3/2004

Compatibilities updated 3/2004

Dose & Administration

0.05 to 0.5 mcg/kg per minute continuous IV infusion.

Maximum dose 2 mcg/kg per minute.

Dosage often titrated according to heart rate.

Acidosis should be corrected before infusion.

Solution Preparation Calculations

To calculate the AMOUNT of drug needed per defined final fluid volume:

Desired final concentration (mg/mL) x defined final fluid volume (mL) = AMOUNT of drug to add to final infusion solution (mg).

To calculate the VOLUME of drug needed per defined final fluid volume:

$$\frac{\text{*AMOUNT of drug to add (mg)}}{\text{drug (vial) concentration (mg/mL)}} = \text{VOLUME of drug to add (mL)}$$

Example (for Isoproterenol): Mix 50 mL of 10 mcg/mL solution using isoproterenol concentration of 0.2 mg/mL.

$$10 \text{ mcg/mL} = 0.01 \text{ mg/mL}$$

$$0.01 \text{ mg/mL} \times 50 \text{ mL} = 0.5 \text{ mg isoproterenol}$$

$$\frac{\text{*0.5 mg}}{0.2 \text{ mg/mL}} = 2.5 \text{ mL of isoproterenol}$$

Add 2.5 mL of isoproterenol (0.2 mg/mL) to 47.5 mL of compatible solution (eg, D₅W) to yield 50 mL of infusion solution with a concentration of 10 mcg/mL.

Maximum concentration 20 mcg/mL.

Isoproterenol Titration Chart

Concentration (mcg/mL)	Dose (mcg/kg/min)	IV Rate (mL/kg/hour)
5	0.05	0.6
	0.1	1.2
	0.5	6
	1	12
10	0.05	0.3
	0.1	0.6
	0.5	3
	1	6
15	0.05	0.2
	0.1	0.4
	0.5	2
	1	4
20	0.05	0.15
	0.1	0.3
	0.5	1.5
	1	3

Uses

Increases cardiac output in patients with cardiovascular shock.
Pulmonary vasodilator (older infants).

continued...

Monitoring

Continuous vital signs, intra-arterial blood pressure, CVP monitoring preferable. Periodic blood glucose reagent strips.

Adverse Effects/Precautions

Cardiac arrhythmias. Tachycardia severe enough to cause CHF. Decreases venous return to heart. Systemic vasodilation. May cause hypoxemia by increasing intrapulmonary shunt. Hypoglycemia.

Pharmacology

β -receptor stimulant, sympathomimetic. Increases cardiac output by 1) increasing rate (major) and 2) increasing strength of contractions (minor). Insulin secretion is stimulated. Afterload reduction via β_2 effects on arterioles.

Special Considerations/Preparation

Supplied as 0.2-mg/mL (1:5000) solution in 1-mL and 5-mL ampuls.

Solution Compatibility: D₅W, D₁₀W, and NS.

Terminal Injection Site Compatibility: Dex/AA solutions, fat emulsion. Aminophylline, amiodarone, caffeine citrate, calcium chloride, calcium gluceptate, calcium gluconate, cimetidine, dobutamine, famotidine, heparin, hydrocortisone succinate, milrinone, netilmicin, nitroprusside, pancuronium bromide, potassium chloride, propofol, prostaglandin E₁, ranitidine, remifentanil, and vecuronium.

Incompatibility: Furosemide and sodium bicarbonate.

Selected References

- ◆ Cabal LA, Devaskar U, Siassi B, et al: Cardiogenic shock associated with perinatal asphyxia in preterm infants. *J Pediatr* 1980;96:705.
- ◆ Daoud FS, Reeves JT, Kelly DB: Isoproterenol as a potential pulmonary vasodilator in primary pulmonary hypertension. *Am J Cardiol* 1978;42:817.
- ◆ Product Information, Hospira, 2006

Text updated 3/2008

Compatibilities updated 3/2005

Dose & Administration

Initial bolus dose: 0.5 to 1 mg/kg IV push over 5 minutes. Repeat Q10 minutes as necessary to control arrhythmia. Maximum total bolus dose should not exceed 5 mg/kg.

Maintenance IV infusion: 10 to 50 mcg/kg per minute. Premature neonates should receive lowest dosage.

Solution Preparation Calculations

To calculate the AMOUNT of drug needed per defined final fluid volume:

Desired final concentration (mg/mL) x defined final fluid volume (mL) = AMOUNT of drug to add to final infusion solution (mg).

To calculate the VOLUME of drug needed per defined final fluid volume:

$$\frac{\text{*AMOUNT of drug to add (mg)}}{\text{drug (vial) concentration (mg/mL)}} = \text{VOLUME of drug to add (mL)}$$

Example (for Lidocaine): Mix 50 mL of 2400 mcg/mL solution using lidocaine concentration of 20 mg/mL.

2400 mcg/mL = 2.4 mg/mL

2.4 mg/mL x 50 mL = 120 mg lidocaine

$$\frac{\text{*120 mg}}{\text{20 mg/mL}} = 6 \text{ mL of lidocaine}$$

Add 6 mL of lidocaine (20 mg/mL) to 44 mL of compatible solution (eg, D₅W) to yield 50 mL of infusion solution with a concentration of 2400 mcg/mL.

Maximum concentration is 8000 mcg/mL.

Lidocaine Titration Chart

Concentration (mcg/mL)	Dose (mcg/kg/min)	IV Rate (mL/kg/hour)
800	10	0.75
	20	1.5
	30	2.25
	40	3
	50	3.75
1600	10	0.375
	20	0.75
	30	1.125
	40	1.5
	50	1.875
2400	10	0.25
	20	0.5
	30	0.75
	40	1
	50	1.25
4000	10	0.15
	20	0.3
	30	0.45
	40	0.6
	50	0.75
6000	10	0.1
	20	0.2
	30	0.3
	40	0.4
	50	0.5
8000	10	0.075
	20	0.15
	30	0.225
	40	0.3
	50	0.375

Uses

Short-term control of ventricular arrhythmias, including ventricular tachycardia, premature ventricular contractions, and arrhythmias resulting from digitalis intoxication.

Monitoring

Continuous monitoring of EKG, heart rate, and blood pressure. Assess level of consciousness. Observe for seizure activity. Therapeutic total lidocaine serum concentrations are 1 to 5 mcg/mL.

Adverse Effects/Precautions

Early signs of CNS toxicity are drowsiness, agitation, vomiting, and muscle twitching. Later signs include seizures, loss of consciousness, respiratory depression, and apnea. Cardiac toxicity is associated with excessive doses and includes bradycardia, hypotension, heart block, and cardiovascular collapse.

Contraindicated in infants with cardiac failure and heart block: Serum lidocaine concentrations increase when using either cimetidine or propranolol in combination.

continued

Pharmacology

Lidocaine is a Type 1b antiarrhythmic agent used intravenously. Onset of action is 1 to 2 minutes after bolus administration. Plasma half-life in neonates is 3 hours. Free drug fraction in both term and premature neonates is approximately twice that found in older children because of significantly reduced protein binding by α_1 -acid glycoprotein. Transformed in the liver to metabolites with antiarrhythmic activity; approximately 30% is excreted unchanged in neonates.

Special Considerations/Preparation

Use only preservative-free lidocaine without epinephrine. Available in multiple concentrations ranging from 1% to 20%. To make a dilution for bolus dosing, dilute 10 mg lidocaine (0.5 mL of 2% solution) in 9.5 mL NS or D₅W, yielding a 1 mg/mL final concentration.

Solution Compatibility: D₅W, D₁₀W, and NS.

Terminal Injection Site Compatibility: Dex/AA solutions, fat emulsion. Alteplase, aminophylline, amiodarone, ampicillin, caffeine citrate, calcium chloride, calcium gluconate, cefazolin, cefoxitin, ceftriaxone, chloramphenicol, cimetidine, dexamethasone, digoxin, dobutamine, dopamine, enalaprilat, erythromycin lactobionate, esmolol, famotidine, fentanyl, flumazenil, furosemide, glycopyrrolate, heparin, hydrocortisone succinate, insulin, linezolid, methicillin, metoclopramide, micafungin, morphine, nafcillin, nicardipine, nitroglycerin, penicillin G, pentobarbital, potassium chloride, procainamide, prostaglandin E₁, ranitidine, sodium bicarbonate, and sodium nitroprusside.

Incompatibility: Phenytoin.

Selected References

- ◆ Lerman J, Strong A, LeDez KM, et al: Effects of age on the serum concentration of α_1 -acid glycoprotein and the binding of lidocaine in pediatric patients. *Clin Pharmacol Ther* 1989;46:219.
- ◆ Mihaly GW, Moore RG, Thomas J: The pharmacokinetics and metabolism of the anilide local anesthetics in neonates. I. Lidocaine. *Eur J Clin Pharmacol* 1978;13:143.
- ◆ Gelband H, Rosen MR: Pharmacologic basis for the treatment of cardiac arrhythmias. *Pediatrics* 1975;55:59.

Text updated 3/2008

Compatibilities updated 3/2007

Dose & Administration

Loading dose: 75 mcg/kg IV infused over 60 minutes, immediately followed by

Maintenance infusion: 0.5 to 0.75 mcg/kg per minute.

Note: Above doses are from studies of older infants and children. Adjust infusion rate based upon hemodynamic and clinical response.

Premature infants < 30 weeks GA:

Loading dose: 0.75 mcg/kg per minute for 3 hours, immediately followed by

Maintenance infusion: 0.2 mcg/kg per minute.

(Preliminary data from pilot study referenced below)

Uses

Short term (<72 hours) treatment of acute low cardiac output after cardiac surgery or due to septic shock.

Monitoring

Continuous monitoring of blood pressure, heart rate and rhythm. Assess signs of cardiac output. Carefully monitor fluid and electrolyte changes and renal function during therapy. Monitor platelet counts.

Adverse Effects/Precautions

Assure adequate vascular volume prior to initiating therapy. Blood pressure will likely fall 5% to 9% after the loading dose, but should gradually return to baseline by 24 hours. Heart rate increases of 5% to 10% are also common. Thrombocytopenia was reported frequently in some studies and rarely in others. Arrhythmias occur occasionally.

Pharmacology

Milrinone improves cardiac output by enhancing myocardial contractility, enhancing myocardial diastolic relaxation and decreasing vascular resistance. It acts via selective phosphodiesterase III inhibition that leads to increased intracellular cyclic AMP, increased myocardial intracellular calcium, and increased reuptake of calcium after systole. Vasodilatation is related to increased levels of cyclic GMP in vascular smooth muscle. Unlike catecholamines, myocardial oxygen consumption is not increased. Elimination is primarily via renal mechanisms. Half-life is quite variable, ranging from approximately 10 hours in ELBW neonates to approximately 3 hours in older and more mature infants.

Special Considerations/Preparation

Available in 1 mg/mL solution for injection in 10-, 20-, and 50-mL single-dose vials. Dilute with compatible diluent prior to administration. Maximum concentration for infusion is 200 mcg/mL. Also available as premixed solution for injection, 200 mcg/mL in 5% Dextrose. pH of 3.2 to 4.

Solution Compatibility: D₅W, NS, and LR.

Terminal Injection Site Compatibility: Dex/AA. Acyclovir, amikacin, aminophylline, amiodarone, ampicillin, atracurium, atropine, bumetanide, calcium chloride, calcium gluconate, cefazolin, cefepime, cefotaxime, ceftazidime, cimetidine, clindamycin, dexamethasone, digoxin, dobutamine, dopamine, epinephrine, fentanyl, gentamicin, heparin, insulin, isoproterenol, lorazepam, meropenem, methylprednisolone, metronidazole, micafungin, midazolam, morphine, nicardipine, nitroglycerin, norepinephrine, oxacillin, pancuronium, piperacillin, piperacillin-tazobactam, potassium chloride, propofol, propranolol, ranitidine, sodium bicarbonate, sodium nitroprusside, theophylline, ticarcillin, ticarcillin-clavulanate, tobramycin, vancomycin, and vecuronium.

Incompatibility: Furosemide, imipenem-cilastatin and procainamide.

Selected References

- ◆ Paradisis M, Jiang X, McLachlan AJ, et al: Population pharmacokinetics and dosing regimen of milrinone in preterm infants. *Arch Dis Child Fetal Neonatal Ed* 2007;92:F204-209.
- ◆ Hoffman TM, Wernovsky G, Atz AM, et al: Efficacy and safety of milrinone in preventing low cardiac output syndrome in infants and children after corrective surgery for congenital heart disease. *Circulation* 2003;107:996-1002.
- ◆ Lindsay CA, Barton P, Lawless S, et al: Pharmacokinetics and pharmacodynamics of milrinone in pediatric patients with septic shock. *J Pediatr* 1998;132:329-34.
- ◆ Chang AC, Atz AM, Wernovsky G, et al: Milrinone: Systemic and pulmonary hemodynamic effects in neonates after cardiac surgery. *Crit Care Med* 1995;23:1907-14.
- ◆ Veltri MA, Conner KG: Physical compatibility of milrinone lactate injection with intravenous drugs commonly used in the pediatric intensive care unit. *Am J Health-Syst Pharm* 2002;59: 452-54.
- ◆ Akkerman SR, Zhang H, Mullins RE, Yaughn K: Stability of milrinone lactate in the presence of 29 critical care drugs and 4 i.v. solutions. *Am J Health-Syst Pharm* 1999;56:63-68.
- ◆ Paradisis M, Evans N, Kluckow M, et al: Pilot study of milrinone for prevention of low systemic blood flow in very preterm infants. *J Pediatr* 2006;148:306-313.
- ◆ Product Information, Sanofi, 2007

Compatibilities and References updated 3/2007

Dose & Administration

Initial dose: 0.5 mcg/kg per minute continuous IV infusion.

Titrate dose to response. Blood pressure will begin to decrease within minutes of starting the infusion, reaching half of its ultimate decrease in approximately 45 minutes. Blood pressure equilibrium will not be achieved for approximately 50 hours (adult data).

Maintenance doses are usually 0.5 to 2 mcg/kg per minute.

Uses

Treatment of acute severe hypertension.

Monitoring

Continuous monitoring of blood pressure, heart rate and rhythm during initiation of therapy, and frequently thereafter. Observe IV site for signs of irritation.

Adverse Effects/Precautions

No adverse effects have been reported in neonates (small numbers). Hypotension and tachycardia are dose-dependent in adults. Headache, nausea, and vomiting were the other common effects reported.

Pharmacology

Nicardipine is a dihydropyridine calcium channel blocker that significantly decreases systemic vascular resistance. Unlike other calcium channel blockers, it has limited effects on the myocardium. It is extensively metabolized by the liver, and is highly protein bound. Following infusion in adults, nicardipine plasma concentrations decline tri-exponentially, with a rapid early distribution phase (alpha half-life of 2.7 minutes), an intermediate phase (beta half-life of 44.8 minutes), and a slow terminal phase (gamma half-life of 14.4 hours) that can only be detected after long-term infusions. Experience in neonates is limited, and there are no reported pharmacokinetic data.

Special Considerations/Preparation

Available as 2.5 mg/mL solution for injection in 10-mL ampuls. **Dilute prior to administration to a concentration of 0.1 mg/mL.** Dilution is stable at room temperature for 24 hours.

Store ampuls at controlled room temperature. Freezing does not adversely affect the product, but exposure to elevated temperatures should be avoided. Protect from light. Store ampuls in carton until used.

Solution Compatibility: D₅W, NS, and D₅NS.

Solution Incompatibility: Lactated Ringers.

Terminal Injection Site Compatibility: No data available for Dex/AA solutions or fat emulsions.

Amikacin, aminophylline, aztreonam, calcium gluconate, cefazolin, ceftizoxime, chloramphenicol, cimetidine, clindamycin, dobutamine, dopamine, enalaprilat, epinephrine, erythromycin lactobionate, esmolol, famotidine, fentanyl, gentamicin, heparin (concentrations ≤ 1 unit/mL), hydrocortisone, lidocaine, linezolid, lorazepam, magnesium sulfate, metronidazole, midazolam, milrinone, morphine, nafcillin, nitroglycerin, norepinephrine, penicillin G potassium, piperacillin, potassium chloride, potassium phosphate, ranitidine, sodium acetate, sodium nitroprusside, tobramycin, trimethoprim-sulfamethoxazole, vancomycin, and vecuronium.

Incompatibility: Ampicillin, cefoperazone, ceftazidime, furosemide, heparin (concentrations > 1 unit/mL), micafungin, sodium bicarbonate and thiopental.

Selected References

- ◆ McBride BF, White CM, Campbell M, Frey BM: Nicardipine to control neonatal hypertension during extracorporeal membrane oxygen support. *Ann Pharmacother* 2003;37:667-670.
- ◆ Tobias JD: Nicardipine to control mean arterial pressure after cardiothoracic surgery in infants and children. *Am J Ther* 2001;8:3-6.
- ◆ Milou C, Debuche-Benouachkou V, Semama DS et al: Intravenous nicardipine as a first-line antihypertensive drug in neonates. *Intensive Care Med* 2000;26:956-958.
- ◆ Gouyon JB, Geneste B, Semama DS, et al: Intravenous nicardipine in hypertensive preterm infants. *Arch Dis Child Fetal Neonatal Ed* 1997;76:F126-127.
- ◆ Product Information, ESP Pharma, 2005.

Added 3/2005

Nicardipine

Solution Compatibility: D₅W, NS, and D₅NS.

Solution Incompatibility: Lactated Ringers.

Terminal Injection Site Compatibility: No data available for Dex/AA solutions or fat emulsions.

Amikacin, aminophylline, aztreonam, calcium gluconate, cefazolin, ceftizoxime, chloramphenicol, cimetidine, clindamycin, dobutamine, dopamine, enalaprilat, epinephrine, erythromycin lactobionate, esmolol, famotidine, fentanyl, gentamicin, heparin (concentrations ≤ 1 unit/mL), hydrocortisone, lidocaine, linezolid, lorazepam, magnesium sulfate, metronidazole, midazolam, milrinone, morphine, nafcillin, nitroglycerin, norepinephrine, penicillin G potassium, piperacillin, potassium chloride, potassium phosphate, ranitidine, sodium acetate, sodium nitroprusside, tobramycin, trimethoprim-sulfamethoxazole, vancomycin, and vecuronium.

Incompatibility: Ampicillin, cefoperazone, ceftazidime, furosemid, heparin (concentrations > 1 unit/mL), micafungin, sodium bicarbonate and thiopental.

Selected References

- ◆ McBride BF, White CM, Campbell M, Frey BM: Nicardipine to control neonatal hypertension during extracorporeal membrane oxygen support. *Ann Pharmacother* 2003;37:667-670.
- ◆ Tobias JD: Nicardipine to control mean arterial pressure after cardiothoracic surgery in infants and children. *Am J Ther* 2001;8:3-6.
- ◆ Milou C, Debuche-Benouachkou V, Semama DS et al: Intravenous nicardipine first-line antihypertensive drug in neonates. *Intensive Care Med* 2000;26:956-958.
- ◆ Gouyon JB, Geneste B, Semama DS, et al: Intravenous nicardipine in hypotension in preterm infants. *Arch Dis Child Fetal Neonatal Ed* 1997;76:F126-127.
- ◆ Product Information, ESP Pharma, 2005.

Added 3/2005

Dose & Administration

30 mg per 250 mL of arterial catheter infusion solution.

Uses

Prolongation of peripheral arterial catheter patency.

Adverse Effects/Precautions

Use with caution in VLBW infants in the first days after birth due to potential of developing or extending an intracranial hemorrhage. Chronic hepatitis, as evidenced by an increase in serum bilirubin and serum glutamic transaminase, has been reported in three adults following long-term papaverine therapy. One patient had jaundice, and another had abnormal liver function on biopsy.

Pharmacology

Papaverine directly relaxes the tonus of various smooth muscle, especially when it has been spasmically contracted. It relaxes the smooth musculature of the larger blood vessels, especially coronary, systemic peripheral and pulmonary arteries. Vasodilation may be related to its ability to inhibit cyclic nucleotide phosphodiesterase, thus increasing levels of intracellular cyclic AMP. During administration, the muscle cell is not paralyzed and still responds to drugs and other stimuli causing contraction. Possibly because of its direct vasodilating action on cerebral blood vessels, papaverine increases cerebral blood flow and decreases cerebral vascular resistance in healthy subjects; oxygen consumption is unaltered. Papaverine is metabolized in the liver and excreted in the urine in an inactive form.

Special Considerations/Preparation

Supplied as 30 mg/mL solution for injection in 2 mL preservative-free vials and 10-mL multiple dose vials containing 0.5% chlorobutanol.

Solution Compatibility: NS, 0.45 NS, both with 1 unit/mL heparin

Solution Incompatibility: Lactated Ringers (precipitate forms)

Terminal Injection Site Compatibility: Phentolamine.

Selected References

- ◆ Griffin MP, Siadaty MS: Papaverine prolongs patency of peripheral arterial catheters in neonates. *J Pediatr* 2005;146:62-65.
- ◆ Heulitt MJ, Farrington EA, O'Shea TM, et al: Double-blind randomized controlled trial of papaverine-containing solutions to prevent failure of arterial catheters in pediatric patients. *Crit Care Med* 1993;21:825-829.
- ◆ Product Information, Parenta Pharmaceuticals, Inc., 2006

Added 3/2005

Phentolamine

Dose & Administration

Inject a 0.5-mg/mL solution of phentolamine subcutaneously into the affected area. Usual amount needed is 1 to 5 mL, depending on the size of the infiltrate. May be repeated if necessary.

Uses

Prevention of dermal necrosis and sloughing caused by extravasation of vasoconstrictive agents, e.g. dopamine.

Monitoring

Assess affected area for reversal of ischemia. Monitor blood pressure.

Adverse Effects/Precautions

Hypotension could potentially occur if a very large dose is administered. Consider using topical 2% nitroglycerin ointment if affected extremity is significantly swollen.

Pharmacology

Alpha-adrenergic blocking agent that produces peripheral vasodilation, thereby reversing ischemia produced by vasoconstrictor infiltration. The effect should be seen almost immediately. Biological half-life when injected subcutaneously is less than 20 minutes.

Special Considerations/Preparation

Available in 5-mg vial as a lyophilized powder.

To prepare:

- 1) Reconstitute one vial with 1 mL of normal saline.
- 2) Dilute to a concentration of 0.5 mg/mL with 9 mL normal saline.
Use immediately.

Do not use if solution is discolored or contains particulate contamination.

Terminal Injection Site Compatibility: Amiodarone, dobutamine, and papaverine.

Selected References

- ◆ Subhani M, Sridhar S, DeCristofaro JD: Phentolamine use in a neonate for the prevention of dermal necrosis caused by dopamine: A case report. *J Perinatol* 2001;21:324-326.
- ◆ Denkler KA, Cohen BE: Reversal of dopamine extravasation injury with topical nitroglycerin ointment. *Plast Reconstr Surg* 1989;84:811.
- ◆ Siwy BK, Sadove AM: Acute management of dopamine infiltration injury with Regitine. *Plast Reconstr Surg* 1987;80:610.
- ◆ Product Information, Bedford, 1999

Updated 3/2006

Compatibilities updated 3/2005

Dose & Administration

Initial bolus dose: 7 to 10 mg/kg IV over 1 hour via syringe pump.

Maintenance IV infusion: 20 to 80 mcg/kg per minute. Premature neonates should receive the lowest dose.

Uses

Acute treatment of supraventricular tachycardia (SVT) refractory to vagal maneuvers and adenosine. Acute treatment of ventricular tachycardia unresponsive to cardioversion and adenosine. Ectopic tachycardia, junctional ectopic tachycardia, and atrial flutter. Consider obtaining expert consultation before use.

Monitoring

Continuous monitoring of the EKG, blood pressure and heart rate. Measure procainamide and N-acetyl procainamide (NAPA) concentrations at 2, 12, and 24 hours after starting the loading dose infusion.

Therapeutic concentrations:

Procainamide: 4-10 mcg/mL, NAPA 6 to 20 mcg/mL.

Sum of procainamide and NAPA: 10-30 mcg/mL.

Adverse Effects/Precautions

Severe hypotension with rapid infusion, bradycardia, A-V block, and ventricular fibrillation have been reported in adult patients. Normal procainamide concentrations widen the QRS complex due to slowing of conduction in the Purkinje system and ventricular muscle. The drug should be discontinued if the QRS duration increases by more than 35 to 50 percent to avoid serious toxicity. Adverse effects are reversible with discontinuation of drug.

Black Box Warning

According to the manufacturer's black box warning, agranulocytosis, bone marrow depression, neutropenia, hypoplastic anemia, and thrombocytopenia, some of which were fatal, have been reported (in adults).

Pharmacology

Procainamide is a class IA antiarrhythmic agent that increases the effective refractory period of the atria and the ventricles of the heart. Onset of action occurs within minutes of starting the loading dose. Half-life is approximately 5 hours in the term neonate, and longer in preterms. Metabolized primarily (60%) in the liver to N-acetylprocainamide (NAPA), an active metabolite. The rate of acetylation is primarily genetically determined in adults and children. Preterm neonates have a higher NAPA:procainamide ratio than term infants presumably due to delayed excretion of NAPA. Renal function is a significant determinant of procainamide clearance. Cimetidine and amiodarone interact when given with procainamide, increasing procainamide serum levels.

Special Considerations/Preparation

Available in 10-mL vials providing 100 mg/mL or 2-mL vials providing 500 mg/mL. Store at room temperature. **DO NOT FREEZE**.

Dilute initial bolus dose to a final concentration of 20 mg/mL and administer over 1 hour. Maintenance infusion should be diluted to 2 mg/mL before administration.

Solution Compatibility: 0.45% NaCl and NS.

Solution Incompatibility: D₅W.

Terminal Injection Site Compatibility: Amiodarone, dobutamine, famotidine, flumazenil, heparin, hydrocortisone, lidocaine, netilmicin, ranitidine, and sodium nitroprusside.

Incompatibility: Esmolol, milrinone, and phenytoin.

Selected References

- ◆ Moffett BS, Cannon BC, Friedman RA, Kertesz NJ: Therapeutic levels of intravenous procainamide in neonates: A retrospective assessment. *Pharmacotherapy* 2006;26:1687-1693.
- ◆ Wong KK, Potts JE, Ethridge SP, Sanatani S: Medications used to manage supraventricular tachycardia in the infant: a North American survey. *Pediatr Cardiol* 2006;27:199-203.
- ◆ Bryson SM, Leson CL, Irwin DB, et al: Therapeutic monitoring and pharmacokinetic evaluation of procainamide in neonates. *DICP* 1991;25:68-71.
- ◆ Product Information, Hospira, 2004
Adverse Effects/Precautions updated 1/2009
Added 3/2007

Dose & Administration

Starting oral dose: 0.25 mg/kg per dose Q6 hours.

Increase as needed to maximum of 3.5 mg/kg per dose Q6 hours.

Starting IV dose: 0.01 mg/kg Q6 hours over 10 minutes.

Increase as needed to maximum of 0.15 mg/kg per dose Q6 hours.

Effective dosage requirements will vary significantly.

Uses

Treatment of tachyarrhythmias and hypertension. Preferred therapy for SVT if associated with Wolff-Parkinson-White syndrome. Palliation of tetralogy of Fallot and hypertrophic obstructive cardiomyopathy. Adjunctive treatment of neonatal thyrotoxicosis.

Monitoring

Continuous EKG monitoring during acute treatment of arrhythmias and during IV therapy. Measure systemic blood pressure frequently. Measure blood glucose during initiation of treatment and after dosage changes. Assess for increased airway resistance.

Adverse Effects/Precautions

Adverse effects are related to beta-receptor blockade: Bradycardia, bronchospasm, and hypoglycemia are most frequently reported. Hypotension occurs in patients with underlying myocardial dysfunction. Contraindicated in patients with reactive airway disease or diminished myocardial contractility. A withdrawal syndrome (nervousness, tachycardia, sweating, hypertension) has been associated with sudden cessation of the drug.

Pharmacology

Propranolol is the most widely used nonselective β -adrenergic-receptor blocking agent. Peak serum concentration is reached approximately 2 hours after an oral dose. Propranolol undergoes significant first-pass hepatic metabolism, resulting in 30% to 40% bioavailability. Protein binding is 70% in neonates. Serum half-life is prolonged in patients with liver disease. Elimination is by renal excretion of metabolites.

Special Considerations/Preparation

Oral solutions are available in concentrations of 4 mg/mL and 8 mg/mL. Injectable form is available in 1-mL ampules containing 1 mg.

Make a 0.1 mg/mL dilution by adding 1 ampul to 9 mL preservative-free normal saline. **Protect from light.** Store at room temperature.

Solution Compatibility: D₅W and NS.

Terminal Injection Site Compatibility: Alteplase, dobutamine, heparin, hydrocortisone succinate, linezolid, milrinone, morphine, potassium chloride, and propofol.

Selected References

- ◆ Schneeweiss A: Neonatal cardiovascular pharmacology, in Long WA (ed): *Fetal and Neonatal Cardiology*. Baltimore: WB Saunders Co, 1990, p 675.
- ◆ Pickoff AS, Zies L, Ferrer PL, et al: High-dose propranolol therapy in the management of supraventricular tachycardia. *J Pediatr* 1979;94:144.
- ◆ Gillette P, Garson A, Eterovic E, et al: Oral propranolol treatment in infants and children. *J Pediatr* 1978;92:141.
- ◆ Product Information, Roxane, 2007

Compatibilities updated 3/2004

Dose & Administration

Time since last heparin dose in minutes and protamine dose:

< 30 min: 1 mg per 100 units heparin received.

30 to 60 min: 0.5 to 0.75 mg per 100 units heparin received.

60 to 120 min: 0.375 to 0.5 mg per 100 units heparin received.

< 120 min: 0.25 to 0.375 mg per 100 units heparin received.

Maximum dose: 50 mg

Infusion rate: should not exceed 5 mg per min

Uses

Heparin antagonist.

Monitoring

Monitor vital signs, clotting functions, and blood pressure continuously. Observe for bleeding.

Adverse Effects/Precautions

Excessive doses can cause serious bleeding problems. Hypotension, bradycardia, dyspnea, and transitory flushing have been reported in adults. Risk factors for severe protamine adverse reactions include high doses, rapid administration, repeated doses, previous exposure to protamine or protamine-containing insulins, severe left ventricular dysfunction, and abnormal preoperative pulmonary hemodynamics.

Pharmacology

Anticoagulant when given alone. Combines ionically with heparin to form a stable complex devoid of anticoagulant activity. Rapid action after IV use (5 minutes).

Special Considerations/Preparation

Available as a 10-mg/mL concentration preservative-free in 5- and 25-mL vials. Store at room temperature.

Can be diluted in D₅W or NS.

Solution Compatibility: D₅W and NS. No data are currently available on Dex/AA.

Terminal Injection Site Compatibility: Cimetidine and ranitidine.

Selected References

- ◆ Monagle P, Chan A, Massicotte P, et al: Antithrombotic therapy in children: the seventh ACCP conference on antithrombotic and thrombolytic therapy. *Chest* 2004;126:645-687.
- ◆ Product Information, Abraxis, 2007

Updated 3/2008

Dose & Administration

0.3 to 1 mg/kg per dose PO every 6 to 12 hours.
Some authors have successfully used doses of 2 mg/kg.

Uses

Limited to treatment of patients with persistent pulmonary hypertension refractory to inhaled nitric oxide and other conventional therapies, those who are persistently unable to be weaned off of inhaled nitric oxide, or in situations where nitric oxide is not available. It has also been reported to improve pulmonary blood flow in patients with severe Ebstein's anomaly.

Monitoring

Continuous monitoring of blood pressure and oxygenation.

Adverse Effects/Precautions

Use in neonates should be restricted and considered experimental. Data in neonates are very limited. The most concerning short term adverse effects are worsening oxygenation and systemic hypotension. There is one case report of bleeding after circumcision in a neonate receiving chronic therapy. Use with caution in infants with sepsis. Sildenafil causes transient impairment of color discrimination in adults, and there is concern that it could increase the risk of severe retinopathy of prematurity.

Pharmacology

Sildenafil is a selective phosphodiesterase (PDE5) inhibitor. This inhibition leads to accumulation of cyclic GMP in pulmonary smooth muscle cells, causing pulmonary vascular relaxation. It may also potentiate the effect of inhaled nitric oxide. Oral absorption is rapid in adults with approximately 40% bioavailability; peak concentrations are reached in 30 to 120 minutes. It is metabolized primarily by hepatic CYP3A4 to an active metabolite (N-desmethyl sildenafil) that has PDE5 inhibitory activity. Both sildenafil and the metabolite have terminal half-lives of 4 hours in adults. Patients with significant hepatic or renal dysfunction have reduced clearance. Significant increases in sildenafil concentrations may occur when used concomitantly with drugs that are CYP3A4 inhibitors: e.g., erythromycin, amiodipine, and cimetidine.

Special Considerations/Preparation

Revatio® is supplied as 20 mg tablets; Viagra® is supplied as 25 mg, 50 mg, and 100 mg tablets. To prepare an oral suspension, thoroughly crush one tablet into a fine powder and add enough Ora-Plus to make a final concentration of 2 mg/mL. Suspension is stable for 1 month if refrigerated.

Selected References

- ◆ Gamboa D, Robbins D, Saba Z: Bleeding after circumcision in a newborn receiving sildenafil. *Clin Pediatr* 2007;46:842-43.
- ◆ Noori S, Friedlich P, Wong P, et al. Cardiovascular effects of sildenafil in neonates and infants with congenital diaphragmatic hernia and pulmonary hypertension. *Neonatology* 2007;91:92-100.
- ◆ Baquero H, Soliz A, Neira F, et al: Oral sildenafil in infants with persistent pulmonary hypertension of the newborn: a pilot randomized blinded study. *Pediatrics* 2006;117:1077-1083.
- ◆ Nahata MC, Morosco RS, Brady MT: Extemporaneous sildenafil citrate oral suspensions for the treatment of pulmonary hypertension in children. *Am J Health-Syst Pharm* 2006;63:254-257.
- ◆ Baquero H, Neira F, Venegas V, et al: Outcome at 18 months of age after sildenafil therapy for refractory neonatal hypoxemia. Poster at 2005 PAS Annual Meeting, Abstract 2119.
- ◆ Pham P, Hoyer A, Shaughnessy R, Law YM: A novel approach incorporating sildenafil in the management of symptomatic neonates with Ebstein's anomaly. *Pediatr Cardiol* 2006;27:614-617.
- ◆ Travadi JN, Patole SK: Phosphodiesterase inhibitors for persistent pulmonary hypertension of the newborn: a review. *Pediatr Pulmonol* 2003;36:529-535.
- ◆ Atz AM, Wessel DL: Sildenafil ameliorates effects of inhaled nitric oxide withdrawal. *Anesthesiology* 1999;91:307-310.
- ◆ Product Information, Pfizer, 2008

Uses and References updated 3/2008

Added 3/2006

Dose & Administration

Initial Dose: 0.25 to 0.5 mcg/kg per minute continuous IV infusion by syringe pump. Use a large vein for IV.

Titrate dose upward Q20 minutes until desired response is attained.

Usual **maintenance dose** is < 2 mcg/kg per minute.

For hypertensive crisis, may use up to 10 mcg/kg per minute, but for no longer than 10 minutes.

Sodium thiosulfate has been coadministered with sodium nitroprusside to accelerate the metabolism of cyanide; however, this has not been extensively studied.

Uses

Acute treatment of hypertensive emergencies. Acute afterload reduction in patients with refractory congestive heart failure.

Monitoring

Continuous heart rate and intra-arterial blood pressure monitoring is mandatory. Daily measurement of RBC cyanide (should be less than 200 ng/mL) and serum thiocyanate (should be less than 50 mcg/mL) concentrations. Assess frequently for development of metabolic acidosis. Daily assessment of renal and hepatic function.

Monitor IV site closely.

Adverse Effects/Precautions

Severe hypotension and tachycardia. Cyanide toxicity may occur with prolonged treatment (> 3 days) and high (> 3 mcg/kg per minute) doses. Use with caution in liver and renal failure patients due to possible impairment of the metabolism of cyanide to thiocyanate. Extravasation can cause tissue sloughing and necrosis.

Black Box Warning

According to the manufacturer's black box warning, nitroprusside is not suitable for direct injection; the reconstituted solution must be further diluted in sterile 5% dextrose injection before infusion. Monitor acid-base balance and venous oxygen concentration while on therapy as these tests may indicate cyanide toxicity.

Pharmacology

Direct-acting nonselective (arterial and venous) vasodilator. Immediately interacts with RBC oxyhemoglobin, dissociating and forming methemoglobin with release of cyanide and nitric oxide. Rapid onset of action with a serum half-life of 3 to 4 minutes in adults. Further metabolized to thiocyanate in the liver and kidney. Thiocyanate is renally eliminated with a half-life of 4 to 7 days.

Special Considerations/Preparation

Available as powder for injection in 2 mL single-dose 50 mg vials. Reconstitute contents of vial with 2 to 3 mL of D₅W or NS.

Do not administer reconstituted drug directly from vial. Dilute entire vial contents to a final concentration less than or equal to 200 mcg/mL (0.2 mg/mL) in D₅W or NS. Use within 24 hours of preparation.

Protect from light with aluminum foil or other opaque material. Blue, green or deep red discoloration indicates nitroprusside inactivation. Slight brownish discoloration is common and not significant.

Solution Compatibility: D₅W and NS only.

Terminal Injection Site Compatibility: Fat emulsion. Aminophylline, caffeine citrate, calcium chloride, cimetidine, dobutamine, dopamine, enalaprilat, epinephrine, esmolol, famotidine, furosemide, heparin, indomethacin, insulin, isoproterenol, lidocaine, magnesium, micafungin, midazolam, milrinone, morphine, nicardipine, nitroglycerin, pancuronium, potassium chloride, procainamide, propofol, prostaglandin E₁, ranitidine, and vecuronium.

Incompatibility: Amiodarone.

Selected References

- ◆ Seto W, Trope A, Carfrae L, et al: Visual compatibility of sodium nitroprusside with other injectable medications given to pediatric patients. *Am J Health-Syst Pharm* 2001;58:1422-6.
- ◆ Friederich JA, Butterworth JF: Sodium nitroprusside: Twenty years and counting. *Anesth Analg* 1995;81:152.
- ◆ Benitz WE, Malachowski N, Cohen RS, et al: Use of sodium nitroprusside in neonates: Efficacy and safety. *J Pediatr* 1985;106:102.
- ◆ Roberts RJ: *Drug Therapy in Infants*. Philadelphia: WB Saunders Co, 1984, p 184.
- ◆ Dillon TR, Janos CG, Meyer RA, et al: Vasodilator therapy for congestive heart failure. *J Pediatr* 1980;96:623.
- ◆ Product Information, Hospira, 2004

Adverse Effects/Precautions updated 1/2009

Text updated 3/2008

Compatibilities updated 3/2007

Added 3/1996

Dose & Administration

Initial dose: 1 mg/kg per dose PO Q12 hours.

Gradually increase as needed every 3 to 5 days until stable rhythm is maintained.

Maximum dose: 4 mg/kg per dose PO Q12 hours.

Uses

Treatment of refractory ventricular and supraventricular tachyarrhythmias.

Monitoring

Frequent EKG during initiation of therapy.

Adverse Effects/Precautions

Proarrhythmic effects occur in 10% of pediatric patients: sinoatrial block, A-V block, torsades de pointes and ventricular ectopic activity. These effects usually occur in the first few days of treatment. Prolongation of the QT interval is dose-dependent. Other adverse effects include fatigue, dyspnea, and hypotension.

Black Box Warning

According to the manufacturer's black box warning, to minimize the risk of induced arrhythmia, patients initiated or re-initiated on sotalol should receive continuous cardiac monitoring for a minimum of three days on maintenance doses.

Pharmacology

Sotalol is an antiarrhythmic agent that combines Class II beta-blocking properties with Class III prolongation of cardiac action potential duration. Betapace® is a racemic mixture of *d*- and *l*-sotalol. Oral bioavailability is good, but absorption is decreased by 20% to 30% by food, especially milk. Sotalol does not bind to plasma proteins, is not metabolized, and is renally excreted as unchanged drug. Limited pharmacokinetic data in infants show a half-life of 8 hours, increasing significantly in elderly patients and those with renal dysfunction.

Special Considerations/Preparation

Supplied in 80-mg, 120-mg, 160-mg, and 240-mg tablets. A 5 mg/mL oral suspension may be made as follows: crush 5 (five) 120-mg tablets, slowly mix in 84 mL of 1% methylcellulose, then add enough simple syrup to make a total volume of 120 mL. Stable for 60 days when kept refrigerated.

Selected References

- ◆ Saul JP, Schaffer MS, Karpwich PP, et al: Single dose pharmacokinetics of sotalol in a pediatric population with supraventricular and/or ventricular tachyarrhythmia. *J Clin Pharmacol* 2001;41:35-43.
- ◆ Pfammatter JP, Paul T, Lehmann C, Kallfelz HC: Efficacy and proarrhythmia of oral sotalol in pediatric patients. *J Am Coll Cardiol* 1995;26:1002.
- ◆ Tanel RE, Walsh EP, Lulu JA, and Saul JP: Sotalol for refractory arrhythmias in pediatric and young adult patients: Initial efficacy and long-term outcome. *Am Heart J* 1995;130:791.
- ◆ Hohnloser SH, Woosley RL: Sotalol. *N Engl J Med* 1994;331:31.
- ◆ Nappi JM, McCollam PL: Sotalol: A breakthrough antiarrhythmic? *Ann Pharmacother* 1993;27:1359.
- ◆ Maragnes P, Tipple M, Fournier A: Effectiveness of oral sotalol for treatment of pediatric arrhythmias. *Am J Cardiol* 1992;69:751.
- ◆ Product Information, Berlex, 2004

Adverse Effects/Precautions updated 1/2009

References and Pharmacology updated 3/2001

CNS DRUGS

Dose & Administration

Oral Loading dose: 20 to 25 mg/kg. Maintenance: 12 to 15 mg/kg per dose.

Rectal Loading dose: 30 mg/kg. Maintenance: 12 to 18 mg/kg per dose.

Maintenance intervals: Term infants: Q6 hours

Preterm infants \geq 32 weeks Postmenstrual Age: Q8 hours

Preterm infants $<$ 32 weeks Postmenstrual Age: Q12 hours

Uses

Fever reduction and treatment of mild to moderate pain.

Monitoring

Assess for signs of pain. Monitor temperature. Assess liver function.

Serum acetaminophen concentration is obtained only to assess toxicity.

Adverse Effects/Precautions

Liver toxicity occurs with excessive doses or after prolonged administration (>48 hours) of therapeutic doses. Rash, fever, thrombocytopenia, leukopenia, and neutropenia have been reported in children.

Pharmacology

Nonnarcotic analgesic and antipyretic. Peak serum concentration occurs approximately 60 minutes after an oral dose. Absorption after rectal administration is variable and prolonged. Extensively metabolized in the liver, primarily by sulfation with a small amount by glucuronidation. Metabolites and unchanged drug are excreted by the kidney. Elimination half-life is approximately 3 hours in term neonates, 5 hours in preterm neonates $>$ 32 weeks gestation, and up to 11 hours in more immature neonates. Elimination is prolonged in patients with liver dysfunction.

Special Considerations/Preparation

Dosage forms: Drops: 100 mg/mL, 48 mg/mL (alcohol-free).

Elixir: 16 mg/mL, 24 mg/mL, 32 mg/mL.

Liquid: 32 mg/mL (alcohol-free). Liquid: 33.33 mg/mL (7% alcohol).

Suppositories: 80,120, 325, and 650 mg.

Inaccurate dosing may occur with rectal administration because of unequal distribution of acetaminophen in the suppositories.

Treatment of Serious Acetaminophen Toxicity: N-acetylcysteine (NAC), 150 mg/kg in 5% dextrose or 1/2 NS given IV over 60 minutes (loading dose), followed by 50 mg/kg in 5% dextrose or 1/2 NS over 4 hours, then 100 mg/kg in 5% dextrose or 1/2 NS over 16 hours. NAC should be continued until clinical and biochemical markers of hepatic injury improve, and acetaminophen concentration is below the limits of detection. NAC solution concentrations of 40 mg/mL have been used to avoid fluid overload and hyponatremia in the neonate.

Selected References

- ◆ Walls L, Baker CF, Sarkar S: Acetaminophen-induced hepatic failure with encephalopathy in a newborn. *J Perinatol* 2007;27:133-135.
- ◆ Anderson BJ, van Lingen RA, Hansen TG, et al: Acetaminophen developmental pharmacokinetics in premature neonates and infants. *Anesthesiology* 2002;96:1336-45.
- ◆ Isbister GK, Bucens IK, Whyte IM: Paracetamol overdose in a preterm neonate. *Arch Dis Child Fetal Neonatal Ed* 2001;85:F70-F72.
- ◆ Arana A, Morton NS, Hansen TG: Treatment with paracetamol in infants. *Acta Anaesthesiol Scand* 2001;45:20-29.
- ◆ Levy G, Khanna NN, Soda DM, et al: Pharmacokinetics of acetaminophen in the human neonate: Formation of acetaminophen glucuronide and sulfate in relation to plasma bilirubin concentration and D-glucuronic acid excretion. *Pediatrics* 1975;55:818.
- ◆ Product Information, Cumberland (acetylcysteine), 2006

Updated 3/2008

Dose & Administration

25 to 75 mg/kg per dose PO or PR. Oral preparation should be diluted or administered after a feeding to reduce gastric irritation.

Uses

Sedative/hypnotic for short-term use only. Chloral hydrate has no analgesic properties; excitement may occur in patients with pain.

Monitoring

Assess level of sedation.

Adverse Effects/Precautions

Episodes of bradycardia are more frequent for up to 24 hours after a single dose in former premature infants. Gastric irritation and paradoxical excitement may also occur after a single dose. Other toxic effects have generally been reported in patients who received either repeated doses at regular intervals or acute overdoses. These effects may persist for days and include CNS, respiratory, and myocardial depression; cardiac arrhythmias; and ileus and bladder atony. Indirect hyperbilirubinemia may occur because TCE and bilirubin compete for hepatic conjugation.

Do not use in patients with significant hepatic and/or renal disease.

Pharmacology

Well absorbed from the oral route, with the onset of action in 10 to 15 minutes. Chloral hydrate is rapidly converted by alcohol dehydrogenase to the active and potentially toxic metabolite trichloroethanol (TCEt), which is excreted renally after glucuronidation in the liver. It is also metabolized to trichloroacetic acid (TCA), which is carcinogenic in mice when given in very high doses. Both TCEt (8 to 64 hours) and TCA (days) have long serum half-lives in neonates and accumulate with repeated doses.

Special Considerations/Preparation

Chloral hydrate is available in syrup as 100-mg/mL concentration. Osmolality is 3285 mOsm/kg of water.

The preparations are light-sensitive: Store in a dark container. Also available as 500 mg suppository. Inaccurate dosing may occur with rectal administration because of unequal distribution of chloral hydrate in the suppositories.

Selected References

- ◆ Allegaert K, Daniels H, Naulaers G, et al: Pharmacodynamics of chloral hydrate in former premature infants. *Eur J Pediatr* 2005;164:403-407.
- ◆ American Academy of Pediatrics, Committee on Drugs and Committee on Environmental Health: Use of chloral hydrate for sedation in children. *Pediatrics* 1993;92:471.
- ◆ Mayers DJ, Hindmarsh KW, Gorecki DKJ, Sankaran K: Sedative/hypnotic effects of chloral hydrate in the neonate: Trichloroethanol or parent drug? *Dev Pharmacol Ther* 1992;19:141.
- ◆ Anyebuno MA, Rosenfeld CR: Chloral hydrate toxicity in a term infant. *Dev Pharmacol Ther* 1991;17:116.
- ◆ Mayers DJ, Hindmarsh KW, Sankaran K, et al: Chloral hydrate disposition following single-dose administration to critically ill neonates and children. *Dev Pharmacol Ther* 1991;16:71.
- ◆ Reimche LD, Sankaran K, Hindmarsh KW, et al: Chloral hydrate sedation in neonates and infants: Clinical and pharmacologic considerations. *Dev Pharmacol Ther* 1989;12:57.

Chloral hydrate

Dose & Administration

25 to 75 mg/kg per dose PO or PR. Oral preparation should be diluted or administered after a feeding to reduce gastric irritation.

Uses

Sedative/hypnotic for short-term use only. Chloral hydrate has no analgesic properties; excitement may occur in patients with pain.

Monitoring

Assess level of sedation.

Adverse Effects/Precautions

Episodes of bradycardia are more frequent for up to 24 hours after a single dose in former premature infants. Gastric irritation and paradoxical excitement may also occur after a single dose. Other toxic effects have generally been reported in patients who received either repeated doses at regular intervals or acute overdoses. These effects may persist for days and include CNS, respiratory, and myocardial depression; cardiac arrhythmias; and ileus and bladder atony. Indirect hyperbilirubinemia may occur because TCE and bilirubin compete for hepatic conjugation.

Do not use in patients with significant hepatic and/or renal disease.

Pharmacology

Well absorbed from the oral route, with the onset of action in 10 to 15 minutes. Chloral hydrate is rapidly converted by alcohol dehydrogenase to the active and potentially toxic metabolite trichloroethanol (TCEt), which is excreted renally after glucuronidation in the liver. It is also metabolized to trichloroacetic acid (TCA), which is carcinogenic in mice when given in very high doses. Both TCEt (8 to 64 hours) and TCA (days) have long serum half-lives in neonates and accumulate with repeated doses.

Special Considerations/Preparation

Chloral hydrate is available in syrup as 100-mg/mL concentration. Osmolality is 3285 mOsm/kg of water.

The preparations are light-sensitive: Store in a dark container. Also available as 500 mg suppository. Inaccurate dosing may occur with rectal administration because of unequal distribution of chloral hydrate in the suppositories.

Selected References

- ◆ Allegaert K, Daniels H, Naulaers G, et al: Pharmacodynamics of chloral hydrate in former premature infants. *Eur J Pediatr* 2005;164:403-407.
- ◆ American Academy of Pediatrics, Committee on Drugs and Committee on Environmental Health: Use of chloral hydrate for sedation in children. *Pediatrics* 1993;92:471.
- ◆ Mayers DJ, Hindmarsh KW, Gorecki DKJ, Sankaran K: Sedative/hypnotic effects of chloral hydrate in the neonate: Trichloroethanol or parent drug? *Dev Pharmacol Ther* 1992;19:141.
- ◆ Anyebuno MA, Rosenfeld CR: Chloral hydrate toxicity in a term infant. *Dev Pharmacol Ther* 1991;17:116.
- ◆ Mayers DJ, Hindmarsh KW, Sankaran K, et al: Chloral hydrate disposition following single-dose administration to critically ill neonates and children. *Dev Pharmacol Ther* 1991;16:71.
- ◆ Reimche LD, Sankaran K, Hindmarsh KW, et al: Chloral hydrate sedation in neonates and infants: Clinical and pharmacologic considerations. *Dev Pharmacol Ther* 1989;12:57.

Updated 3/2006

Dose & Administration

Sedation and analgesia: 0.5 to 4 mcg/kg per dose IV slow push.
Repeat as required (usually Q2 to 4 hours).

Infusion rate: 1 to 5 mcg/kg per hour.
Tolerance may develop rapidly following constant infusion.

Anesthesia: 5 to 50 mcg/kg per dose.

Uses

Analgesia. Sedation. Anesthesia.

Monitoring

Monitor respiratory and cardiovascular status closely. Observe for abdominal distention, loss of bowel sounds, and muscle rigidity.

Adverse Effects/Precautions

Respiratory depression occurs when anesthetic doses (>5 mcg/kg) are used and may also occur unexpectedly because of redistribution. Chest wall rigidity has occurred in 4% of neonates who received 2.2 to 6.5 mcg/kg per dose, occasionally associated with laryngospasm. This was reversible with administration of naloxone. Urinary retention may occur when using continuous infusions. Tolerance may develop to analgesic doses with prolonged use. Significant withdrawal symptoms have been reported in patients treated with continuous infusion for 5 days or longer.

Pharmacology

Synthetic opioid narcotic analgesic that is 50 to 100 times more potent than morphine on a weight basis. Extremely lipid soluble. Penetrates the CNS rapidly. Transient rebound in fentanyl serum concentration may reflect sequestration and subsequent release of fentanyl from body fat. Metabolized extensively in the liver by CYP 3A4 enzyme system and then excreted by the kidney. Serum half-life is prolonged in patients with liver failure. Highly protein bound. Wide variability in apparent volume of distribution (10 to 30 L/kg) and serum half-life (1 to 15 hours).

Special Considerations/Preparation

Naloxone should be readily available to reverse adverse effects.

Available in 2-, 5-, 10-, and 20-mL ampules in a concentration of 50 mcg/mL. A 10 mcg/mL dilution may be made by adding 1 mL of the 50 mcg/mL concentration to 4 mL preservative-free normal saline. Stable for 24 hours refrigerated.

Solution Compatibility: D₅W and NS.

Terminal Injection Site Compatibility: Dex/AA solutions, fat emulsion. Amiodarone, atropine, caffeine citrate, cimetidine, dexamethasone, dobutamine, dopamine, enalaprilat, epinephrine, esmolol, furosemide, heparin, hydrocortisone succinate, lidocaine, linezolid, lorazepam, metoclopramide, midazolam, milrinone, mivacurium, morphine, nafcillin, nicardipine, pancuronium bromide, potassium chloride, propofol, ranitidine, remifentanil, sodium bicarbonate, and vecuronium.

Incompatibility: Azithromycin, pentobarbital and phenytoin.

continued...

Selected References

- ◆ Anand KJS and the International Evidence-Based Group for Neonatal Pain: Consensus statement for the prevention and management of pain in the newborn. *Arch Pediatr Adolesc Med* 2001;155:173-180.
- ◆ Fahnstich H, Steffan J, Kau N, Bartmann P: Fentanyl-induced chest wall rigidity and laryngospasm in preterm and term infants. *Crit Care Med* 2000;28:836-839.
- ◆ Saarenmaa E, Neuvonen PJ, Fellman V: Gestational age and birth weight effects on plasma clearance of fentanyl in newborn infants. *J Pediatr* 2000;136:767-770.
- ◆ Muller P and Vogtmann C: Three cases with different presentation of fentanyl-induced muscle rigidity-A rare problem in intensive care of neonates. *Am J Perinatol* 2000;17:23-26.
- ◆ Santeiro ML, Christie J, Stromquist C, et al: Pharmacokinetics of continuous infusion fentanyl in newborns. *J Perinatol* 1997;17:135-139.
- ◆ Arnold JH, Truog RD, Orav EJ, et al: Tolerance and dependence in neonates sedated with fentanyl during extracorporeal membrane oxygenation. *Anesthesiology* 1990;73:1136.
- ◆ Koehntop DE, Rodman JH, Brundage DM, et al: Pharmacokinetics of fentanyl in neonates. *Anesth Analg* 1986;65:227.
- ◆ Johnson KL, Erickson JP, Holley FO, Scott JC: Fentanyl pharmacokinetics in the pediatric population. *Anesthesiology* 1984;61:A441.
- ◆ Reilly CS, Wood AJ, Wood M: Variability of fentanyl pharmacokinetics in man. *Anaesthesia* 1984;40:837.
- ◆ Mather LE: Clinical pharmacokinetics of fentanyl and its newer derivatives. *Clin Pharmacokinet* 1983;8:422.
- ◆ Product Information, Hospira, 2005

References updated 3/2008

Text updated 3/2002

Compatibilities updated 3/2007

Dose & Administration

IV: 5 to 10 mcg/kg per dose IV over 15 seconds. May repeat every 45 seconds until the patient is awake. Maximum total cumulative dose should not exceed 50 mcg/kg (0.05 mg/kg) or 1 mg in infants, whichever is smaller (data in infants older than 1 year). No reported maximum dose in neonates has been tested. Administer intravenously through a freely running large vein to minimize pain upon injection.

Intranasal: 40 mcg/kg per dose divided equally between both nostrils. Administer via TB syringe for accurate equal dosing.

Rectal: 15 to 30 mcg/kg per dose, may repeat if sedation not reversed within 15 to 20 minutes.

Uses

Reversal of sedative effect from benzodiazepines, in cases of suspected benzodiazepines overdose, and in neonatal apnea secondary to prenatal benzodiazepine exposure.

Monitoring

Monitor for the return of sedation and respiratory depression. Continuous EKG and blood pressure.

Adverse Effects/Precautions

The reported experience in neonates is very limited. Use with caution in neonates with pre-existing seizure disorders. Hypotension has been reported in adults following rapid administration. Resedation has been reported in 10% of treated pediatric patients, occurring 19 to 50 minutes after initial dosing. May cause pain on injection. Observe IV site for extravasation.

Black Box Warning

According to the manufacturer's black box warning, the use of flumazenil has been associated with the occurrence of seizures. Seizures are most frequent in patients who have been on benzodiazepines for long-term sedation.

Pharmacology

Imidazobenzodiazepine that is a benzodiazepine receptor antagonist. Competitively inhibits the activity at the benzodiazepine recognition site on the GABA/benzodiazepine receptor. Eliminated rapidly by hepatic metabolism to three inactive metabolites. Highly lipid soluble and penetrates the brain rapidly. Elimination half-life in children 20 to 75 minutes. Peak concentration reached in 3 minutes when delivered intravenously (children). Limited pharmacokinetic data in neonates.

Flumazenil

Special Considerations/Preparation

Available in an injectable form as a 0.1 mg/mL concentration in 5- and 10-mL multi-dose vials. If drawn into a syringe or mixed with D5W, LR, or NS, discard solution after 24 hours. Discard opened vials within 24 hours. Store at room temperature.

Solution Compatibility: D₅W, LR, and NS.

Terminal Injection Site Compatibility: Aminophylline, cimetidine, dobutamine, dopamine, famotidine, heparin, lidocaine, procainamide, and ranitidine.

Selected References

- ◆ Phelps SJ, Hak EB: *Pediatric Injectable Drugs*. Maryland: American Society of Health System Pharmacists, 2004, p176.
- ◆ Zaw W, Knoppert DC, da Silva O: Flumazenil's reversal of myoclonic-like movements associated with midazolam in term newborns. *Pharmacotherapy* 2001;21:642-6.
- ◆ Carbajal R, Simon N, Blanc P, et al: Rectal flumazenil to reverse midazolam sedation in children. *Anest Analog* 1996;82:895.
- ◆ Richard P, Autret E, Bardol J, et al: The use of flumazenil in a neonate. *Clin Toxicol* 1991;29:137-40.
- ◆ Brogden RN, Goa KL: Flumazenil. A review of its benzodiazepine antagonist properties, intrinsic activity and therapeutic use. *Drugs* 1988;35:448-67.
- ◆ Product Information, Roche, 2007.

Adverse Effects/Precautions updated 1/2009

Compatibilities updated 3/2007

Added 3/2005

Dose & Administration

Note: Fosphenytoin dosing is expressed in phenytoin equivalents (PE). (Fosphenytoin 1 mg PE = phenytoin 1 mg)

Loading dose: 15 to 20 mg PE/kg IM or IV infusion over at least 10 minutes.

Maintenance dose: 4 to 8 mg PE/kg Q24 hours IM or IV slow push. Begin maintenance 24 hours after loading dose.

Maximum rate of infusion 1.5 mg PE/kg per minute. May be administered more rapidly than phenytoin due to less infusion-related toxicity. Flush IV with saline before and after administration.

Term infants older than 1 week of age may require up to 8 mg PE/kg per dose Q8 to 12 hours.

Uses

Anticonvulsant. Generally used to treat seizures that are refractory to phenobarbital. Can be administered with lorazepam for rapid onset of seizure control.

Monitoring

Monitor blood pressure closely during infusion. Measure trough serum phenytoin (not fosphenytoin) concentration; obtain 48 hours after IV loading dose. Therapeutic serum phenytoin concentration: Probably 6 to 15 mcg/mL (up to 10 to 20 mcg/mL). Collect blood samples in EDTA tubes to minimize fosphenytoin to phenytoin conversion in the tube.

Adverse Effects/Precautions

Clinical signs of toxicity, such as drowsiness, are difficult to identify in infants, but are dose and infusion rate dependent. Minor venous irritation upon IV administration. Fosphenytoin drug interactions are similar to phenytoin (i.e. carbamazepine, cimetidine, corticosteroids, digoxin, furosemide, phenobarbital, and valproate).

FDA ALERT [11/24/08]: FDA is investigating new preliminary data regarding a potential increased risk of serious skin reactions including Stevens Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) from phenytoin therapy in Asian patients positive for a particular human leukocyte antigen (HLA) allele, HLA-B*1502. This allele occurs almost exclusively in patients with ancestry across broad areas of Asia, including Han Chinese, Filipinos, Malaysians, South Asian Indians, and Thais. Because fosphenytoin is a prodrug and is converted to phenytoin after administration, any concern regarding this association is also applicable to fosphenytoin.

Use with caution in neonates with hyperbilirubinemia: both fosphenytoin and bilirubin displace phenytoin from protein-binding sites, resulting in increased serum free phenytoin concentration.

Fosphenytoin

Pharmacology

Fosphenytoin is a water-soluble prodrug of phenytoin rapidly converted by phosphatases in blood and tissue. It has no known intrinsic pharmacologic activity before conversion to phenytoin. Each 1.5 mg of fosphenytoin is metabolically converted to 1 mg phenytoin. Conversion half-life of fosphenytoin administered intravenously to young pediatric patients is approximately 7 minutes. Data obtained using spiked blood samples from term and preterm neonates demonstrated similar conversion rates. No drugs have been identified to interfere with the conversion of fosphenytoin to phenytoin. Fosphenytoin is highly protein bound (adults 95% to 99%) and does not penetrate the blood-brain barrier. Serum half-life reflects that of phenytoin (18 to 60 hours) due to rapid conversion. The conversion of fosphenytoin to phenytoin yields very small amounts of formaldehyde and phosphate. This is only significant in cases of large overdosage. Phenytoin serum concentrations measured up to two hours after IV and four hours after IM dose may be falsely elevated due to fosphenytoin interaction with immunoanalytic methods (e.g. TDx fluorescence polarization).

Special Considerations/Preparation

Available as an injectable solution in a concentration equivalent to 50 mg PE/mL, in 2- and 10-mL vials. Administer IM undiluted. Administer IV after diluting in NS or D₅W to a concentration of 1.5 to 25 mg PE/mL. The pH is 8.6 to 9.0.

Store refrigerated. Stable for 48 hours at room temperature. Do not use vials containing particulate matter.

Solution Compatibility: D₅W, D₁₀W and NS.

Terminal Injection Site Compatibility: Lorazepam, phenobarbital, and potassium chloride.

Incompatibility: Midazolam.

Selected References

- ◆ FDA Alert [11/24/08]. Information for Healthcare Professionals: Phenytoin and Fosphenytoin. Available at: http://www.fda.gov/cder/drug/InfoSheets/HCP/phenytoin_fosphenytoinHCP.htm.
- ◆ Fischer JH, Patel TV, Fischer PA: Fosphenytoin: Clinical pharmacokinetics and comparative advantages in the acute treatment of seizures. *Clin Pharmacokinet* 2003;42:33-58.
- ◆ Takeoka M, Krishnamoorthy KS, Soman TB, et al: Fosphenytoin in infants. *J Child Neurol* 1998;13:537-540.
- ◆ Morton LD: Clinical experience with fosphenytoin in children. *J Child Neurol* 1998;13(Suppl 1): S19-S22.
- ◆ Hatzopoulos FK, Carlos MA, Fischer JH: Safety and pharmacokinetics of intramuscular fosphenytoin in neonates. *Pediatr Res* 1998;43:60A.
- ◆ Fischer JH, Cwik MJ, Luer MS, et al: Stability of fosphenytoin sodium with intravenous solutions in glass bottles, polyvinyl chloride bags, and polypropylene syringes. *Ann Pharmacother* 1997;31:553-559.
- ◆ English BA, Riggs RM, Webster AA, Benner KW: Y-site stability of fosphenytoin and sodium phenobarbital. *Int J Pharm Compound* 1999;3:64-66.
- ◆ Riggs RM, English BA, Webster AA, et al: Fosphenytoin Y-site stability studies with lorazepam and midazolam hydrochloride. *Int J Pharm Compound* 1999;3:235-238.
- ◆ Product Information, Teva, 2007

Adverse Effects/Precautions and References updated 1/2009

Dose & Administration

Initial dose: 10 mg/kg per dose Q24 hours IV or PO in the neonatal period, Q12 hours later in infancy.

Adjust dosage upward as needed every 1 to 2 weeks to a maximum of 30 mg/kg per dose.

Frequency: Administer every 24 hours in the immediate neonatal period, every 12 hours later in infancy.

Administer IV slowly over 15 minutes. Dilute to a concentration of 5 mg/mL with a compatible diluent prior to administration.

Uses

Anticonvulsant. In the neonatal period, it has been used as a second line of therapy for seizures refractory to phenobarbital and other anticonvulsants.

Monitoring

Serum trough concentrations are not routinely monitored, although they may be useful when determining the magnitude of dosing adjustments. Therapeutic concentrations are approximately 10 to 40 mcg/mL.

Adverse Effects/Precautions

Data in neonates are limited to case reports and abstracts. Sedation and irritability have been reported in neonates and young infants. When discontinuing therapy, wean the dose gradually to minimize the potential of increased seizure frequency.

Pharmacology

Rapidly and completely absorbed after oral administration, with the onset of action by 30 minutes and peak concentration within 2 hours. Bioavailability is not affected by food. Half-life in the immediate neonatal period is approximately 18 hours, decreasing to 6 hours by 6 months of age. Minimal protein binding. Linear pharmacokinetics. Primarily (66%) excreted unchanged in the urine, with some metabolism via enzymatic hydrolysis to inactive metabolites (no cytochrome p450 involvement). Dose should be adjusted in patients with renal impairment. The precise mechanism of action is unknown. Levetiracetam inhibits burst firing without affecting normal neuronal excitability, suggesting that levetiracetam may selectively prevent hypersynchronization of epileptiform burst firing and propagation of seizure activity. There are no known significant drug interactions.

Special Considerations/Preparation

Kepra® Injection for intravenous use is available in single-use 5 mL vials containing 500 mg (100 mg/mL). Kepra® Oral Solution is available in a concentration of 100 mg/mL (dye- and alcohol-free). Store both products at controlled room temperature.

Solution Compatibility: NS, Lactated Ringer's, and D₅W.

Terminal Injection Site Compatibility: Lorazepam.

Levetiracetam

Selected References

- ◆ Shoemaker MT, Rotenberg JS: Levetiracetam for the treatment of neonatal seizures. *J Child Neurol* 2007;22:95-98.
- ◆ Grosso S, Cordelli DM, Franzoni E, et al: Efficacy and safety of levetiracetam in infants and young children with refractory epilepsy. *Seizure* 2007;16:345-350.
- ◆ Striano P, Coppola A, Pezzella M, et al: An open-label trial of levetiracetam in severe myoclonic epilepsy of infancy. *Neurology* 2007;69:250-254.
- ◆ Allegaert K, Lewi L, Naulaers G, et al: Levetiracetam pharmacokinetics in neoates at birth. *Epilepsia* 2006;47:1068-1069.
- ◆ Glauser TA, Mitchell WG, Weinstock A, et al: Pharmacokinetics of levetiracetam in infants and children with epilepsy. *Epilepsia* 2007;48:1117-22.
- ◆ Tomson T, Palm R, Kallen K, et al: Pharmacokinetics of levetiracetam during pregnancy, delivery, in the neonatal period, and lactation. *Epilepsia* 2007;48:1111-1116.
- ◆ De Smedt T, Raedt R, Vonck K, Boon P: Levetiracetam: Part II, the clinical profile of a novel anticonvulsant drug. *CNS Reviews* 2007;13:57-78.
- ◆ Product information, UCB, 2008.

Added 3/2008

Dose & Administration**Term, normothermic newborns:**

Loading dose: 2 mg/kg IV over 10 minutes, followed immediately by a

Maintenance infusion: 6 mg/kg per hour for 6 hours, then 4 mg/kg per hour for 12 hours, then 2 mg/kg per hour for 12 hours.

Caution: Preterm newborns and term newborns undergoing hypothermia treatment are at risk for drug accumulation due to slower drug clearance. Precise dosing in these infants is uncertain.

Uses

Treatment of severe recurrent or prolonged seizures that do not respond to first-line therapies.

Monitoring

Continuous monitoring of EKG, heart rate, and blood pressure. Observe for worsening of seizure activity. Measuring blood concentrations is not clinically useful except when accumulation is suspected.

Adverse Effects/Precautions

Do not use concurrently with phenytoin due to cardiac effects. Stop infusion immediately if significant cardiac arrhythmia occurs. Arrhythmias and significant bradycardia have occurred in 5% of reported cases. Slowing of the heart rate is common.

Pharmacology

The mode of action for lidocaine as an anticonvulsant drug is unknown. Lidocaine is metabolized in the liver into 2 active metabolites: monoethylglycinexylidide (MEGX) and glycinxylidide (GX). Approximately 30% is excreted unchanged in the urine. The half-life in neonates is at least 3 hours, and clearance is dose-dependent. The clinically effective dose of 6 mg/kg/hr will lead to accumulation of both lidocaine and metabolites within several hours. Free drug fraction in both term and premature neonates is approximately twice that found in older children because of significantly reduced protein binding by alpha 1-acid glycoprotein.

Special Considerations/Preparation

Use only preservative-free lidocaine without epinephrine. Available in multiple concentrations ranging from 1% to 20%. To make a dilution for bolus dosing, dilute 10 mg lidocaine (0.5 mL of 2% solution) in 9.5 mL NS or D₅W, yielding a 1 mg/mL final concentration.

Solution Compatibility: D₅W, D₁₀W, and NS.

Terminal Injection Site Compatibility: Dex/AA solutions, fat emulsion. Alteplase, aminophylline, amiodarone, ampicillin, caffeine citrate, calcium chloride, calcium gluconate, cefazolin, cefoxitin, ceftriaxone, chloramphenicol, cimetidine, dexamethasone, digoxin, dobutamine, dopamine, enalaprilat, erythromycin lactobionate, famotidine, fentanyl, flumazenil, furosemide, glycopyrrolate, heparin, hydrocortisone succinate, insulin, linezolid, methicillin, metoclopramide, micafungin, morphine, nafcillin, nicardipine, nitroglycerin, penicillin G, pentobarbital, potassium chloride, procainamide, prostaglandin E1, ranitidine, sodium bicarbonate, and sodium nitroprusside.

Incompatibility: Phenytoin.

Selected References

- ◆ Shany E, Benzaqen O, Watemberg N: Comparison of continuous drip of midazolam or lidocaine in the treatment of intractable neonatal seizures. *J Child Neurol* 2007;22:255-259.
- ◆ Rademaker CMA, de Vries LS: Lidocaine for neonatal seizure management. *NeoReviews* 2008;9:e585-e589.
- ◆ Malingre MM, Van Rooij LGM, Rademaker CMA, et al: Development of an optimal lidocaine infusion strategy for neonatal seizures. *Eur J Pediatr* 2006;165:598-604.
- ◆ Van Rooij LGM, Toet MC, Rademaker KMA, et al: Cardiac arrhythmias in neonates receiving lidocaine as anticonvulsive treatment. *Eur J Pediatr* 2004;163:637-641.
- ◆ Hellstrom-Westas L, Svenningsen NW, Westgren U, et al: Lidocaine for treatment of severe seizures in newborn infants. II. Blood concentrations of lidocaine and metabolites during intravenous infusion. *Acta Paediatr* 1992;81:35-39.
- ◆ Hellstrom-Westas L, Westgren U, Rosen I, Svenningsen NW: Lidocaine for treatment of severe seizures in newborn infants. I. Clinical effects and cerebral electrical activity monitoring. *Acta Paediatr Scand* 1988;77:79-84.
- ◆ Rey E, Radvanyi-Bouvet MF, Bodiou C, et al: Intravenous lidocaine in the treatment of convulsions in the neonatal period: Monitoring plasma levels. *Ther Drug Monit* 1990;12:316-320.

Dose & Administration and References updated 1/2009
Added 3/2006

Dose & Administration

0.05 to 0.1 mg/kg per dose IV slow push. Repeat doses based on clinical response.

Uses

Anticonvulsant—acute management of patients with seizures refractory to conventional therapy.

Monitoring

Monitor respiratory status closely. Observe IV site for signs of phlebitis or extravasation.

Adverse Effects/Precautions

Respiratory depression. Rhythmic myoclonic jerking has occurred in premature neonates receiving lorazepam for sedation.

Pharmacology

Dose-dependent CNS depression. Onset of action within 5 minutes; peak serum concentration within 45 minutes. Duration of action is 3 to 24 hours. Mean half-life in term neonates is 40 hours. Metabolized to an inactive glucuronide, which is excreted by the kidneys. Highly lipid-soluble.

Special Considerations/Preparation

Limited data are available for neonates. Available in 2-mg/mL and 4-mg/mL concentrations (1 mL preservative free vial) and 2 mg/mL multidose vial (10 mL). Some available products contain 2% (20 mg/mL) benzyl alcohol and 18% polyethylene glycol 400 in propylene glycol. A dilution of 0.4 mg/mL may be prepared by adding 1 mL of 4 mg/mL concentration in 9 mL of preservative-free sterile water for injection. This will make it easier to measure the dose and decrease the benzyl alcohol content to 0.5 mg/kg per dose.

Solutions should not be used if they are discolored or contain a precipitate.

Solution Compatibility: D₅W, NS, and sterile water for injection.

Terminal Injection Site Compatibility: Dex/AA solutions. Acyclovir, amikacin, amiodarone, bumetanide, cefepime, cefotaxime, cimetidine, dexamethasone, dobutamine, dopamine, epinephrine, erythromycin lactobionate, famotidine, fentanyl, fluconazole, fosphenytoin, furosemide, gentamicin, heparin, hydrocortisone succinate, labetalol, levetiracetam, linezolid, metronidazole, midazolam, milrinone, morphine, nicardipine, nitroglycerin, pancuronium bromide, piperacillin, piperacillin-tazobactam, potassium chloride, propofol, ranitidine, remifentanil, trimethoprim-sulfamethoxazole, vancomycin, vecuronium, and zidovudine.

Incompatibility: Fat emulsion. Aztreonam, caffeine citrate, imipenem/cilastatin, and omeprazole.

Lorazepam

Selected References

- ◆ Sexson WR, Thigpen J, Stajich GV: Stereotypic movements after lorazepam administration in premature neonates: a series and review of the literature. *J Perinatol* 1995;15:146-49.
- ◆ McDermott CA, Kowalczyk AL, Schnitzler ER, et al: Pharmacokinetics of lorazepam in critically ill neonates with seizures. *J Pediatr* 1992;120:479.
- ◆ Deshmukh A, Wittert W, Schnitzler E, Mangurten HH: Lorazepam in the treatment of refractory neonatal seizures. *Am J Dis Child* 1986;140:1042.
- ◆ Product Information, Bedford, 2004

Compatibilities updated 3/2006

Text updated 3/98

Dose & Administration

Initial dose: 0.05 to 0.2 mg/kg per dose Q12 to 24 hours PO.

Reduce dose by 10% to 20% per week over 4 to 6 weeks. Adjust weaning schedule based on signs and symptoms of withdrawal.

Uses

Treatment of opiate withdrawal.

Monitoring

Monitor respiratory and cardiac status closely. A 12-lead ECG should be obtained on methadone-exposed infants experiencing bradycardia or tachycardia. Assess for gastric residuals, abdominal distention, and loss of bowel sounds.

Adverse Effects/Precautions

Respiratory depression in excessive doses. Ileus and delayed gastric emptying. In a single case report, QTc prolongation was noted in a term infant born to a mother receiving methadone maintenance therapy (50 mg/day). After birth, the infant's resting HR was 80 to 90 beats per minute and ECG showed a QTc of 510 ms. This resolved spontaneously over 5 days.

Black Box Warning

According to the manufacturer's black box warning, deaths have been reported during initiation of methadone treatment for opioid dependence. In some cases, deaths appear to have occurred due to respiratory or cardiac effects of methadone and too-rapid titration without appreciation for the accumulation of methadone over time. It is critical to understand the pharmacokinetics of methadone and to exercise vigilance during treatment initiation and dose titration. Respiratory depression is the chief hazard associated with methadone, and its peak respiratory depressant effects typically occur later, and persist longer than its peak analgesic effects, particularly in the early dosing period. Cases of QT interval prolongation and serious arrhythmia (torsades de pointes) have been observed (in adults). Most cases involve (adult) patients being treated for pain with large, multiple daily doses, although cases have been reported in patients receiving doses used for maintenance treatment of opioid addiction. Special requirements for dispensing exist, and the oral solution must not be injected.

Pharmacology

Long-acting narcotic analgesic. Oral bioavailability is 50%, with peak plasma levels obtained in 2 to 4 hours. Metabolized extensively via hepatic N-demethylation. Highly protein bound (90% adults). Serum half-life ranges from 16 to 25 hours in neonates and is prolonged in patients with renal failure. Rifampin and phenytoin accelerate the metabolism of methadone and can precipitate withdrawal symptoms.

Special Considerations/Preparation

Available as oral solutions in 1- and 2-mg/mL concentrations containing 8% alcohol, and a 10-mg/mL alcohol-free solution. May dilute 1 mL of the 10-mg/mL concentrated solution with 19 mL of sterile water to provide an oral dilution with a final concentration of 0.5 mg/mL. Stable for 24 hours refrigerated. Also available as 5- and 10-mg tablets.

continued...

Selected References

- ◆ Krantz MJ, Martin J, Stimmel B, et al: QTc interval screening in methadone treatment. *Ann Intern Med* 2009;150:1-9.
- ◆ Hussain T, Ewer AK: Maternal methadone may cause arrhythmias in neonates. *Acta Paediatr* 2007;96:768-769.
- ◆ Guo J, Greenberg M, Finer NN, Heldt GP: Methadone is a superior detoxification agent compared to tincture opium for treatment of neonatal narcotic abstinence syndrome (NAS). Abstract 4850.230, 2006 Pediatric Academic Societies Annual Meeting.
- ◆ Tobias JD, Schleien CL, Haun SE: Methadone as treatment for iatrogenic narcotic dependency in pediatric intensive care unit patients. *Crit Care Med* 1990;18:1292.
- ◆ Koren G, Maurice L: Pediatric uses of opioids. *Ped Clin North Am* 1989;36:1141.
- ◆ Rosen TS, Pippenger CE: Pharmacologic observations on the neonatal withdrawal syndrome. *J Pediatr* 1976;88:1044.
- ◆ Product Information, Roxane, 2007

Adverse Effects/Precautions, Monitoring and References updated 3/2009
Added 1/1995

Dose & Administration**Sedation:**

IV: 0.05 to 0.15 mg/kg over at least 5 minutes. Repeat as required, usually Q2 to 4 hours. May also be given IM. Dosage requirements are decreased by concurrent use of narcotics.

Continuous IV infusion: 0.01 to 0.06 mg/kg per hour (10 to 60 mcg/kg/hour). Dosage may need to be increased after several days of therapy because of development of tolerance and/or increased clearance.

Intranasal: 0.2 to 0.3 mg/kg per dose using 5-mg/mL injectable form.

Sublingual: 0.2 mg/kg per dose using 5-mg/mL injectable form mixed with a small amount of flavored syrup.

Oral: 0.25 mg/kg per dose using Versed® oral syrup.

Anticonvulsant: Loading dose: 0.15 mg/kg (150 mcg/kg) IV over at least 5 minutes, followed by

Maintenance infusion: 0.06 to 0.4 mg/kg per hour (1 to 7 mcg/kg per minute).

Uses

Sedative/hypnotic. Anesthesia induction. Treatment of refractory seizures.

Monitoring

Follow respiratory status and blood pressure closely, especially when used concurrently with narcotics. Assess hepatic function. Observe for signs of withdrawal after discontinuation of prolonged therapy.

Adverse Effects/Precautions**Black Box Warning**

According to the manufacturer's black box warning, midazolam has been associated with respiratory depression and respiratory arrest, especially when used for sedation in noncritical care settings. Doses should be titrated slowly. Midazolam should not be given by rapid injection in the neonatal population, as severe hypotension and seizures have been reported.

Respiratory depression and hypotension are common when used in conjunction with narcotics, or following rapid bolus administration. Seizure-like myoclonus has been reported in 8% of premature infants receiving continuous infusions - this also may occur following rapid bolus administration and in patients with underlying CNS disorders. Nasal administration may be uncomfortable because of a burning sensation.

Pharmacology

Relatively short-acting benzodiazepine with rapid onset of action. Sedative and anticonvulsant properties related to GABA accumulation and occupation of benzodiazepine receptor. Antianxiety properties related to increasing the glycine inhibitory neurotransmitter. Metabolized by hepatic CYP 3A4 to a less active hydroxylated metabolite, then glucuronidated before excretion in urine. Drug accumulation may occur with repeated doses, prolonged infusion therapy, or concurrent administration of cimetidine, erythromycin or fluconazole. Highly protein bound. Duration of action is 2 to 6 hours. Elimination half-life is approximately 4 to 6 hours in term neonates, and quite variable, up to 22 hours, in premature babies and those with impaired hepatic function. Bioavailability is approximately 36% with oral administration and 50% with sublingual and intranasal administration. Midazolam is water soluble in acidic solutions and becomes lipid soluble at physiologic pH.

Special Considerations/Preparation

A preservative-free preparation is available as 1- and 5-mg/mL concentrations in 1-, 2-, and 5-mL vials.

Versed® is available in an injectable form as 1- and 5-mg/mL concentrations in 1-, 2-, 5-, and 10-mL vials. Contains 1% (10mg/mL) benzyl alcohol as a preservative. To decrease benzyl alcohol content, a 0.5 mg/mL dilution may be made by adding 1 mL of the 5-mg/mL concentration to 9 mL preservative-free sterile water for injection. Dilution stable for 24 hours refrigerated.

Versed® oral syrup is available in a 2 mg/mL concentration. Store at room temperature.

Solution Compatibility: D₅W, NS, and sterile water for injection.

Terminal Injection Site Compatibility: Dex/AA solutions. Amikacin, aminophylline, amiodarone, atropine, calcium gluconate, cefazolin, cefotaxime, cimetidine, clindamycin, digoxin, dobutamine, dopamine, epinephrine, erythromycin lactobionate, esmolol, famotidine, fentanyl, fluconazole, gentamicin, glycopyrrolate, heparin, imipenem/cilastatin, insulin, linezolid, lorazepam, methadone, metoclopramide, metronidazole, milrinone, mivacurium, morphine, nicardipine, nitroglycerin, nitroprusside, pancuronium bromide, piperacillin, potassium chloride, propofol, prostaglandin E₁, ranitidine, remifentanil, sodium nitroprusside, theophylline, tobramycin, vancomycin, and vecuronium.

Incompatibility: Fat emulsion. Albumin, ampicillin, bumetanide, ceftazidime, dexamethasone, fosphenytoin, furosemide, hydrocortisone succinate, micafungin, nafcillin, omeprazole, pentobarbital, phenobarbital, and sodium bicarbonate.

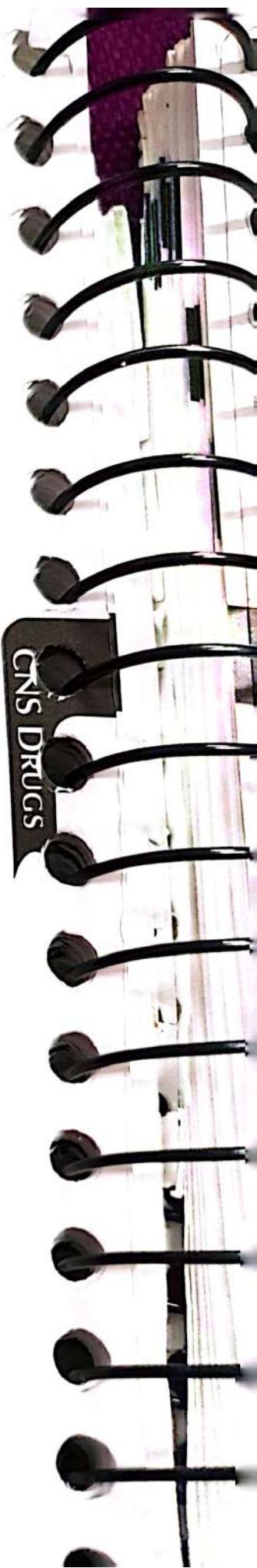
Selected References

- ◆ Casto Conde JR, Hernandez Borges AA, Martinez E, et al: Midazolam in neonatal seizures with no response to phenobarbital. *Neurology* 2005;64:876-879.
- ◆ van Leuven K, Groenendaal F, Toet MC, et al: Midazolam and amplitude-integrated EEG in asphyxiated full-term neonates. *Acta Paediatr* 2004;93:1221-1227.
- ◆ de Wildt SN, Kearns GL, Hop WCJ, et al: Pharmacokinetics and metabolism of intravenous midazolam in preterm infants. *Clin Pharmacol Ther* 2001;70:525-531.
- ◆ Coté CJ, Cohen IT, Suresh S, et al: A comparison of three doses of a commercially prepared oral midazolam syrup in children. *Anesth Analg* 2002;94:37-43.
- ◆ Sheth RD, Buckley DJ, Gutierrez AR: Midazolam in the treatment of refractory neonatal seizures. *Clin Neuropharmacol* 1996;2:165-70.
- ◆ Olkkola KT, Ahonen J, Neuvonen PJ: The effect of the systemic antimycotics, itraconazole and fluconazole, on the pharmacokinetics and pharmacodynamics of intravenous and oral midazolam. *Anesth Analg* 1996;82:511.
- ◆ Jacqz-Aigrain E, Daoud P, Burtin P, et al: Placebo-controlled trial of midazolam sedation in mechanically ventilated newborn babies. *Lancet* 1994;344:646-50.
- ◆ Magnyn JF, d'Allest AM, Nedelcoux H, et al: Midazolam and myoclonus in neonate. *Eur J Pediatr* 1994;153:389.
- ◆ Karl HW, Rosenberger JL, Larach MG, Ruffie JM: Transmucosal administration of midazolam for premedication of pediatric patients: Comparison of the nasal and sublingual routes. *Anesthesiology* 1993;78:885.
- ◆ Jacqz-Aigrain E, Daoud P, Burtin P, et al: Pharmacokinetics of midazolam during continuous infusion in critically ill neonates. *Eur J Clin Pharmacol* 1992;42:329.
- ◆ van Straaten HLM, Rademaker CMA, de Vries LS: Comparison of the effect of midazolam or vecuronium on blood pressure and cerebral blood flow velocity in the premature newborn. *Dev Pharmacol Ther* 1992;19:191.
- ◆ Product Information, Hospira, 2004

Dose & Administration, Adverse Effects/Precautions, and References updated 1/2009

Compatibilities updated 3/2005

Pharmacology updated 3/2003



Dose & Administration

0.05 to 0.2 mg/kg per dose IV over at least 5 minutes, IM, or SC. Repeat as required (usually Q4 hours).

Continuous infusion: Give a loading dose of 100 to 150 mcg/kg over 1 hour followed by 10 to 20 mcg/kg per hour.

Treatment of opioid dependence: Begin at most recent IV morphine dose equivalent. Taper 10 to 20% per day as tolerated. Oral dose is approximately 3 to 5 times IV dose.

Initial treatment of neonatal narcotic abstinence: 0.03 to 0.1 mg/kg per dose PO Q3 to 4 hours. Wean dose by 10 to 20% every 2 to 3 days based on abstinence scoring. (The Finnegan score should be < 9). Use a 0.4-mg/mL dilution made from a concentrated oral morphine sulfate solution.

Uses

Analgesia. Sedation. Treatment of opioid withdrawal and abstinence.

Monitoring

Monitor respiratory and cardiovascular status closely. Observe for abdominal distention and loss of bowel sounds. Consider urine retention if output is decreased.

Adverse Effects/Precautions

Naloxone should be readily available to reverse adverse effects. Marked respiratory depression (decreases the responsiveness of the respiratory center to CO₂ tension). Hypotension and bradycardia. Transient hypertonia. Ileus and delayed gastric emptying. Urine retention. Tolerance may develop after prolonged use—wean slowly. Seizures reported in two infants who received bolus plus infusion.

Pharmacology

Morphine is a narcotic analgesic that stimulates brain opioid receptors. Increases venous capacitance, caused by release of histamine and central suppression of adrenergic tone. GI secretions and motility decreased. Increases smooth muscle tone. Morphine is converted in the liver to two glucuronide metabolites (morphine-6-glucuronide and morphine-3-glucuronide) that are renally excreted. Morphine-6-glucuronide (M6G) is a potent respiratory-depressant and analgesic. Morphine-3-glucuronide (M3G) is an antagonist to the effects of morphine and morphine-6-glucuronide. Morphine is 20% to 40% bioavailable when administered orally. Pharmacokinetics are widely variable. Elimination half-life is approximately 9 hours for morphine and 18 hours for morphine-6-glucuronide. Steady state concentrations of morphine are reached by 24 to 48 hours.

Special Considerations/Preparation

Injectable solutions are available in dosage strengths ranging from 0.5- to 50-mg/mL.

Oral morphine sulfate solutions are available in concentrations of 2, 4, and alcohol-free 20 mg/mL.

A 0.4-mg/mL oral morphine dilution may be made by adding 1 mL of the 4-mg/mL injectable solution to 9 mL preservative-free normal saline. Stable for 7 days refrigerated. **Protect from light.**

continued...

Morphine

Solution Compatibility: D₅W, D₁₀W, and NS.

For continuous infusions of morphine **containing heparin:** Use only NS; maximum morphine concentration 5 mg/mL.

Terminal Injection Site Compatibility: Dex/AA solutions, fat emulsion. Acyclovir, alteplase, amikacin, aminophylline, amiodarone, ampicillin, atropine, aztreonam, bumetanide, caffeine citrate, calcium chloride, cefotaxime, cefoxitin, ceftazidime, ceftriaxone, chloramphenicol, cefazolin, cimetidine, clindamycin, dexamethasone, digoxin, dobutamine, dopamine, enalaprilat, epinephrine, erythromycin lactobionate, esmolol, famotidine, fentanyl, fluconazole, furosemide, gentamicin, glycopyrrolate, heparin, hydrocortisone succinate, insulin, lidocaine, linezolid, lorazepam, meropenem, metoclopramide, metronidazole, mezlocillin, midazolam, milrinone, nafcillin, nicardipine, nitroglycerin, oxacillin, pancuronium bromide, penicillin G, phenobarbital, piperacillin, piperacillin-tazobactam, potassium chloride, propofol, propranolol, prostaglandin E₁, ranitidine, remifentanil, sodium bicarbonate, sodium nitroprusside, ticarcillin/clavulanate, tobramycin, trimethoprim-sulfamethoxazole, vancomycin, vecuronium, and zidovudine.

Incompatibility: Azithromycin, cefepime, micafungin, pentobarbital, and phenytoin.

Selected References

- ◆ Langenfeld S, Birkenfeld L, Herkenrath P, et al: Therapy of the neonatal abstinence syndrome with tincture of opium or morphine drops. *Drug Alcohol Depend* 2005;77:31-36.
- ◆ Oei J, Lui K: Management of the newborn infant affected by maternal opiates and other drugs of dependency. *J Paediatr Child Health* 2007;43:9-18.
- ◆ Saarenmaa E, Neuvonen PJ, Rosenberg P, Fellman V: Morphine clearance and effects in newborn infants in relation to gestational age. *Clin Pharmacol Ther* 2000;68:160-166.
- ◆ American Academy of Pediatrics Committee on Drugs: Neonatal drug withdrawal. *Pediatrics* 1998;101:1079-1088.
- ◆ Yaster M, Kost-Byerly S, Berde C, Billet C: The management of opioid and benzodiazepine dependence in infants, children, and adolescents. *Pediatrics* 1996;98:135-40.
- ◆ Barrett DA, Barker DP, Rutter N, et al: Morphine, morphine-6-glucuronide and morphine-3-glucuronide pharmacokinetics in newborn infants receiving diamorphine infusions. *Br J Clin Pharmacol* 1996;41:531.
- ◆ Hartley R, Green M, Quinn M, Levene MI: Pharmacokinetics of morphine infusion in premature neonates. *Arch Dis Child* 1993;69:55.
- ◆ Chay PCW, Duffy BJ, Walker JS: Pharmacokinetic-pharmacodynamic relationships of morphine in neonates. *Clin Pharmacol Ther* 1992;51:334.
- ◆ Koren G, Butt W, Chinyanga H, et al: Postoperative morphine infusion in newborn infants: Assessment of disposition characteristics and safety. *J Pediatr* 1985;107:963.
- ◆ Product Information, Mayne, 2004

Dose and References updated 3/2007

Dose & Administration

Suggested dose: 0.1 mg/kg IV push.

Doses needed to reverse narcotic-induced depression may be as low as 0.01 mg/kg.

May give IM if adequate perfusion. Tracheal administration is not recommended. There are no studies to support or refute the current dosing recommendations.

Uses

Narcotic antagonist. Adjuvant therapy to customary resuscitation efforts for narcotic-induced respiratory (CNS) depression. Naloxone is not recommended as part of the initial resuscitation of newborns with respiratory depression in the delivery room. Before naloxone is given, providers should restore heart rate and color by supporting ventilation.

Monitoring

Assess respiratory effort and neurologic status.

Adverse Effects/Precautions

No short-term toxicity observed. One case report of seizures secondary to acute opioid withdrawal after administration to an infant born to an opioid abuser. Long-term safety has not been investigated.

Pharmacology

Reverses respiratory depression by competing for CNS narcotic receptor sites. Onset of action is variable, but usually within minutes after IV administration, and approximately 1 hour after IM administration. Half-life in neonates is approximately 70 minutes. Metabolized by the liver and excreted in the urine. Increases circulating catecholamines.

Special Considerations/Preparation

Do not mix in an alkaline solution. Available in 0.4 mg/mL and 1 mg/mL concentrations. **Store at room temperature and protect from light.**

Solution Compatibility: No data are currently available on Dex/AA.

Terminal Injection Site Compatibility: Heparin, linezolid, and propofol. No data are currently available on potassium chloride and other medications.

Selected References

- ◆ The International Liaison Committee on Resuscitation: The International Liaison Committee on Resuscitation (ILCOR) Consensus on Science With Treatment Recommendations for Pediatric and Neonatal Patients: Neonatal Resuscitation. *Pediatrics* 2006;117(5).
- URL:<http://www.pediatrics.org/cgi/content/full/117/5/e978> .
- ◆ Guinsburg R, Wyckoff MH. Naloxone during neonatal resuscitation: acknowledging the unknown. *Clin Perinatol* 2006;33:121132.
- ◆ Herschel M, Khoshnood B, Lass N. Role of naloxone in newborn resuscitation. *Pediatrics* 2000;106:831-834.
- ◆ McGuire W, Fowlie PW. Naloxone for narcotic exposed newborn infants: systematic review. *Arch Dis Child Fetal Neonatal Ed* 2003;88:F308F311.
- ◆ Product Information, Hospira, 2005

Dose & Administration

Myasthenia gravis: 0.1 mg IM (give 30 minutes before feeding). 1 mg PO (give 2 hours before feeding). Dose may have to be increased and should be titrated.

Reversal of neuromuscular blockade: 0.04 to 0.08 mg/kg IV, in addition to atropine 0.02 mg/kg.

Uses

Neonatal transient myasthenia gravis. Neonatal persistent (congenital) myasthenia gravis. Reversing effects of neuromuscular blocking drugs.

Monitoring

Monitor respiratory and cardiovascular status closely.

Adverse Effects/Precautions

Contraindicated in presence of intestinal or urinary obstruction, bradycardia, or hypotension. Use cautiously in patients with bronchospasm or cardiac arrhythmia. Adverse effects include muscle weakness, tremors, bradycardia, hypotension, respiratory depression, bronchospasm, diarrhea, and excessive salivation.

Pharmacology

Inhibits acetylcholinesterase at the neuromuscular junction, allowing accumulation of acetylcholine and thus restoring activity.

Special Considerations/Preparation

Available as injectable solution in 1-mL ampules and 10-mL vials in concentrations of 1:1000 (1 mg/mL) and 1:2000 (0.5 mg/mL). **Protect from light.**

Solution Compatibility: No data.

Terminal Injection Site Compatibility: Glycopyrrolate, heparin, hydrocortisone succinate, netilmicin, pentobarbital and potassium chloride.

Selected References

- ◆ Fisher DM, Cronnelly R, Miller RD, Sharma M: The neuromuscular pharmacology of neostigmine in infants and children. *Anesthesiology* 1983;59:220.
- ◆ Goudsouzian NG, Crone RK, Todres ID: Recovery from pancuronium blockade in the neonatal intensive care unit. *Br J Anaesth* 1981;53:1303.
- ◆ Sarnat HB: Neuromuscular disorders in the neonatal period, in Korobkin R, Guillemain C (eds): *Advances in Perinatal Neurology*. New York: Spectrum Publications, 1979, p 153.
- ◆ Product Information, Abraxis, 2006

Text updated 3/2001

Compatibilities updated 3/2001

Dose & Administration

0.1 mg/kg (0.04 to 0.15 mg/kg) IV push, as needed for paralysis. Usual dosing interval is 1 to 2 hours. Adjust dose as needed based on duration of paralysis.

Uses

Skeletal muscle relaxation/paralysis in infants requiring mechanical ventilation. Proposed desirable effects are improved oxygenation/ventilation, reduced barotrauma, and reduced fluctuations in cerebral blood flow.

Monitoring

Monitor vital signs frequently, blood pressure continuously. Use some form of eye lubrication.

Adverse Effects/Precautions

Hypoxemia may occur because of inadequate mechanical ventilation and deterioration in pulmonary mechanics. Tachycardia and blood pressure changes (both hypotension and hypertension) occur frequently. Increased salivation.

Black Box Warning

According to the manufacturer's black box warning, pancuronium should be administered by adequately trained individuals familiar with its actions, characteristics, and hazards.

Pharmacology

Nondepolarizing muscle-relaxant that competitively antagonizes autonomic cholinergic receptors and also causes sympathetic stimulation. Partially hydroxylated by the liver, 40% excreted unchanged in urine. Onset of action is 1 to 2 minutes; duration varies with dose and age. Reversed by neostigmine and atropine.

Factors affecting duration of neuromuscular blockade:

Potentiation: Acidosis, hypothermia, neuromuscular disease, hepatic disease, renal failure, cardiovascular disease, younger age, aminoglycosides, hypermagnesemia, and hypokalemia.

Antagonism: Alkalosis, epinephrine, and hyperkalemia.

Sensation remains intact; analgesia should be used for painful procedures.

Special Considerations/Preparation

Available in concentrations of 1-mg/mL (10 mL vials) and 2-mg/mL (2- and 5-mL vials). Products contain 1% (10 mg/mL) benzyl alcohol. **Refrigerate.**

Solution Compatibility: D₅W and NS.

Terminal Injection Site Compatibility: Dex/AA. Aminophylline, caffeine citrate, cefazolin, cimetidine, dobutamine, dopamine, epinephrine, esmolol, fentanyl, fluconazole, gentamicin, heparin, hydrocortisone succinate, isoproterenol, lorazepam, midazolam, milrinone, morphine, netilmicin, nitroglycerin, nitroprusside, propofol, prostaglandin E₁, ranitidine, trimethoprim-sulfamethoxazole, and vancomycin.

Incompatibility: Pentobarbital and phenobarbital.

Selected References

- ◆ Bhutani VK, Abbasi S, Sivieri EM: Continuous skeletal muscle paralysis: Effect on neonatal pulmonary mechanics. *Pediatrics* 1988;81:419.
- ◆ Costarino AT, Polin RA: Neuromuscular relaxants in the neonate. *Clin Perinatol* 1987;14:965.
- ◆ Cabal LA, Siassi B, Artal R, et al: Cardiovascular and catecholamine changes after administration of pancuronium in distressed neonates. *Pediatrics* 1985;75:284.
- ◆ Product Information, Sicor, 2003

Adverse Effects/Precautions updated 1/2009

Compatibilities updated 3/2005

Text updated 1/1993

Dose & Administration

2 to 6 mg/kg IV slow push.

Uses

Sedative/hypnotic, for short-term use.

Monitoring

Monitor respiratory status and blood pressure closely.

Serum concentration for sedation: 0.5 to 3 mcg/mL.

Adverse Effects/Precautions

Respiratory depression. Tolerance, dependence, and cardiovascular depression occur with continued use. Enhances metabolism of phenytoin, sodium valproate, and corticosteroids by microsomal enzyme induction.

Pharmacology

Short-acting barbiturate. Pentobarbital has no analgesic effects. Serum half-life is dose-dependent (15 to 50 hours in adults) and unknown in neonates. Metabolized by hepatic microsomal enzyme system.

Special Considerations/Preparation

Available as a 50-mg/mL solution in 20 mL and 50 mL multidose vials. Solution contains propylene glycol 40%, and alcohol 10%. Irritating to veins—pH is 9.5.

A 5-mg/mL dilution may be made by adding 1 mL of the 50-mg/mL solution to 9 mL of preservative-free normal saline. Use immediately.

Solution Compatibility: D₅W, D₁₀W, and NS. No data are currently available on Dex/AA.

Terminal Injection Site Compatibility: Acyclovir, amikacin, aminophylline, atropine, calcium chloride, chloramphenicol, erythromycin lactobionate, hyaluronidase, insulin, lidocaine, linezolid, neostigmine, penicillin G, propofol, and sodium bicarbonate.

Incompatibility: Fat emulsion. Cefazolin, cimetidine, clindamycin, fentanyl, hydrocortisone succinate, midazolam, mivacurium, morphine, pancuronium bromide, phenytoin, ranitidine, and vancomycin. No data are currently available on heparin and potassium chloride.

Selected References

- ◆ Strain JD, Harvey LA, Foley LC, Campbell JB: Intravenously administered pentobarbital sodium for sedation in pediatric CT. *Radiology* 1986;161:105.
- ◆ Product Information, Ovation, 2005

Text updated 3/97

Compatibilities updated 3/2005



Dose & Administration

Loading dose: 20 mg/kg IV, given slowly over 10 to 15 minutes.

Refractory seizures: Additional 5-mg/kg doses, up to a total of 40 mg/kg.

Maintenance: 3 to 4 mg/kg per day beginning 12 to 24 hours after the load.

Frequency/Route: Daily (Q12 hours probably unnecessary). IV slow push (most rapid control of seizures), IM, PO, or PR.

Uses

Anticonvulsant. May improve outcomes in severely asphyxiated infants (40 mg/kg IV infusion over 1 hour, prior to onset of seizures). May enhance bile excretion in patients with cholestasis before ⁹⁹Tc-IDA scanning.

Monitoring

Phenobarbital monotherapy will control seizures in 43 to 85% of affected neonates - adding a second drug (phenytoin or lorazepam) is often needed. Therapeutic serum concentration is 15 to 40 mcg/mL. Drug accumulation may occur using recommended maintenance dose during the first two weeks of life. Altered (usually increased) serum concentrations may occur in patients also receiving phenytoin or valproate. Observe IV site for signs of extravasation and phlebitis.

Adverse Effects/Precautions

Sedation at serum concentrations above 40 mcg/mL. Respiratory depression at concentrations above 60 mcg/mL. Irritating to veins - pH is approximately 10 and osmolality is approximately 15,000 mOsm/kg H₂O.

Pharmacology

Phenobarbital limits the spread of seizure activity, possibly by increasing inhibitory neurotransmission. Approximately 30% protein bound. Primarily metabolized by liver, then excreted in the urine as p-hydroxyphenobarbital (no anticonvulsant activity). Serum half-life in neonates is 40 to 200 hours.

Special Considerations/Preparation

Injectable solution available in concentrations of 60-, 65-, and 130-mg/mL, all containing 10% (100 mg/mL) alcohol and 67.8% propylene glycol.

Oral elixir is available in 20 mg/5 mL concentration.

Solution Compatibility: D₅W, D₁₀W, and NS. No data are currently available on neonatal Dex/AA solutions.

Terminal Injection Site Compatibility: Amikacin, aminophylline, caffeine citrate, calcium chloride, calcium gluconate, enalaprilat, fentanyl, fosphenytoin, heparin, linezolid, meropenem, morphine, propofol, prostaglandin E₁, and sodium bicarbonate.

Incompatibility: Fat emulsion. Cimetidine, clindamycin, hydralazine, hydrocortisone succinate, insulin, methadone, midazolam, pancuronium, ranitidine, and vancomycin. No data available on potassium chloride.

Selected References

- ◆ Volpe JJ: *Neurology of the Newborn*, ed 4. Philadelphia: WB Saunders Co, 2001, p 203-204.
- ◆ Hall RT, Hall FK, Daily SK: High-dose phenobarbital therapy in term newborn infants with severe perinatal asphyxia: A randomized, prospective study with three-year follow-up. *J Pediatr* 1998;132:345-348.
- ◆ Product Information, PAI, 2005
- ◆ Product Information, Hospira, 2004

Compatibilities updated 3/2005

Text updated 3/2002

Dose & Administration

Loading dose: 15 to 20 mg/kg IV infusion over at least 30 minutes.

Maintenance dose: 4 to 8 mg/kg Q24 hours IV slow push, or PO.

(Up to 8 mg/kg per dose Q8 to 12 hours after 1 week of age).

Maximum rate of infusion 0.5 mg/kg per minute. Flush IV with saline before and after administration. **Phenytoin is highly unstable in any IV solution. Avoid using in central lines because of the risk of precipitation. IM route not acceptable; drug crystallizes in muscle.**

Oral absorption is erratic.

Uses

Anticonvulsant often used to treat seizures refractory to phenobarbital.

Monitoring

Monitor for bradycardia, arrhythmias, and hypotension during infusion. Observe IV site for extravasation. Follow serum concentration closely: therapeutic range is 6 to 15 mcg/mL in the first weeks, then 10 to 20 mcg/mL due to changes in protein binding. Obtain initial trough level 48 hours after IV loading dose.

Adverse Effects/Precautions

Extravasation causes tissue inflammation and necrosis due to high pH and osmolality. High serum concentrations are associated with seizures. Drowsiness may be difficult to identify. Hypersensitivity reactions have been reported in infants. Toxicities with long-term therapy include cardiac arrhythmias, hypotension, gingivitis, nystagmus, rickets, hyperglycemia, and hypoinsulinemia. Phenytoin interacts with carbamazepine, cimetidine, corticosteroids, digoxin, furosemide, phenobarbital, and valproate.

FDA ALERT [11/24/08]: FDA is investigating new preliminary data regarding a potential increased risk of serious skin reactions including Stevens Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) from phenytoin therapy in Asian patients positive for a particular human leukocyte antigen (HLA) allele, HLA-B*1502. This allele occurs almost exclusively in patients with ancestry across broad areas of Asia, including Han Chinese, Filipinos, Malaysians, South Asian Indians, and Thais.

Pharmacology

Hepatic metabolism capacity is limited—saturation may occur within therapeutic range. Pharmacokinetics are dose-dependent. Elimination rate is increased during first few weeks of life. Serum half-life is 18 to 60 hours. 85% to 90% protein bound. Bilirubin displaces phenytoin from protein-binding sites, resulting in increased free drug.

Special Considerations/Preparation

Injectable solution available in a concentration of 50 mg/mL. Contains 40% propylene glycol and 10% alcohol (100 mg/mL).

Oral suspension available in a concentration of 25 mg/mL.

Solution Compatibility: Phenytoin is highly unstable in any IV solution.

Solution Incompatibility: D₅W and D₁₀W.

Terminal Injection Site Compatibility: Esmolol, famotidine, fluconazole, sodium bicarbonate.

Incompatibility: Dex/AA solutions, fat emulsion. Amikacin, aminophylline, chloramphenicol, ciprofloxacin, clindamycin, dobutamine, enalaprilat, fentanyl, heparin, hyaluronidase, hydrocortisone succinate, insulin, lidocaine, linezolid, methadone, micafungin, mivacurium, morphine, nitroglycerin, pentobarbital, potassium chloride, procainamide, propofol, ranitidine, and vitamin K₁.

Selected References

- ◆ FDA Alert [11/24/08]. Information for Healthcare Professionals: Phenytoin and Fosphenytoin. Available at: http://www.fda.gov/cder/drug/InfoSheets/HCP/phenytoin_fosphenytoinHCP.htm.
- ◆ Volpe JJ: *Neurology of the Newborn*, ed 4. Philadelphia: WB Saunders Co, 2001, p 204-205.
- ◆ Wheless JW: Pediatric use of intravenous and intramuscular phenytoin: lessons learned. *J Child Neurol* 1998;13(Suppl 1): S11-14.
- ◆ Product Information, Hospira, 2004
- ◆ Product Information, Pfizer, 2006

Adverse Effects/Precautions and References updated 1/2009

Compatibilities updated 3/2007

Text updated 3/2002

Dose & Administration

0.3 to 0.6 mg/kg per dose IV push over 5 to 10 seconds. Do not give IM.
Must be accompanied by adequate analgesia and/or sedation.

Uses

Skeletal muscle relaxation/paralysis in infants requiring endotracheal intubation.

Monitoring

Assess vital signs frequently and blood pressure continuously if possible.

Adverse Effects/Precautions

The use of rocuronium in infants has only been studied in patients under halothane anesthesia. The overall analysis of ECG data in pediatric patients indicates that the concomitant use of rocuronium with general anesthetic agents can prolong the QTc interval. Most pediatric patients anesthetized with halothane who did not receive atropine for induction experienced a transient increase (30% or greater) in heart rate after intubation, whereas only 1 of 19 infants anesthetized with halothane and fentanyl who received atropine for induction experienced this magnitude of change. Aminoglycosides, vancomycin, and hypermagnesemia may enhance neuromuscular blockade. Propofol has no effect. Phenytoin may diminish neuromuscular blockade. Respiratory and metabolic acidosis prolong the recovery time, respiratory alkalosis shortens it. Rocuronium may be associated with increased pulmonary vascular resistance, so caution is appropriate in patients with pulmonary hypertension. Extravasations cause local tissue irritation. The package insert statement that rocuronium is not recommended for rapid sequence intubations in pediatric patients is due to the lack of studies.

Pharmacology

Rocuronium is an aminosteroid nondepolarizing neuromuscular blocking agent that is an analog of vecuronium with 10 to 15% of its potency. It has a rapid to intermediate onset depending on dose and intermediate duration. It acts by competing for cholinergic receptors at the motor end-plate. This action is antagonized by acetylcholinesterase inhibitors, such as neostigmine and edrophonium. Plasma levels of rocuronium follow a three compartment open model following intravenous administration. The rapid distribution half-life is 1 to 2 minutes and the slower distribution half-life is 14 to 18 minutes. Onset of clinical effect usually occurs within 2 minutes and the duration ranges from 20 minutes to 2 hours. Larger doses (0.9 to 1.2 mg/kg) lead to more rapid onset and longer duration of clinical effect. It can have differential effects on various muscle groups (e.g., laryngeal vs. adductor pollicis vs. diaphragm). The onset of laryngeal adductor paralysis is significantly slower with rocuronium compared with succinylcholine. Despite this difference, rocuronium has the fastest onset of any currently available nondepolarizing muscle relaxant. Average half-life in newborns is 1.1 hours. Rocuronium is approximately 30% protein bound, and is primarily excreted by the liver. There are no known metabolites.

continued...

Special Considerations/Preparation

Zemuron® for intravenous injection is available in 5 mL and 10 mL multiple-dose vials containing 10 mg/mL. Each mL contains 10 mg rocuronium bromide and 2 mg sodium acetate. The solution is clear, colorless to yellow/orange, and is adjusted to isotonicity with sodium chloride and to a pH of 4 with acetic acid and/or sodium hydroxide. Store refrigerated, 2 to 8°C (36 to 46°F). DO NOT FREEZE. Upon removal from refrigeration to room temperature storage conditions (25°C/77°F), use within 60 days. Use opened vials within 30 days. To prepare a 1 mg/mL solution, dilute 1 mL of the 10 mg/mL solution up to a final volume of 10 mL with NS.

Solution Compatibility: D₅W, Lactated Ringer's, and NS.

Terminal Injection Site Compatibility: Milrinone.

Incompatibility: Micafungin.

Selected References

- ◆ Perry JJ, Lee JS, Sillberg VAH, Wells GA. Rocuronium versus succinylcholine for rapid sequence induction intubation. *Cochrane Database of Systematic Reviews* 2008, Issue 2. Art. No.: CD002788. DOI:10.1002/14651858.CD002788.pub2.
- ◆ Rapp H-J, Altenmueller CA, Waschke C: Neuromuscular recovery following rocuronium bromide single dose in infants. *Pediatr Anesth* 2004; 14:329-355.
- ◆ Eikermann M, Hunkemöller I, Peine L, et al: Optimal rocuronium dose for intubation during inhalation induction with sevoflurane in children. *Br J Anesthaes* 2002;89:277-281.
- ◆ Sparr HJ, Beaufort TM, Fuchs-Buder T: Newer neuromuscular blocking agents: how do they compare with established agents. *Drugs* 2001;61:919-942.
- ◆ Product information, Schering, 2008.

Added 3/2009

Dose & Administration

Administer orally 2 minutes prior to the painful procedure by using a pacifier dipped in the sweet solution, up to a maximum of 2 mL.

0.5 mL of 24% sucrose is equivalent to 0.12 grams of sucrose. Other solutions containing 50% sucrose and artificial sweetener have also been shown to be effective.

Uses

Mild analgesia and behavioral comforting.

Monitoring

Assess for signs of pain and discomfort.

Adverse Effects/Precautions

Sucrose 24% has an osmolarity of ≈1000 mOsm/L. The adverse effects of repeated doses in premature infants are unknown.

Special Considerations/Preparation

Sweet-Ease®, a 24% sucrose and water solution, is aseptically packaged in an 15 ml cup with a peel off lid that is suitable for dipping a pacifier or for administration via a dropper.

Selected References

- ◆ Stevens B, Yamada J, Ohlsson A: Sucrose for analgesia in newborn infants undergoing painful procedures (Cochrane Review). In: *The Cochrane Library*, Issue 1, 2003. Oxford Update Software.
- ◆ Abad F, Diaz-Gomez NM, Domenech E, et al: Oral sucrose compares favorably with lidocaine-prilocaine cream for pain relief during venepuncture in neonates. *Acta Paediatr* 2001;90:160-165.
- ◆ Blass EM, Watt LB: Suckling and sucrose-induced analgesia in human newborns. *Pain* 1999;83:611-623.
- ◆ Bucher H-U, Moser T, Von Siebenthal K, et al: Sucrose reduces pain reaction to heel lancing in preterm infants: A placebo-controlled, randomized and masked study. *Pediatr Res* 1995;38:332-335.
- ◆ Product Information, Sweetease® website: <http://sweetease.respironics.com/>

Added 3/2003

Updated 3/2008

Dose & Administration

0.1 mg/kg (0.03 to 0.15 mg/kg) IV push, as needed for paralysis. Usual dosing interval is 1 to 2 hours. Adjust dose as needed based on duration of paralysis.

Uses

Skeletal muscle relaxation/paralysis in infants requiring mechanical ventilation. Proposed desirable effects are improved oxygenation/ventilation, reduced barotrauma, and reduced fluctuations in cerebral blood flow.

Monitoring

Monitor vital signs frequently, blood pressure continuously. Use some form of eye lubrication.

Adverse Effects/Precautions

Hypoxemia may occur because of inadequate mechanical ventilation and deterioration in pulmonary mechanics. When used alone, cardiovascular side effects are minimal; however, decreases in heart rate and blood pressure have been observed when used concurrently with narcotics.

Black Box Warning

According to the manufacturer's black box warning, vecuronium should be administered by adequately trained individuals familiar with its actions, characteristics, and hazards.

Pharmacology

Nondepolarizing muscle-relaxant that competitively antagonizes autonomic cholinergic receptors. Sympathetic stimulation is minimal. Vecuronium is metabolized rapidly in the liver to 3-desacetyl-vecuronium, which is 50% to 70% active, and is excreted renally. Newborns, particularly premature infants, are especially sensitive to vecuronium; this sensitivity diminishes with age. Onset of action is 1 to 2 minutes; duration of effect is prolonged with higher doses and in premature infants. Skeletal relaxation/paralysis is reversed by neostigmine and atropine.

Factors affecting duration of neuromuscular blockade:

Potentiation: Acidosis, hypothermia, neuromuscular disease, hepatic disease, cardiovascular disease, aminoglycosides, hypokalemia, hypermagnesemia, renal failure, and younger age.

Antagonism: Alkalosis, epinephrine, and hyperkalemia.

Sensation remains intact; analgesia should be used for painful procedures.

Vecuronium

Special Considerations/Preparation

Available as powder for injection in 10-mg and 20-mg vials. After reconstitution- 24 hrs stability in refrigerator. Single use only, discard unused portion. After dilution, use within 24 hours after admixing.

A 0.4-mg/mL dilution may be made by diluting 1 mL of 1-mg/mL concentration with 1.5 mL of preservative-free normal saline. Dilution is stable for 24 hours in refrigerator.

Solution Compatibility: D₅W, LR, and NS.

Terminal Injection Site Compatibility: Dex/AA solutions. Aminophylline, amiodarone, cefazolin, cefoxitin, cimetidine, ciprofloxacin, dobutamine, dopamine, epinephrine, esmolol, fentanyl, fluconazole, gentamicin, heparin, hydrocortisone succinate, isoproterenol, linezolid, lorazepam, midazolam, milrinone, morphine, nicardipine, nitroglycerin, nitroprusside, propofol, ranitidine, trimethoprim-sulfamethoxazole, and vancomycin.

Incompatibility: Diazepam, furosemide, micafungin, and sodium bicarbonate.

Selected References

- ◆ Martin LD, Bratton SL, O'Rourke P: Clinical uses and controversies of neuromuscular blocking agents in infants and children. *Crit Care Med* 1999;27:1358-1368.
- ◆ Segredo V, Matthay MA, Sharma ML, et al: Prolonged neuromuscular blockage after long-term administration of vecuronium in two critically ill patients. *Anesthesiology* 1990;72:566.
- ◆ Bhutani VK, Abbasi S, Sivieri EM: Continuous skeletal muscle paralysis: Effect on neonatal pulmonary mechanics. *Pediatrics* 1988;81:419.
- ◆ Gravlee GP, Ramsey FM, Roy RC, et al: Rapid administration of a narcotic and neuromuscular blocker: A hemodynamic comparison of fentanyl, sufentanil, pancuronium, and vecuronium. *Anesth Analg* 1988;67:39.
- ◆ Meretoja OA, Wirtavuori K, Neuvonen PJ: Age-dependence of the dose-response curve of vecuronium in pediatric patients during balanced anesthesia. *Anesth Analg* 1988;67:21.
- ◆ Costarino AT, Polin RA: Neuromuscular relaxants in the neonate. *Clin Perinatol* 1987;14:965.
- ◆ Product Information, Hospira, 2005

Adverse Effects/Precautions updated 1/2009

Compatibilities updated 3/2008

References updated 3/2002

DIURETICS

DIURETICS

Dose & Administration

0.005 to 0.1 mg/kg per dose IV slow push, IM, or PO.

Preterm infants < 34 weeks gestation in the first 2 months of life:
Q24 hours.

Afterward: Q12 hours.

Preterm infants \geq 34 weeks gestation in the first month of life:
Q24 hours.

Afterward: Q12 hours.

Infants with lung disease and normal renal function should be started on a low dose. Infants with congestive heart failure or abnormal renal function will need a higher dose.

Uses

Diuretic used in patients with renal insufficiency, congestive heart failure, or significant edema that is refractory to furosemide.

Monitoring

Serum electrolytes and urine output. Assess patients receiving digoxin concurrently for potassium depletion. Follow weight changes.

Adverse Effects/Precautions

Water and electrolyte imbalances occur frequently, especially hyponatremia, hypokalemia, and hypochloremic alkalosis. Potentially ototoxic, but less so than furosemide. May displace bilirubin from albumin binding sites when given in high doses or for prolonged periods.

Black Box Warning According to the manufacturer's black box warning, bumetanide is a potent diuretic which, if given in excessive amounts, can lead to profound diuresis with water and electrolyte depletion.

Pharmacology

Bumetanide is a loop diuretic with a similar mechanism of action to furosemide. Inhibits chloride reabsorption in the ascending limb of Henle's loop and inhibits tubular sodium transport, causing major loss of sodium and chloride. Increases urinary losses of potassium, calcium, and bicarbonate. Urine sodium losses are lower with bumetanide than furosemide, but urine calcium losses are higher. Decreases CSF production by weak carbonic anhydrase inhibition. Decreases pulmonary transvascular fluid filtration. Increases renal blood flow and prostaglandin secretion. Highly protein bound (>97%). Data from adults indicate excellent oral bioavailability and significant hepatic metabolism (40%) via the cytochrome CYP pathway. Serum half-life varies from 4 to 19 hours in neonates, determined by gestational age, postnatal age, and disease state.

Special Considerations/Preparation

Supplied as 2-, 4-, and 10-mL vials (0.25-mg/mL solution). Contains 1% (10 mg/mL) benzyl alcohol; pH adjusted to 7.

A 0.125 mg/mL dilution may be made by adding 3 mL of 0.25 mg/mL injectable solution to 3 mL preservative-free normal saline for injection. Refrigerated dilution is stable for 24 hours. Discolors when exposed to light.

There is no oral dosing formulation available for neonates. The intravenous formulation, diluted in sterile water and given orally, has been used successfully in infants with congenital heart disease.

Solution Compatibility: D₅W and NS. No data are available on Dex/AA.

Terminal Injection Site Compatibility: Fat emulsion. Aztreonam, cefepime, furosemide, lorazepam, micafungin, milrinone, morphine, piperacillin-tazobactam, and propofol.

Incompatibility: Dobutamine and midazolam.

Selected References

- ◆ Eades SK, Christensen ML: The clinical pharmacology of loop diuretics in the pediatric patient. *Pediatr Nephrol* 1998;12:603-616.
- ◆ Lopez-Samblas AM, Adams JA, Goldberg RN, Modi MW: The pharmacokinetics of bumetanide in the newborn infant. *Biol Neonate* 1997;72:265-272.
- ◆ Sullivan JE, Witte MK, Yamashita TS, Myers CM, Blumer JL: Dose-ranging evaluation of bumetanide pharmacodynamics in critically ill infants. *Clin Pharmacol Ther* 1996;60:424-434. (2 other related articles by same authors in same issue).
- ◆ Shankaran S, Liang K-C, Ilagan N, Fleischmann L: Mineral excretion following furosemide compared with bumetanide therapy in premature infants. *Pediatr Nephrol* 1995;9:159-62.
- ◆ Ward OC, Lam LKT: Bumetanide in heart failure of infancy. *Arch Dis Child* 1977;52:877-882.
- ◆ Product Information, Bedford, 2005

Dose, Pharmacology, Special Considerations, and References updated 1/2009

Compatibilities updated 3/2004

Dose & Administration

Diuresis: 10 to 20 mg/kg per dose Q12 hours PO.

Adjuvant treatment of central diabetes insipidus: 5 mg/kg per dose Q12 hours PO.

Administer with food (improves absorption).

IV administration not recommended because of a lack of data.

Note: Do not confuse with hydrochlorothiazide.

Uses

Diuretic used in treating both mild to moderate edema and mild to moderate hypertension. Effects increased when used in combination with furosemide or spironolactone. May improve pulmonary function in patients with BPD. Adjuvant treatment of central diabetes insipidus.

Monitoring

Serum electrolytes, calcium, phosphorus, and glucose; urine output and blood pressure.

Adverse Effects/Precautions

Hypokalemia and other electrolyte abnormalities. Hyperglycemia. Hyperuricemia.

Do not use in patients with significant impairment of renal or hepatic function.

Pharmacology

Limited data in neonates. Variable absorption from GI tract. Onset of action within 1 hour. Elimination half-life depends on GFR, and is approximately 5 hours. Major diuretic effect results from inhibition of sodium reabsorption in the distal nephron. Increases urinary losses of sodium, potassium, magnesium, chloride, bicarbonate, and phosphorus. Decreases renal excretion of calcium. Inhibits pancreatic release of insulin. Displaces bilirubin from albumin binding sites.

Special Considerations/Preparation

Available as a 250 mg/5mL suspension for oral use.

Selected References

- ◆ Pogacar PR, Mahnke S, Rivkees SA: Management of central diabetes insipidus in infancy with low renal solute load formula and chlorothiazide. *Curr Opin Pediatr* 2000;12:405-411.
- ◆ Wells TG: The pharmacology and therapeutics of diuretics in the pediatric patient. *Pediatr Clin North Am* 1990;37:463.
- ◆ Albersheim SG, Solimano AJ, Sharma AK, et al: Randomized, double-blind, controlled trial of long-term diuretic therapy for bronchopulmonary dysplasia. *J Pediatr* 1989;115:615.
- ◆ Roberts RJ: *Drug Therapy in Infants*. Philadelphia: WB Saunders Co, 1984, p 244.
- ◆ Kao LC, Warburton D, Cheng MH, et al: Effect of oral diuretics on pulmonary mechanics in infants with chronic bronchopulmonary dysplasia: Results of a double-blind crossover sequential trial. *Pediatrics* 1984;74:37.
- ◆ Product Information, Merck, 2007

Updated 3/2003

EDUCATION

Dose & Administration

Initial dose: 1 mg/kg IV slow push, IM, or PO.
May increase to a maximum of 2 mg/kg per dose IV or
6 mg/kg per dose PO.

Initial intervals: Premature infant: Q24 hours.
Fullterm infant: Q12 hours.
Fullterm infant older than 1 month: Q6 to 8 hours.
Consider alternate-day therapy for long-term use.

Uses

Diuretic that may also improve pulmonary function.

Monitoring

Follow urine output and serum electrolytes and phosphorus. Assess closely for potassium depletion in patients receiving digoxin concurrently. Follow weight changes.

Adverse Effects/Precautions

Water and electrolyte imbalances occur frequently, especially hyponatremia, hypokalemia, and hypochloremic alkalosis. Hypercalciuria and development of renal calculi occur with long-term therapy. Potentially ototoxic, especially in patients also receiving aminoglycosides. Cholelithiasis has been reported in patients with BPD or congenital heart disease who received long-term TPN and furosemide therapy.

Pharmacology

The diuretic actions of furosemide are primarily at the ascending limb of Henle's loop, and are directly related to renal tubular drug concentration. Furosemide causes major urinary losses of sodium, potassium, and chloride. Urinary calcium and magnesium excretion, and urine pH are also increased. Prostaglandin production is stimulated, with increases in renal blood flow and renin secretion. Free water clearance is increased and CSF production is decreased by weak carbonic anhydrase inhibition. Nondiuretic effects include decreased pulmonary transvascular fluid filtration and improved pulmonary function. Protein binding is extensive, but bilirubin displacement is negligible when using normal doses. Oral bioavailability is good. Time to peak effect when given IV is 1 to 3 hours; duration of effect is approximately 6 hours, although half-life may be as long as 67 hours in the most immature neonates.

continued...

Furosemide

Special Considerations/Preparation

Furosemide oral solution is available in 8-mg/mL and 10-mg/mL concentrations. Protect from light and discard open bottle after 90 days. The injectable solution may also be used for oral administration.

Furosemide for injection is available as a 10-mg/mL concentration in 2-, 4-, and 10-mL single use vials.

A 2-mg/mL dilution may be made by adding 2 mL of the 10 mg/mL injectable solution to 8 mL preservative-free normal saline for injection. Dilution should be used within 24 hours. Protect from light and do not refrigerate.

Solution Compatibility: NS and sterile water for injection.

Acidic solutions (pH <5.5) such as D₅W, D₁₀W, and Dex/AA cause furosemide to degrade when they are mixed together for several hours.

Terminal Injection Site Compatibility: Fat emulsion. Amikacin, aminophylline, amiodarone, ampicillin, atropine, aztreonam, bumetanide, calcium gluconate, cefepime, ceftazidime, cimetidine, dexamethasone, digoxin, epinephrine, famotidine, fentanyl, heparin, hydrocortisone succinate, indomethacin, lidocaine, lorazepam, linezolid, meropenem, morphine, nitroglycerin, penicillin G, piperacillin-tazobactam, potassium chloride, propofol, prostaglandin E₁, ranitidine, remifentanil, sodium bicarbonate, sodium nitroprusside, and tobramycin.

Incompatibility: Azithromycin, ciprofloxacin, dobutamine, dopamine, erythromycin lactobionate, esmolol, fluconazole, gentamicin, hydralazine, isoproterenol, metoclopramide, midazolam, milrinone, netilmicin, nicardipine, and vecuronium.

Selected References

- ◆ Stefano JL, Bhutani VK: Role of furosemide after booster-packed erythrocyte transfusions in infants with bronchopulmonary dysplasia. *J Pediatr* 1990;117:965.
- ◆ Rush MG, Engelhardt B, Parker RA, Hazinski TA: Double-blind, placebo-controlled trial of alternate-day furosemide therapy in infants with chronic bronchopulmonary dysplasia. *J Pediatr* 1990;117:112.
- ◆ Mirochnick MH, Miceli JJ, Kramer PA, et al: Furosemide pharmacokinetics in very low birth weight infants. *J Pediatr* 1988;112:653.
- ◆ Green TP: The pharmacologic basis of diuretic therapy in the newborn. *Clin Perinatol* 1987;14:951.
- ◆ Hufnagle KG, Khan SN, Penn D: Renal calcifications: A complication of long-term furosemide therapy in preterm infants. *Pediatrics* 1982;70:360.
- ◆ Ross BS, Pollak A, Oh W: The pharmacological effects of furosemide therapy in the low-birth-weight infant. *J Pediatr* 1978;92:149.
- ◆ Ghanekar AG, Das Gupta V, Gibbs CW Jr: Stability of furosemide in aqueous systems. *J Pharm Sci* 1978;67:808.
- ◆ Product Information, Roxane, 2007
- ◆ Product Information, Abraxis, 2006

Text updated 3/2008

Compatibilities updated 3/2007

Dose & Administration

1 to 2 mg/kg per dose Q12 hours PO.
Administer with food (improves absorption).
Note: Do not confuse with chlorothiazide.

Uses

Diuretic used in treating both mild to moderate edema and mild to moderate hypertension. Effects increased when used in combination with furosemide or spironolactone. May improve pulmonary function in patients with BPD.

Monitoring

Serum electrolytes, calcium, phosphorus, and glucose; urine output and blood pressure.

Adverse Effects/Precautions

Hypokalemia and other electrolyte abnormalities. Hyperglycemia. Hyperuricemia.

Do not use in patients with significant impairment of renal or hepatic function.

Pharmacology

Limited data in neonates. Rapidly absorbed from GI tract. Onset of action is within 1 hour. Elimination half-life depends on GFR and is longer than that of chlorothiazide. Major diuretic effect results from inhibition of sodium reabsorption in the distal nephron. Increases urinary losses of sodium, potassium, magnesium, chloride, phosphorus, and bicarbonate. Decreases renal excretion of calcium. Inhibits pancreatic release of insulin. Displaces bilirubin from albumin.

Special Considerations/Preparation

Supplied as a 50-mg/5mL oral solution.

Selected References

- ◆ Albersheim SG, Solimano AJ, Sharma AK, et al: Randomized, double-blind, controlled trial of long-term diuretic therapy for bronchopulmonary dysplasia. *J Pediatr* 1989;115:615.
- ◆ Roberts RJ: *Drug Therapy in Infants*. Philadelphia: WB Saunders Co, 1984, p 244.

Updated 1/2005

Dose & Administration

1 to 3 mg/kg per dose Q24 hours PO.

Uses

Used in combination with other diuretics in the treatment of congestive heart failure and BPD (situations of increased aldosterone secretion).

Monitoring

Follow serum potassium closely during long-term therapy. Also, measuring urinary potassium is a useful indicator of effectiveness.

Adverse Effects/Precautions

Rashes, vomiting, diarrhea, paresthesias. Dose-dependent androgenic effects in females. Gynecomastia in males. Headaches, nausea, and drowsiness. Use with caution in patients with impaired renal function. May cause false positive ELISA screening tests for congenital adrenal hyperplasia.

Black Box Warning

According to the manufacturer's black box warning, spironolactone has been shown to be a tumorigen in chronic animal toxicity studies.

Pharmacology

Competitive antagonist of mineralocorticoids (e.g. aldosterone). Metabolized to canrenone and 7-a-thiomethylspironolactone, active metabolites with extended elimination half-lives. Decreases excretion of potassium. Highly protein bound. Increases excretion of calcium, magnesium, sodium, and chloride (small effect). Serum half-life with long term use is 13 to 24 hours. Addition of spironolactone to thiazide diuretic therapy in patients with BPD may yield little, if any, additional benefit.

Special Considerations/Preparation

Available in 25-mg, 50-mg, and 100-mg tablets. A simple syrup suspension can be made by crushing eight 25-mg spironolactone tablets and suspending the powder in 50 mL of simple syrup. Final concentration is 4 mg/mL; solution is stable for 1 month refrigerated.

Selected References

- ◆ Brion LP, Primhak RA, Ambrosio-Perz I: Diuretics acting on the distal renal tubule for preterm infants with (or developing) chronic lung disease (Cochrane Review). In: *The Cochrane Library* Issue 1, 2003. Oxford: Update Software.
- ◆ Hoffman DJ, Gerdes JS, Abbasi S: Pulmonary function and electrolyte balance following spironolactone treatment in preterm infants with chronic lung disease: a double-blind, placebo-controlled randomized trial. *J Perinatol* 2000;20:41-45.
- ◆ Terai I, Yamano K, Ichihara N, et al: Influence of spironolactone on neonatal screening for congenital adrenal hyperplasia. *Arch Dis Child Fetal Neonatal Ed* 1999;81:F179.
- ◆ Mathur LK, Wickman A: Stability of extemporaneously compounded spironolactone suspensions. *Am J Hosp Pharm* 1989;46:2040.
- ◆ Overdiek HW, Hermens WA, Merkus FW: New insights into the pharmacokinetics of spironolactone. *Clin Pharmacol Ther* 1985;38:469.
- ◆ Karim A: Spironolactone: Disposition, metabolism, pharmacodynamics, and bioavailability. *Drug Metab Rev* 1978;8:151.
- ◆ Loggie JMH, Kleinman LI, Van Maanen EF: Renal function and diuretic therapy in infants and children. Part II. *J Pediatr* 1975;86:657.
- ◆ Product Information, Actavis, 2006

Adverse Effects/Precautions updated 1/2009

Preparation and References updated 3/2004



GI DRUGS

Dose & Administration

2.5 to 5 mg/kg per dose Q6 to 12 hours PO or IV infusion over 15 to 30 minutes.

Uses

Prevention and treatment of stress ulcers and GI hemorrhage aggravated by gastric acid secretion.

Monitoring

Gastric pH may be measured to assess efficacy. Observe for impaired consciousness and reduced spontaneous movements.

Adverse Effects/Precautions

Known adverse effects of cimetidine in adults include mental confusion, seizures, renal dysfunction, hepatic dysfunction, flushing and transpiration, neutropenia, diarrhea, hypothalamic-pituitary-gonadal dysfunction, and muscular pain. Cimetidine has been reported to increase the serum level and potentiate toxicity of other drugs such as aminophylline, carbamazepine, diazepam, lidocaine, morphine, phenytoin, procainamide, propranolol, quinidine, theophylline, and warfarin.

Contraindicated in patients receiving cisapride due to precipitation of life-threatening arrhythmias.

Pharmacology

Inhibits gastric acid secretion by histamine H₂-receptor antagonism. Peak inhibition occurs in 15 to 60 minutes after both oral and IV administration. Metabolized in the liver via sulfation and hydroxylation to inactive compounds that are 90% renally eliminated. Half-life in neonates is 1.1 to 3.4 hours, and is prolonged in patients with renal or hepatic insufficiency. The sulfoxide metabolite may accumulate in the CNS and cause toxicity. Antacids interfere with absorption; therefore concomitant administration is not recommended.

Special Considerations/Preparation

Available as a 150-mg/mL injectable solution in 2-mL single-use vials and 8-mL multidose vials. A 15-mg/mL dilution may be made by adding 1 mL of 150 mg/mL concentration to 9 mL of preservative-free normal saline. Dilution stable for 48 hours. Manufacturer's oral solution (60 mg/mL) contains 2.8% alcohol. A 2.4 mg/mL oral dilution may be prepared by adding 1 mL (60 mg) of manufacturer's oral solution to 24 mL of sterile water. Stable for 14 days refrigerated. Also available in 200-, 300-, 400-, and 800-mg tablets.

Solution Compatibility: D₅W, D₁₀W, and NS.

Terminal Injection Site Compatibility: Dex/AA solutions, fat emulsion. Acetazolamide, acyclovir, amikacin, aminophylline, ampicillin, atropine, aztreonam, caffeine citrate, cefoxitin, ceftazidime, clindamycin, dexamethasone, diazepam, digoxin, enalaprilat, epinephrine, erythromycin lactobionate, esmolol, fentanyl, fluconazole, flumazenil, furosemide, gentamicin, glycopyrrolate, heparin, insulin, isoproterenol, lidocaine, linezolid, lorazepam, meperidine, meropenem, metoclopramide, midazolam, milrinone, morphine, nafcillin, nicardipine, nitroprusside, pancuronium, penicillin G, piperacillin-tazobactam, potassium chloride, propofol, prostaglandin E₁, protamine, remifentanil, sodium bicarbonate, vancomycin, vecuronium, vitamin K₁, and zidovudine.

Incompatibility: Amphotericin B (Immediate precipitation occurs), cefazolin, cefepime, indomethacin, pentobarbital, phenobarbital, and secobarbital.

Selected References

- ◆ Vandenplas Y, Sacre L: The use of cimetidine in newborns. *Am J Perinatol* 1987;4:131.
- ◆ Lloyd CW, Martin WJ, Taylor BD: The pharmacokinetics of cimetidine and metabolites in a neonate. *Drug Intell Clin Pharm* 1985;19:203.
- ◆ Ziemniak JA, Wynn RJ, Aranda JV, et al: The pharmacokinetics and metabolism of cimetidine in neonates. *Dev Pharmacol Ther* 1984;7:30.
- ◆ Aranda JV, Outerbridge EW, Shentag JJ: Pharmacodynamics and kinetics of cimetidine in a premature newborn. *Am J Dis Child* 1983;137:1207.
- ◆ Product Information, Hospira, 2004

Text Updated 3/97

Compatibilities updated 3/2005

Dose & Administration

IV: 0.25 to 0.5 mg/kg per dose Q24 hours, IV slow push;

Continuous infusion of the daily dose in adults provides better gastric acid suppression than intermittent dosing.

PO: 0.5 to 1 mg/kg per dose Q24 hours orally.

Uses

Prevention and treatment of stress ulcers and GI hemorrhage aggravated by gastric acid secretion.

Monitoring

Gastric pH may be measured to assess efficacy (>4.0).

Adverse Effects/Precautions

No adverse events have been reported in infants and children, although data are limited to a few small studies. The most common (<5% of patients) adverse effects noted in adults were headache, dizziness, constipation, and diarrhea.

Pharmacology

Inhibits gastric acid secretion by histamine H₂-receptor antagonism. Elimination half-life is dependent on renal function, and decreases with age from 11 hours (range 5 to 22) in neonates to 8 hours (range 4 to 12) by 3 months of age. Oral bioavailability is 42 to 50%.

Special Considerations/Preparation

Available as 10-mg/mL solution for intravenous use in 2-mL preservative-free single-dose vials, and 4-mL multidose vials containing 0.9% (9 mg/mL) benzyl alcohol as a preservative. A 1-mg/mL dilution may be made by adding 1 mL of the 10 mg/mL concentrated solution to 9 mL of sterile water for injection. Dilution stable for 7 days at room temperature. Although diluted Pepcid® Injection has been shown to be physically and chemically stable for 7 days at room temperature, there are no data on the maintenance of sterility after dilution. Therefore, it is recommended that if not used immediately after preparation, diluted solutions of Pepcid® Injection should be refrigerated and used within 48 hours.

Pepcid® for oral suspension is supplied as a powder containing 400 mg famotidine. Constitute by slowly adding 46 mL Purified Water and shaking vigorously for 5-10 seconds. Final concentration 40 mg/5 mL (8 mg/mL). Stable at room temperature for 30 days. Shake bottle before each use.

Solution Compatibility: D₅W, D₁₀W, NS. Dex/AA solutions, fat emulsion.

Terminal Injection Site Compatibility: Acyclovir, aminophylline, amiodarone, ampicillin, atropine, aztreonam, calcium gluconate, cefazolin, cefotaxime, cefoxitin, ceftazidime, ceftriaxone, dexamethasone, digoxin, dobutamine, dopamine, enalaprilat, epinephrine, erythromycin lactobionate, esmolol, fluconazole, flumazenil, furosemide, gentamicin, heparin, hydrocortisone succinate, imipenem/cilastatin, insulin, isoproterenol, lidocaine, linezolid, lorazepam, magnesium sulfate, metoclopramide, mezlocillin, midazolam, morphine, nafcillin, nicardipine, nitroglycerin, oxacillin, phenytoin, piperacillin, potassium chloride, procainamide, propofol, remifentanil, sodium bicarbonate, sodium nitroprusside, ticarcillin/clavulanate, vancomycin, and vitamin K₁.

Incompatibility: Azithromycin, cefepime and piperacillin-tazobactam.

Selected References

- ◆ Wenning LA, Murphy MG, James LP, et al: Pharmacokinetics of famotidine in infants. *Clin Pharmacokinet* 2005;44:395-406.
- ◆ James LP, Marotti T, Stowe CD, et al: Pharmacokinetics and pharmacodynamics of famotidine in infants. *J Clin Pharmacol* 1998;38:1089-1095.
- ◆ James LP, Marshall JD, Heulitt MJ, et al: Pharmacokinetics and pharmacodynamics of famotidine in children. *J Clin Pharmacol* 1996;21:48-54.
- ◆ Bullock L, Fitzgerald JF, Glick MR: Stability of famotidine 20 and 50 mg/L in total nutrient admixtures. *Am J Hosp Pharm* 1989;46:2326-29.
- ◆ Product information, Merck Inc., 2006.
- ◆ Product information, Salix, 2007

Completely updated 3/2006

Compatibilities updated 3/2007

Dose & Administration

0.73 to 1.66 mg/kg per dose PO, once a day.

See Special Considerations/Preparation for preparation.

Uses

Treatment of reflux esophagitis.

Monitoring

Observe for symptomatic improvement within 3 days. Consider intraesophageal pH monitoring to assess for efficacy (pH >4.0). Measure AST and ALT if duration of therapy is greater than 8 weeks.

Adverse Effects/Precautions

Hypergastrinemia and mild transaminase elevations are the only Adverse Effects reported in children who received lansoprazole for extended periods of time. Available data are limited to small studies of infants and children.

Pharmacology

Lansoprazole inhibits gastric acid secretion by inhibition of hydrogen-potassium ATPase, the enzyme responsible for the final step in the secretion of hydrochloric acid by the gastric parietal cell ("proton pump"). Extensively metabolized in the liver by CYP 2C19 and 3A4. Onset of action is within one hour of administration, maximal effect is at approximately 1.5 hours. Average elimination half-life is 1.5 hours. Inhibition of acid secretion is about 50% of maximum at 24 hours and the duration of action is approximately 72 hours. The absorption of weakly acidic drugs (e.g., digoxin, furosemide) is enhanced. The absorption of weakly basic drugs (e.g., ketoconazole) is inhibited.

Special Considerations/Preparation

Prevacid® is supplied in packets for oral suspension containing either 15 mg or 30 mg lansoprazole as enteric-coated granules and delayed-release capsules. Also available in 15 mg and 30 mg orally disintegrating tablets and 30 mg IV injection.

For patients able to drink, prepare the oral suspension as follows: empty the packet contents into a container containing 30 mL of water. Stir well. Draw up the patient-specific dose and administer immediately after mixing. Do not administer the oral suspension via enteral tubes.

For administration via nasogastric tube, use the capsules or orally disintegrating tablets. For capsules, open the capsule and mix thoroughly in 30 mL of apple, orange, or tomato juice. Do not use other liquids. Immediately draw up the patient-specific dose and inject through the NG tube into the stomach. After administering the granules, flush the NG tube with additional juice to clear the tube.

For orally disintegrating tablets, place the 15 mg tablet in a syringe and draw up 4 mL of water or 30 mg tablet in a syringe and draw up 10 mL of water. Shake gently and allow dispersal. Inject patient-specific dose into the NG tube within 15 minutes. Refill the syringe with approximately 5 mL of water and flush the NG tube.

Selected References

- ◆ Gibbons TE, Gold BD: The use of proton pump inhibitors in children: a comprehensive review. *Paediatr Drugs* 2003;5:25-40.
- ◆ Scott LJ: Lansoprazole in the management of gastroesophageal reflux disease in children. *Paediatr Drugs* 2003;5:57-61.
- ◆ Tran A, Rey E, Pons G, Pariente-Khayat A, et al: Pharmacokinetic-pharmacodynamic study of oral lansoprazole in children. *Clin Pharmacol Ther* 2002;71:359-67.
- ◆ Franco M, Salvia G, Terrin G, Spadaro R, et al: Lansoprazole in the treatment of gastroesophageal reflux disease in childhood. *Dig Liver Dis* 2000;32:660-6.
- ◆ Product information, TAP Pharmaceuticals, 2007.

Special Considerations/Preparation updated 3/2008

Dose & Administration

0.033 to 0.1 mg/kg per dose PO or IV slow push Q8 hours.

Uses

To facilitate gastric emptying and GI motility. May improve feeding intolerance. Use in GE reflux patients is controversial.
(Also used to enhance lactation—10 mg Q8 hours.)

Monitoring

Measure gastric residuals. Observe for increased irritability or vomiting.

Adverse Effects/Precautions

Intended for short-term use (several weeks). Dystonic reactions and extrapyramidal symptoms are seen frequently at higher doses and with prolonged use; children are more susceptible than adults.

Pharmacology

Derivative of procainamide. Exact mode of action is unknown; however, metoclopramide has both dopamine-receptor blocking activity and peripheral cholinergic effects. Well absorbed from GI tract. Variable first-pass metabolism by liver. Significant fraction excreted unchanged in urine. Lipid-soluble, large volume of distribution. Serum half-life in adults is 4 hours; prolonged in patients with renal failure.

Special Considerations/Preparation

Available as a 5-mg/mL injectable solution (osmolarity 280 mOsm/kg).

Protect from light. A 0.1 mg/mL dilution may be made by adding 0.4 mL of the 5-mg/mL concentration to 19.6 mL of preservative-free NS. Dilution is stable for 24 hours at room temperature.

Oral preparation available in 1-mg/mL concentration. A 0.1 mg/mL oral dilution may be made by adding 1 mL of the 1 mg/mL concentration to 9 mL simple syrup. Stable for 4 weeks at room temperature.

Solution Compatibility: D₅W, and NS.

Terminal Injection Site Compatibility: Dex/AA solutions, fat emulsion. Acyclovir, aminophylline, atropine, aztreonam, caffeine citrate, cimetidine, ciprofloxacin, clindamycin, dexamethasone, famotidine, fentanyl, fluconazole, heparin, hydrocortisone, insulin, lidocaine, linezolid, meropenem, midazolam, morphine, multivitamins, piperacillin-tazobactam, potassium chloride, potassium phosphate, prostaglandin E₁, quinupristin-dalfopristin, ranitidine, remifentanil, and zidovudine.

Incompatibility: Ampicillin, calcium chloride, calcium gluconate, cefepime, chloramphenicol, erythromycin lactobionate, furosemide, penicillin G, propofol, and sodium bicarbonate.

Selected References

- ◆ Meadow WL, Bui K, Strates E, et al: Metoclopramide promotes enteral feeding in preterm infants with feeding intolerance. *Dev Pharmacol Ther* 1989;13:38.
- ◆ Machida HM, Forbes DA, Gall DG, et al: Metoclopramide in gastroesophageal reflux of infancy. *J Pediatr* 1988;112:483.
- ◆ Ehrenkranz RA, Ackerman BA: Metoclopramide effect on faltering milk production by mothers of premature infants. *Pediatrics* 1986;78:614.
- ◆ Sankaran K, Yeboah E, Bingham WT, Ninan A: Use of metoclopramide in premature infants. *Dev Pharmacol Ther* 1982;5:114.
- ◆ Product Information, Baxter, 2004

Compatibilities updated 3/2005

NEOFAX® 2009

Dose & Administration

PO: 2 to 5 mg/kg per dose Q12 hours orally.

Uses

Prevention and treatment of stress ulcers and GI hemorrhage aggravated by gastric acid secretion.

Monitoring

Gastric pH may be measured to assess efficacy.

Adverse Effects/Precautions

Limited data in neonatal patients. One case report of thrombocytopenia. No other adverse effects have been reported in infants or children. Elevations in hepatic enzymes and asymptomatic ventricular tachycardia have been reported in adults.

Pharmacology

Inhibits gastric acid secretion by histamine H₂-receptor antagonism. Peak serum concentration occurs 0.5 to 3 hours after oral administration and is not influenced by food. Bioavailability is quite variable. Greater than 90% eliminated in the urine within 12 hours with 60% excreted unchanged. Elimination half-life in neonates is 3 to 7 hours, and is prolonged in preterm infants and patients with renal insufficiency.

Special Considerations/Preparation

Axid® alcohol-free oral solution (15 mg/mL) is supplied in 480 mL bottles. Store at room temperature.

Selected References

- ◆ Orenstein SR, Gremse DA, Pantaleon CD, et al: Nizatidine for the treatment of pediatric gastroesophageal reflux symptoms: An open-label, multiple-dose, randomized, multicenter clinical trial in 210 children. *Clin Therapeutics* 2005;27:472-483.
- ◆ Hamamoto N, Hashimoto T, Adachi K, et al: Comparative study of nizatidine and famotidine for maintenance therapy of erosive esophagitis. *J Gastroenterol Hepatol* 2005;20:281-286.
- ◆ Abdel-Rahman SM, Johnson FK, Connor JD, et al: Developmental pharmacokinetics and pharmacodynamics of nizatidine. *JPGN* 2004;38:442-451.
- ◆ Abdel-Rahman SM, Johnson FK, Gauthier-Dubois G, et al: The bioequivalence of nizatidine (Axid®) in two extemporaneously and one commercially prepared oral liquid formulations compared with capsule. *J Clin Pharmacol* 2003;43:148-153.
- ◆ Abdel-Rahman SM, Johnson FK, Manowitz N, et al: Single-dose pharmacokinetics of nizatidine (Axid®) in children. *J Clin Pharmacol* 2002;42:1089-1096.
- ◆ Product information, Braintree Laboratories, Inc., 2005.

Added 2006

Dose & Administration

0.5 to 1.5 mg/kg per dose PO, once a day.

See Special Considerations/Preparation section for oral preparation.

Uses

Short-term (less than 8 weeks) treatment of documented reflux esophagitis or duodenal ulcer refractory to conventional therapy.

Monitoring

Observe for symptomatic improvement within 3 days. Consider intraesophageal pH monitoring to assess for efficacy (pH >4.0). Measure AST and ALT if duration of therapy is greater than 8 weeks.

Adverse Effects/Precautions

Hypergastrinemia and mild transaminase elevations are the only Adverse Effects reported in children who received omeprazole for extended periods of time. Available data are limited to small studies of infants and children.

Pharmacology

Omeprazole inhibits gastric acid secretion by inhibition of hydrogen-potassium ATPase, the enzyme responsible for the final step in the secretion of hydrochloric acid by the gastric parietal cell ("proton pump"). Onset of action is within one hour of administration, maximal effect is at approximately 2 hours. Inhibition of acid secretion is about 50% of maximum at 24 hours and the duration of action is approximately 72 hours.

Special Considerations/Preparation

Zegerid® (omeprazole/sodium bicarbonate) is supplied as a 20 mg powder for suspension packet. A 2-mg/mL concentration can be prepared by reconstituting up to a total volume of 10 mL with water. The appropriate dose can be administered through a nasogastric or orogastric tube. The suspension should be flushed through the tube with water or normal saline. A stability study of a 2-mg/mL concentration showed stability for up to 28 days in refrigerator.

Prilosec® is supplied as 2.5-mg and 10-mg unit dose packets for delayed-release oral suspension (omeprazole magnesium) and as delayed-release capsules containing 10, 20, or 40-mg omeprazole as enteric-coated granules.

To prepare the delayed-release suspension, empty the 2.5 mg packet into a container containing 5 mL of water (or the 10 mg packet into a container containing 15 mL of water). Stir and leave 2 to 3 minutes to thicken. Stir and administer appropriate patient-specific dose within 30 minutes. For nasogastric or gastric tube administration, add 5 mL of water to a catheter-tipped syringe then add contents of 2.5 mg packet (or add 15 mL of water to syringe for adding 10 mg packet). Shake syringe immediately and leave 2 to 3 minutes to thicken. Shake syringe and inject patient-specific dose through the tube within 30 minutes. Flush tube with an appropriate amount of water.

Selected References

- ◆ Burnett JE, Balkin ER: Stability and viscosity of a flavored omeprazole oral suspension for pediatric use. *Am J Health-Syst Pharm* 2006;63:2240-2247.
- ◆ Johnson CE, Cober MP, Ludwig JL: Stability of partial doses of omeprazole-sodium bicarbonate oral suspension. *Ann Pharmacother* 2007;41:1954-61.
- ◆ Alliet P, Raes M, Bruneel E, Gillis P: Omeprazole in infants with cimetidine-resistant peptic esophagitis. *J Pediatr* 1998;132:352-354.
- ◆ Quercia RA, Fan C, Liu X, et al: Stability of omeprazole in an extemporaneously prepared oral liquid. *Am J Health-Syst Pharm* 1997;54:1833-1836.
- ◆ Kato S, Ebina K, Fujii K, et al: Effect of omeprazole in the treatment of refractory acid-related diseases in childhood: endoscopic healing and twenty-four-hour intragastric acidity. *J Pediatr* 1996;128:415-421.
- ◆ Faure C, Michaud L, Shaghagi EK, Popon M, et al: Intravenous omeprazole in children: pharmacokinetics and effect on 24-hour intragastric pH. *J Pediatr Gastroenterol Nutr* 2001;33:144-8.
- ◆ Product Information, Santarus, 2008
- ◆ Product Information, AstraZeneca, 2008

Special Considerations/Preparation and References updated 1/2009

Dose & Administration

PO: 2 mg/kg per dose Q8 hours.

IV: Term: 1.5 mg/kg per dose Q8 hours slow push.

Preterm: 0.5 mg/kg per dose Q12 hours slow push.

Continuous IV infusion: 0.0625 mg/kg per hour; dose range, 0.04 to 0.1 mg/kg per hour.

Uses

Prevention and treatment of stress ulcers and GI hemorrhage aggravated by gastric acid secretion.

Monitoring

Gastric pH may be measured to assess efficacy.

Adverse Effects/Precautions

One case report of thrombocytopenia. No other adverse effects have been reported in infants or children. Elevations in hepatic enzymes, leukopenia, and bradycardia have been reported in adults.

Pharmacology

Inhibits gastric acid secretion by histamine H₂-receptor antagonism. Peak serum concentration occurs 1 to 3 hours after oral administration and is not influenced by food. Bioavailability is quite variable. Hepatic biotransformation predominates after oral absorption, with 30% excreted unchanged in the urine. In contrast, 70% of an IV dose is excreted unchanged in the urine. Elimination half-life in neonates is 3 to 7 hours, and is prolonged in preterm infants and patients with renal or hepatic insufficiency.

Special Considerations/Preparation

Available as a 1 mg/mL preservative-free solution for injection in 50 mL single-dose plastic containers, and a 25 mg/mL injectable solution in 2- and 6-mL vials. A 2 mg/mL dilution may be made by adding 0.8 mL of the 25 mg/mL concentration to 9.2 mL preservative-free sterile water or normal saline for injection. Stable for 48 hours at room temperature. May be given orally; absorption is equivalent to that of the oral solution.

Manufacturer's oral solution (15 mg/mL) contains 7.5% alcohol.

Also available as 150- and 300-mg tablets. May prepare oral solution by crushing a 150-mg tablet and dissolving in 30 mL of sterile water to yield a final concentration of 5 mg/mL. Stable for 28 days refrigerated.

Solution Compatibility: D₅W, D₁₀W, and NS.

Terminal Injection Site Compatibility: Dex/AA solutions, fat emulsion. Acyclovir, acetazolamide, amikacin, aminophylline, ampicillin, atropine, aztreonam, cefazolin, cefepime, cefoxitin, ceftazidime, chloramphenicol, clindamycin, dexamethasone, digoxin, dobutamine, dopamine, enalaprilat, epinephrine, erythromycin lactobionate, fentanyl, fluconazole, flumazenil, furosemide, gentamicin, glycopyrrolate, heparin, insulin, isoproterenol, lidocaine, linezolid, lorazepam, meropenem, metoclopramide, midazolam, milrinone, morphine, nicardipine, nitroprusside, pancuronium bromide, penicillin G, piperacillin, piperacillin-tazobactam, potassium chloride, propofol, prostaglandin E₁, protamine, remifentanil, tobramycin, vancomycin, vecuronium, vitamin K₁, and zidovudine.

Incompatibility: Amphotericin B, pentobarbital, phenobarbital, and phenytoin.

Selected References

- ◆ Wells TG, Heulitt MJ, Taylor BJ et al: Pharmacokinetics and pharmacodynamics of ranitidine in neonates treated with extracorporeal membrane oxygenation. *J Clin Pharmacol* 1998;38:402-407.
- ◆ Kuusela A-L: Long term gastric pH monitoring for determining optimal dose of ranitidine for critically ill preterm and term neonates. *Arch Dis Child Fetal Neonatal Ed* 1998;78:F151-F153.
- ◆ Kelly EJ, Chatfield SL, Brownlee KG, et al: The effect of intravenous ranitidine on the intragastric pH of preterm infants receiving dexamethasone. *Arch Dis Child* 1993;69:37.
- ◆ Fontana M, Massironi E, Rossi A, et al: Ranitidine pharmacokinetics in newborn infants. *Arch Dis Child* 1993;68:602.
- ◆ Sutphen JL, Dillard VL: Effect of ranitidine on twenty-four-hour gastric acidity in infants. *J Pediatr* 1989;114:472.
- ◆ Grant SM, Langtry HD, Brogden RN: Ranitidine: An updated review of its pharmacodynamic and pharmacokinetic properties and therapeutic use in peptic ulcer disease and other allied diseases. *Drugs* 1989;37:801.
- ◆ Product Information, GlaxoSmithKline, 2007

Dose & Administration and References updated 1/2009

Compatibilities updated 3/2005

Text updated 3/2002

Dose & Administration

10 to 15 mg/kg per dose Q 12 hours PO.

Uses

Treatment of cholestasis associated with parenteral nutrition, biliary atresia, and cystic fibrosis. Also used to dissolve cholesterol gallstones.

Monitoring

Hepatic transaminases and direct bilirubin concentration.

Adverse Effects/Precautions

Nausea/vomiting, abdominal pain, constipation, and flatulence.

Pharmacology

Ursodiol is a hydrophilic bile acid that decreases both the secretion of cholesterol from the liver and its intestinal absorption. It is well absorbed orally. After conjugation with taurine or glycine, it then enters the enterohepatic circulation where it is excreted into the bile and intestine. It is hydrolyzed back to the unconjugated form or converted to lithocholic acid which is excreted in the feces. Serum half-life is 3 to 4 days in adults. Dissolution of gallstones may take several months. Aluminum-containing antacids bind ursodiol and inhibit absorption.

Special Considerations/Preparation

Available in 300-mg capsules. A liquid suspension may be made by opening ten (10) 300-mg capsules into a glass mortar. Mix this powder with 10 mL of glycerin and stir until smooth. Add 60 mL of Ora-Plus® to the mixture and stir. Transfer the contents of the mortar to a glass amber bottle and shake well. Add a small amount of Orange Syrup to the mortar and rinse. Pour the remaining contents into the amber glass bottle, then add enough simple syrup to make the final volume 120 mL, with a final concentration of 25-mg/mL. Shake vigorously. Mixture is stable for 60 days stored at room temperature or refrigerated.

Selected References

- ◆ Chen C-Y, Tsao P-N, Chen H-L, et al: Ursodeoxycholic acid (UDCA) therapy in very-low-birth-weight infants with parenteral nutrition-associated cholestasis. *J Pediatr* 2004;145:317-321.
- ◆ Levine A, Maayan A, Shamir R, et al: Parenteral nutrition-associated cholestasis in preterm neonates: Evaluation of ursodeoxycholic acid treatment. *J Pediatr Endocrinol Metab* 1999;12:549-553.
- ◆ Balisteri WF: Bile acid therapy in pediatric hepatobiliary disease: the role of ursodeoxycholic acid. *J Pediatr Gastroenterol Nutr* 1997;24:573-89.
- ◆ Teitelbaum DH: Parenteral nutrition-associated cholestasis. *Curr Opin Pediatr* 1997;9:270-75.
- ◆ Mallett MS Hagan RL, Peters DA: Stability of ursodiol 25mg/mL in an extemporaneously prepared oral liquid. *Am J Health-Syst Pharm* 1997;54:1401.
- ◆ Spagnuolo MI, Iorio R, Vignente A, Guarino A: Ursodeoxycholic acid for treatment of cholestasis in children. *Gastroenterol* 1996;111:716-719.
- ◆ Ward A, Brogden RN, Heel RC, et al: Ursodeoxycholic acid: A review of its pharmacological properties and therapeutic efficacy. *Drugs* 1984;27:95.

References updated 3/2005

RESPIRATORY DRUGS

Dose & Administration

Bronchodilation: 0.1 to 0.5 mg/kg per dose Q2 to 6 hours via nebulizer.

1 MDI actuation per dose (approx. 0.1 mg or 100 mcg) Q2 to 6 hours via MDI with spacer device placed in the inspiratory limb of the ventilator circuit. Simulated neonatal lung models suggest greater delivery when using a spacer with the MDI. Use chlorofluorocarbon free preparations when administering to neonates.

Oral: 0.1 to 0.3 mg/kg per dose Q6 to 8 hours PO.

Treatment of hyperkalemia: 0.4 mg/kg per dose Q2 hours via nebulizer.

Uses

Bronchodilator. Treatment of hyperkalemia.

Monitoring

Assess degree of bronchospasm. Continuous EKG monitoring. Consider not administering when heart rate is greater than 180 beats per minute. Serum potassium.

Adverse Effects/Precautions

Tachycardia, arrhythmias, tremor, hypokalemia, and irritable behavior.

Pharmacology

Specific β_2 -adrenergic agonist. Minimal cardiovascular effects unless used concurrently with aminophylline. Stimulates production of intracellular cyclic AMP, enhancing the binding of intracellular calcium to the cell membrane and endoplasmic reticulum, resulting in bronchodilation. Enhances mucociliary clearance. Drives potassium intracellular. Studies in vitro indicate that approximately 5% of a MDI dose administered using an in-line holding chamber/spacer device, versus less than 1% of a nebulizer dose, is delivered to the lung. Optimal aerosol dose in neonates is uncertain due to differences in aerosol drug delivery techniques. The therapeutic margin appears to be wide.

Well absorbed when administered PO. Onset of action is 30 minutes; duration is 4 to 8 hours. Serum half-life is approximately 6 hours (adults). Time to peak serum concentration is 3 to 4 hours. Tolerance may develop.

Special Considerations/Preparation

Oral dosage form: Syrup, 2 mg/5 mL.

Inhalation solution: Available as either 5 mg/mL, 0.83 mg/mL, 0.42 mg/mL, or 0.21 mg/mL.

A 0.1 mg/mL dilution for inhalation may be made by adding 3 mL of 0.83 mg/mL albuterol concentration to 22 mL of preservative-free normal saline. Label for inhalation use only. Stable for 7 days refrigerated.

MDI: Available in a pressurized hydrofluoroalkane metered dose inhaler (contains no chlorofluorocarbons (CFC)). Proventil® HFA and Ventolin® HFA 90 mcg albuterol base per actuation.

continued...

NEOFAX 2009

Selected References

- ◆ Ballard J, Lugo RA, Salyer JW: A survey of albuterol administration practices in intubated patients in the neonatal intensive care unit. *Respir Care* 2002;47:31-38.
- ◆ Singh BS, Sadiq HF, Noguchi A, Keenan WJ: Efficacy of albuterol inhalation in treatment of hyperkalemia in premature neonates. *J Pediatr* 2002;141:16-20.
- ◆ Lugo RA, Kenney JK, Keenan J: Albuterol delivery in a neonatal ventilated lung model: nebulization versus chlorofluorocarbon- and, hydrofluoroalkane- pressurized metered dose inhalers. *Pediatr Pulmonol* 2001;31:247-254.
- ◆ Stefano JL, Bhutani VK, Fox WW: A randomized placebo-controlled study to evaluate the effects of oral albuterol on pulmonary mechanics in ventilator-dependent infants at risk of developing BPD. *Pediatr Pulmonol* 1991;10:183-90.
- ◆ Wong CS, Pavord ID, Williams J, et al: Bronchodilator, cardiovascular, and hypokalemic effects of fenoterol, salbutamol, and terbutaline in asthma. *Lancet* 1990;336:1396.
- ◆ Morgan DJ, Paull JD, Richmond BH, et al: Pharmacokinetics of intravenous and oral salbutamol and its sulphate conjugate. *Br J Clin Pharmacol* 1986;22:587.
- ◆ Beck R, Robertson C, Galdes-Sebaldt M, Levison H: Combined salbutamol and ipratropium bromide by inhalation in the treatment of severe acute asthma. *J Pediatr* 1985;107:605.
- ◆ Product information, Dey, 2007
- ◆ Product Information, GlaxoSmithKline, 2008

Dose & Administration, Special Considerations, and References updated 1/2009

Dose & Administration

Loading dose: 8 mg/kg IV infusion over 30 minutes, or PO.

Maintenance: 1.5 to 3 mg/kg per dose PO, or IV slow push Q8 to 12 hours (start maintenance dose 8 to 12 hours after the loading dose). In older infants (greater than 55 weeks PMA), dosage may need to be increased to 25 to 30 mg/kg per day in divided doses Q4 to 8 hours.

If changing from IV to PO aminophylline: increase dose 20%.

If changing from IV aminophylline to PO theophylline: no adjustment.

Uses

Treatment of neonatal apnea, including post-extubation, post-anesthesia, and prostaglandin E₁-induced. Bronchodilator. May improve respiratory function.

Monitoring

Monitor heart rate and check blood glucose periodically with reagent strips. Assess for agitation and feeding intolerance.

Consider withholding next dose if heart rate is greater than 180 beats per minute.

When indicated by lack of efficacy or clinical signs of toxicity, serum trough concentration should be obtained. Therapeutic ranges are:

1) Apnea of prematurity: 7 to 12 mcg/mL.

2) Bronchospasm: 10 to 20 mcg/mL (older infants with bronchospasm may need these higher levels because of increased protein binding).

Adverse Effects/Precautions

GI irritation. Hyperglycemia. CNS irritability and sleeplessness. May be associated with renal calcifications when used concurrently with furosemide and/or dexamethasone.

Signs of toxicity: Sinus tachycardia, failure to gain weight, vomiting, jitteriness, hyperreflexia, and seizures.

Treatment of Serious Theophylline Toxicity: Activated charcoal, 1 g/kg as a slurry by gavage tube Q2 to 4 hours. Avoid sorbitol-containing preparations: They may cause osmotic diarrhea.

Pharmacology

Stimulates central respiratory drive and peripheral chemoreceptor activity. May increase diaphragmatic contractility. Cerebral blood flow is acutely decreased following IV bolus dose. Renal effects include diuresis and increased urinary calcium excretion. Stimulates gastric acid secretion and may cause GE reflux. Cardiac output is increased due to higher sensitivity to catecholamines. Elimination in preterm infants is primarily as unchanged drug, although significant interconversion to caffeine occurs. In the very immature neonate, the serum half-life of theophylline is prolonged (20 to 30 hours). Theophylline metabolism and clearance mature to adult values by 55 weeks postmenstrual age. Aminophylline salt is 78.9% theophylline. Theophylline administered orally is approximately 80% bioavailable; therefore, no dosage adjustment is necessary when changing from IV aminophylline to PO theophylline.

continued...

Aminophylline

Special Considerations/Preparation

Available as aminophylline for IV use (25 mg/mL) in 10- and 20-mL vials. Dilute 1 mL (25 mg) with 4 mL NS or D₅W to yield a final concentration of 5 mg/mL. Stable for 4 days refrigerated.

Aminophylline oral solution is available in a concentration of 21 mg/mL. Dilute with sterile water to a final concentration of 2 to 4 mg/mL for oral use.

Theophylline oral solution is available as an alcohol- and dye-free preparation in a concentration of 5.33 mg/mL.

Solution Compatibility: D₅W, D₁₀W, and NS.

Terminal Injection Site Compatibility: Dex/AA (white precipitate forms within 2 hours) solutions, fat emulsion. Acyclovir, ampicillin, amikacin, aztreonam, caffeine citrate, calcium gluconate, cefazolin, ceftazidime, chloramphenicol, cimetidine, dexamethasone, dopamine, enalaprilat, erythromycin lactobionate, esmolol, famotidine, fluconazole, flumazenil, furosemide, heparin, hydrocortisone succinate, isoproterenol, lidocaine, linezolid, methicillin, meropenem, metoclopramide, metronidazole, micafungin, midazolam, morphine, nafcillin, netilmicin, nicardipine, nitroglycerin, nitroprusside, pancuronium bromide, pentobarbital, phenobarbital, piperacillin, piperacillin-tazobactam, potassium chloride, propofol, prostaglandin E₁, ranitidine, remifentanil, sodium bicarbonate, ticarcillin/clavulanate, tobramycin, vancomycin, and vecuronium.

Incompatibility: Amiodarone, cefepime, cefotaxime, ceftriaxone, ciprofloxacin, clindamycin, dobutamine, epinephrine, hydralazine, insulin, methadone, methylprednisolone, penicillin G, and phenytoin.

Selected References

- ◆ Lim DS, Kulik TJ, Kim DW: Aminophylline for the prevention of apnea during prostaglandin E₁ infusion. *Pediatrics* 2003;112:e27-e29.
- ◆ Hochwald C, Kennedy K, Chang J, Moya F: A randomized, controlled, double-blind trial comparing two loading doses of aminophylline. *J Perinatol* 2002;22:275-278.
- ◆ Carnielli VP, Verlato G, Benini F, et al: Metabolic and respiratory effects of theophylline in the preterm infant. *Arch Dis Child Fetal Neonatal Ed* 2000;83:F39-F43.
- ◆ Zanardo V, Dani C, Trevisanuto D: Methylxanthines increase renal calcium excretion in preterm infants. *Biol Neonate* 1995;68:169-74.
- ◆ Reese J, Prentice G, Yu VYH: Dose conversion from aminophylline to theophylline in preterm infants. *Arch Dis Child* 1994;71:F51-F52.
- ◆ Kraus DM, Fischer JH, Reitz SJ, et al: Alterations in theophylline metabolism during the first year of life. *Clin Pharmacol Ther* 1993;54:351-59.
- ◆ Shannon M, Amitai Y, Lovejoy FH: Multiple dose activated charcoal for theophylline poisoning in young infants. *Pediatrics* 1987;80:368.
- ◆ Gal P, Boer HR, Toback J, et al: Effect of asphyxia on theophylline clearance in newborns. *South Med J* 1982;75:836.
- ◆ Srinivasan G, Pildes RS, Jaspan JB, et al: Metabolic effects of theophylline in preterm infants. *J Pediatr* 1981;98:815.
- ◆ Aranda JV, Sitar DS, Parsons WD, et al: Pharmacokinetic aspects of theophylline in premature newborns. *N Engl J Med* 1976;295:413.
- ◆ Product Information, Hospira, 2004

Uses and references updated 3/2004

Compatibilities updated 3/2005

Dose & Administration

Loading dose: 20 to 25 mg/kg of caffeine citrate IV over 30 minutes or PO.

(Equivalent to 10 to 12.5 mg/kg caffeine base).

Maintenance dose: 5 to 10 mg/kg per dose of caffeine citrate IV slow push or PO Q24 hours. (Equivalent to 2.5 to 5 mg/kg caffeine base).

Maintenance dose should be started 24 hours after the loading dose.

May consider an additional loading dose and higher maintenance doses if able to monitor serum concentrations.

(Please note that emphasis has changed to caffeine citrate due to commercially available product. This product (Cafcit®) may be administered both intravenously and orally).

Uses

Treatment of neonatal apnea, including post-extubation and post-anesthesia. (More favorable therapeutic index than aminophylline).

Monitoring

If using the suggested doses above, measuring serum concentrations is probably not necessary. Monitoring of serum drug concentration should be based on a trough level determined on approximately day 5 of therapy. Therapeutic trough serum concentration is 5 to 25 mcg/mL. Concentrations greater than 40 to 50 mcg/mL are toxic. Assess for agitation. Monitor heart rate; **consider withholding dose if greater than 180 beats per minute.**

Adverse Effects/Precautions

Adverse effects are usually mild, and include restlessness, vomiting, and functional cardiac symptoms. There has been a suggested association with NEC, but causality has never been proven. Loading doses of 25 mg/kg caffeine (50 mg/kg caffeine citrate) have been reported to decrease cerebral and intestinal blood flow velocity.

Pharmacology

The pharmacological effects of caffeine are mediated by its antagonism of the actions of adenosine at cell surface receptors. It is rapidly distributed in the brain, with CNS levels approximating plasma levels. Caffeine increases the respiratory center output, chemoreceptor sensitivity to CO₂, smooth muscle relaxation, and cardiac output. Oxygen consumption may be increased and weight gain may be reduced. Renal effects include diuresis and increased urinary calcium excretion. Orally administered caffeine citrate is rapidly and completely absorbed. There is almost no first-pass metabolism. In neonates, approximately 86% is excreted unchanged in the urine, with the remainder metabolized via the CYP1A2 enzyme system. The serum half-life of caffeine ranges from 40 to 230 hours, decreasing with advancing postmenstrual age until 60 weeks PMA. Half-life is prolonged in infants with cholestatic hepatitis.

Special Considerations/Preparation

Both Cafcit® Oral Solution and Cafcit® Injection for intravenous administration are preservative free and available in 3-mL single use vials. Each mL of Cafcit® contains 20 mg of caffeine citrate (equivalent to 10 mg caffeine base). Store at room temperature.

Alternatively, an oral solution may be prepared by dissolving 2.5 g of caffeine anhydrous powder in 250 mL of water, yielding a final concentration of 10 mg/mL. Solution is stable for 4 weeks refrigerated. Crystals form when stored at low temperature but dissolve at room temperature without loss of potency. **Do not freeze.**

Solution Compatibility: D₅W, D₅₀W, and NS.

Terminal Injection Site Compatibility: Dex/AA solutions, fat emulsion. Alprostadil, amikacin, aminophylline, calcium gluconate, cefotaxime, cimetidine, clindamycin, dexamethasone, dobutamine, dopamine, doxapram, epinephrine, fentanyl, gentamicin, heparin (concentration < 1 unit/mL), isoproterenol, lidocaine, metoclopramide, morphine, nitroprusside, pancuronium, penicillin G, phenobarbital, sodium bicarbonate, and vancomycin.

Incompatibility: Acyclovir, furosemide, lorazepam, nitroglycerin, and oxacillin.

Selected References

- ◆ Schmidt B, Roberts RS, Davis P, et al: Long-term effects of caffeine therapy for apnea of prematurity. *N Engl J Med* 2007;357:1893-1902.
- ◆ Schmidt B, Roberts RS, Davis P, et al: Caffeine therapy for apnea of prematurity. *N Engl J Med* 2006;354:2112-2121.
- ◆ Steer P, Flenady V, Shearman A, et al: High dose caffeine citrate for extubation of preterm infants: a randomized controlled trial. *Arch Dis Child Fetal Neonatal Ed* 2004;89:F499-F503.
- ◆ Comer AM, Perry CM, Figgitt DP: Caffeine citrate: A review of its use in apnoea of prematurity. *Paediatr Drugs* 2001;3:61-70.
- ◆ Bauer J, Maier K, Linderkamp O, Hentschel R: Effect of caffeine on oxygen consumption and metabolic rate in very low birth weight infants with idiopathic apnea. *Pediatrics* 2001;107:660-663.
- ◆ Erenberg A, Leff RD, Haack DG, et al: Caffeine citrate for the treatment of apnea of prematurity: A double-blind, placebo-controlled study. *Pharmacotherapy* 2000;20:644-652.
- ◆ Anderson BJ, Gunn TR, Holford NHG, et al: Caffeine overdose in a premature infant: Clinical course and pharmacokinetics. *Anaesth Intensive Care* 1999;27:307-311.
- ◆ Lane AJP, Coombs RC, Evans DH, et al: Effect of caffeine on neonatal splanchnic blood flow. *Arch Dis Child Fetal Neonatal Ed* 1999;80:F-128-F129.
- ◆ Lee TC, Charles B, Steer P: Population pharmacokinetics of intravenous caffeine in neonates with apnea of prematurity. *Clin Pharmacol Ther* 1997;61:628-640.
- ◆ Falcao AC, Fernandez de Gatta MM, Delgado Iribarnegaray MF, et al: Population pharmacokinetics of caffeine in premature neonates. *Eur J Clin Pharmacol* 1997;52:211-217.
- ◆ Zanardo V, Dani C, Trevisanuto D: Methylxanthines increase renal calcium excretion in preterm infants. *Biol Neonate* 1995;68:169-74.
- ◆ Product Information, Bedford Laboratories, 2008

Dose, Monitoring and References updated 3/2008
Compatibilities updated 3/2005

Dose & Administration

DART trial protocol: 0.075 mg/kg per dose Q12 hours for 3 days, 0.05 mg/kg per dose Q12 hours for 3 days, 0.025 mg/kg per dose Q12 hours for 2 days, and 0.01 mg/kg per dose Q12 hours for 2 days. Doses may be administered IV slow push or PO.

Uses

Anti-inflammatory glucocorticoid used to facilitate extubation and improve lung function in infants at high risk for developing chronic lung disease.

Monitoring

Assess for hyperglycemia and hyperlipidemia. Monitor blood pressure. Guaiac gastric aspirates. Echocardiogram if treating longer than 7 days.

Adverse Effects/Precautions

The February 2002 AAP and CPS statement strongly discourages routine use of dexamethasone. If dexamethasone is used for CLD risk reduction, 1) Treat only those infants at highest risk; 2) Use lower than traditional pharmacologic doses; 3) Begin treatment after Day 7 but before Day 14 of life; 4) Do not give concurrently with indomethacin; 5) Use preservative-free drug wherever possible.

The DART trial found no association with long-term morbidity, but other studies have reported an increased risk of cerebral palsy. Most evidence suggests no increase in the incidence of ROP or the need for cryotherapy. Gastrointestinal perforation and GI hemorrhage occur more frequently in patients treated beginning on Day 1 and in those also being treated concurrently with indomethacin. Hyperglycemia and glycosuria occur frequently after the first few doses, and one case of diabetic ketoacidosis has been reported. Blood pressure increases are common, and hypertension occurs occasionally. Cardiac effects noted by Day 14 of therapy include increased left ventricular wall thickness with outflow tract obstruction and transient impairment of left ventricular filling, systolic anterior motion of the mitral valve, and ST-segment depression. Other potential short-term adverse effects include sodium and water retention, hypokalemia, hypocalcemia, hypertriglyceridemia, increased risk of sepsis, renal stones (in patients receiving furosemide), osteopenia, and inhibition of growth. Adrenal insufficiency may occur secondary to pituitary suppression.

Pharmacology

Stabilizes lysosomal and cell membranes, inhibits complement-induced granulocyte aggregation, improves integrity of alveolar-capillary barrier, inhibits prostaglandin and leukotriene production, rightward shifts oxygen-hemoglobin dissociation curve, increases surfactant production, decreases pulmonary edema, relaxes bronchospasm. Hyperglycemia is caused by inhibition of glucose uptake into cells and decreased glucokinase activity. Increased triglyceride synthesis is due to hyperinsulinemia and increased acetyl-CoA carboxylase activity. Blood pressure is increased due to increased responsiveness to endogenous catecholamines. Increases protein catabolism with potential loss of muscle tissue, increases urinary calcium excretion because of bone resorption, and suppresses pituitary ACTH secretion. Biologic half-life is 36 to 54 hours.

Special Considerations/Preparation

Dexamethasone sodium phosphate for injection is available in concentrations of 4 mg/mL (benzyl alcohol preservative 10 mg/mL) and 10 mg/mL (preservative free or benzyl alcohol preservative 10 mg/mL). A 0.2 mg/mL dilution may be made by adding 1 mL of the 4 mg/mL concentration to 19 mL preservative-free sterile water for injection. Dilution is stable for 24 hours refrigerated and may be used for PO administration.

A 0.5 mg/mL oral suspension can be made by diluting 1 mL of the 4 mg/mL IV solution up to a total volume of 8 mL with a 1:1 mixture of Ora-Sweet® and Ora-Plus®. The oral suspension is physically and chemically stable for up to 91 days with or without refrigeration.

Solution Compatibility: D₅W, D₁₀W, and NS.

Terminal Injection Site Compatibility: Dex/AA solutions, fat emulsion. Acyclovir, amikacin, aminophylline, aztreonam, caffeine citrate, cefepime, cimetidine, famotidine, fentanyl, fluconazole, furosemide, heparin, hydrocortisone succinate, lidocaine, linezolid, lorazepam, meropenem, metoclopramide, milrinone, morphine, nafcillin, netilmicin, piperacillin-tazobactam, potassium chloride, propofol, prostaglandin E₁, ranitidine, remifentanil, sodium bicarbonate, and zidovudine.

Incompatibility: Ciprofloxacin, glycopyrrolate, midazolam and vancomycin.

Selected References

- ◆ Doyle LW, Davis PG, Morley CJ, et al. DART Study Investigators: Low-dose dexamethasone facilitates extubation among chronically ventilator-dependent infants: a multicenter, international, randomized, controlled trial. *Pediatrics* 2006;117:75-83.
- ◆ Wen-Lin Chou J, Decarie D, Dumont RJ, et al. Stability of dexamethasone in extemporaneously prepared oral suspensions. *Can J Hosp Pharm* 2001;54:96-101.

Reviews

- ◆ Eichenwald EC, Stark AR: Are postnatal steroids ever justified to treat severe bronchopulmonary dysplasia? *Arch Dis Child Fetal Neonatal Ed* 2007;92:334-337.
- ◆ American Academy of Pediatrics, Canadian Paediatric Society: Postnatal corticosteroids to treat or prevent chronic lung disease in preterm infants. *Pediatrics* 2002;109:330.
- ◆ Kennedy KA: Controversies in the use of postnatal steroids. *Semin Perinatol* 2001;25:397-405.
- ◆ Halliday HL, Ehrenkranz RA, Doyle LW: Moderately early (7-14 days) postnatal corticosteroids for preventing chronic lung disease in preterm infants. (Cochrane Review). In: *The Cochrane Library*, Issue 1, 2003. Oxford: Update Software.

Adverse Effects

- ◆ Stark AR, Carlo W, Tyson JE, et al: Adverse effects of early dexamethasone treatment extremely low birth weight infants. *N Engl J Med* 2001;344:95-101.
- ◆ Stoll BJ, Temporda MS, Tyson JE, et al: Dexamethasone therapy increases infection in very low birth weight infants. *Pediatrics* 1999;104(5). URL:[http://www.pediatrics.org/cgi/content/full/104\(5\)/e63](http://www.pediatrics.org/cgi/content/full/104(5)/e63).
- ◆ Amin SB, Sinkin RA, McDermott MP, Kendig JW: Lipid intolerance in neonates receiving dexamethasone for bronchopulmonary dysplasia. *Arch Pediatr Adolesc Med* 1999;153:795-800.
- ◆ Bensky AS, Kothadia JM, Covitz, W: Cardiac effects of dexamethasone in very low birth weight infants. *Pediatrics* 1996;97:818.
- ◆ Wright K, Wright SP: Lack of association of glucocorticoid therapy and retinopathy of prematurity. *Arch Pediatr Adolesc Med* 1994;148:848.
- ◆ Ng PC: The effectiveness and side effects of dexamethasone in preterm infants with bronchopulmonary dysplasia. *Arch Dis Child* 1993;68:330.

Developmental Follow-up

- ◆ Doyle LW, Davis PG, Morley CJ, et al. DART Study Investigators: Outcome at 2 years of age of infants from the DART study: a multicenter, international, randomized, controlled trial of low-dose dexamethasone. *Pediatrics* 2007;119:716-21.
- ◆ O'Shea TM, Kothadia JM, Klinepeter KL, et al: Randomized placebo-controlled trial of a 42-day tapering course of dexamethasone to reduce the duration of ventilator dependency in very low birth weight infants: Outcome of study participants at 1 year adjusted age. *Pediatrics* 1999;104:15-21.
- ◆ Shinwell ES, Karplus M, Reich D, et al: Early postnatal dexamethasone therapy and increased incidence of cerebral palsy. *Arch Dis Child Fetal Neonatal Ed* 2000; 83:F177-181.
- ◆ Product Information, Abraxis, 2006

Special Considerations and References updated 3/2009
Compatibilities updated 3/2005

Dose & Administration

1.25 mL to 2.5 mL via nebulizer, or 0.2 mL/kg instilled directly into the endotracheal tube.
Administer once or twice per day.

Uses

Treatment of atelectasis, secondary to mucus plugging, that is unresponsive to conventional therapies.

Monitoring

Monitor airway patency. Suction the airway as needed.

Adverse Effects/Precautions

Desaturation and/or airway obstruction may occur due to rapid mobilization of secretions.

Pharmacology

Pulmozyme® is a highly purified solution of recombinant human deoxyribonuclease (rhDNase, an enzyme that selectively cleaves DNA). The protein is produced by genetically engineered Chinese hamster ovary cells. Purulent pulmonary secretions contain very high concentrations of extracellular DNA released by degenerating leukocytes. rhDNase hydrolyzes this DNA to decrease the viscoelasticity of the secretions. Clinical improvements in the thickness of secretions and ventilation usually occur within 3 hours of administration.

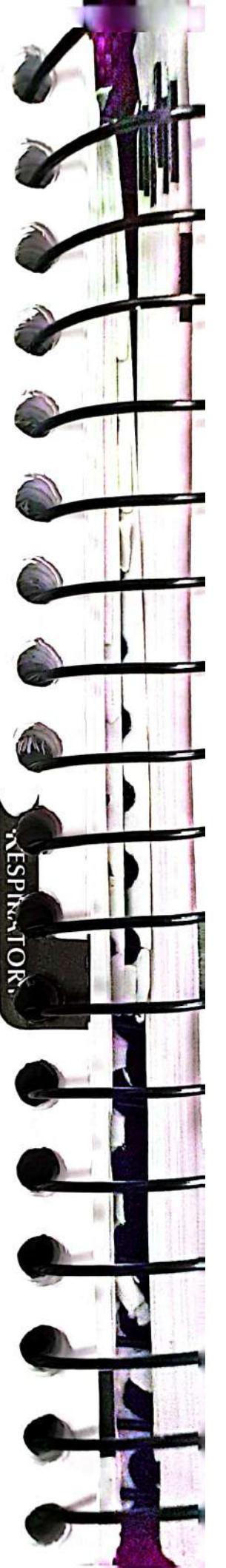
Special Considerations/Preparation

Pulmozyme® is supplied in single-use ampules. Each ampule contains 2.5 mL of a sterile, clear, colorless, aqueous solution containing 1 mg/mL dornase alfa (2.5 mg per ampule), 0.15 mg/mL calcium chloride dihydrate, and 8.77 mg/mL sodium chloride (22 mg per ampule) with no preservative. The nominal pH of the solution is 6.3. The ampules should be stored in their protective foil pouch under refrigeration (2-8° C, 36-46° F) and protected from strong light. Do not use beyond the expiration date on the ampule.

Selected References

- ◆ Erdeve O, Uras N, Atasay B, Arsan S: Efficacy and safety of nebulized recombinant human DNase as rescue treatment for persistent atelectasis in newborns: case-series. *Croat Med J* 2007;48:234-239.
- ◆ Riethmueller J, Borth-Bruhns T, Kumpf M, et al: Recombinant human deoxyribonuclease shortens ventilation time in young, mechanically ventilated children. *Pediatr Pulmonol* 2006;41:61-66.
- ◆ Hendricks T, de Hoog M, Lequin MH, et al: DNase and atelectasis in non-cystic fibrosis patients. *Crit Care* 2005;9:R351-R356.
- ◆ Ratjen F: Dornase in non-CF. *Pediatr Pulmonol* 2004;26:S154-155.
- ◆ Kupeli S, Teksam O, Dogru D, Yurdakok M: Use of recombinant human DNase in a premature infant with recurrent atelectasis. *Pediatrics International* 2003;45:584-586.
- ◆ El Hassan NO, Chess PR, Huysman MWA, et al: Rescue use of DNase in critical lung atelectasis and mucus retention in premature neonates. *Pediatrics* 2001;108:468-471.
- ◆ Reiter PD, Townsend SF, Velasquez R: Dornase alfa in premature infants with severe respiratory distress and early bronchopulmonary dysplasia. *J Perinatol* 2000;20:530-534.
- ◆ Product information, Genentech, 2005.

Added 03/2008



Dose & Administration

Administer Q6 to 8 hours as a metered dose inhaler (MDI) or nebulized solution.

Doses studied in intubated neonates range from 2 puffs (34 mcg) to 4 puffs (68 mcg) via MDI with spacer device placed in the inspiratory limb of the ventilator circuit, and 75 to 175 mcg via jet nebulizer. Simulated neonatal lung models suggest greater delivery when using a spacer with the MDI. Use chlorofluorocarbon free preparations when administering to neonates.

Optimal dose in neonates has yet to be determined due to differences in aerosol drug delivery techniques, although the therapeutic margin appears to be wide.

Uses

Anticholinergic bronchodilator for primary treatment of chronic obstructive pulmonary diseases and adjunctive treatment of acute bronchospasm. Ipratropium is not useful in the treatment of bronchiolitis.

Monitoring

Assess degree of bronchospasm.

Adverse Effects/Precautions

Temporary blurring of vision, precipitation of narrow-angle glaucoma, or eye pain may occur if solution comes into direct contact with the eyes.

Pharmacology

Ipratropium bromide is a quaternary ammonium derivative of atropine. It produces primarily large airway bronchodilation by antagonizing the action of acetylcholine at its receptor site. It is relatively bronchospecific when administered by inhalation because of limited absorption through lung tissue. Peak effect occurs 1 to 2 hours after administration. Duration of effect is 4 to 6 hours in children. The combination of ipratropium with a beta-agonist produces more bronchodilation than either drug individually.

Special Considerations/Preparation

Inhalation Solution: Supplied in 2.5-mL vials, containing ipratropium bromide 0.02% (200 mcg/mL) in a sterile, preservative-free, isotonic saline solution that is pH-adjusted to 3.4 with hydrochloric acid. It may be mixed with albuterol or metaproterenol if used within 1 hour. Compatibility data are not currently available with other drugs.

Store at room temperature in foil pouch provided. Protect from light.

MDI: Atrovent® HFA is available in a pressurized metered-dose aerosol unit (contains no chlorofluorocarbons (CFC)). Each actuation delivers 21 mcg of ipratropium from the valve and 17 mcg from the mouthpiece.

Selected References

- ◆ Fayon M, Tayara N, Germain C et al: Efficacy and tolerance of high-dose ipratropium bromide vs. terbutaline in intubated premature human neonates. *Neonatology* 2007;91:167-173.
- ◆ Lee H, Arnon S, Silverman M: Bronchodilator aerosol administered by metered dose inhaler and spacer in subacute neonatal respiratory distress syndrome. *Arch Dis Child* 1994;70:F218.
- ◆ Consensus Conference in Aerosol Delivery: Aerosol Consensus Statement. *Respir Care* 1991;36:916.
- ◆ Brundage KL, Mohsini KJ, Froese AB, Fisher JT: Bronchodilator response to ipratropium bromide in infants with bronchopulmonary dysplasia. *Am Rev Respir Dis* 1990;142:1137.
- ◆ Gross NJ: Ipratropium bromide. *N Engl J Med* 1988;319:486.
- ◆ Product Information, Dey, 2006
- ◆ Product Information, Boehringer-Ingelheim, 2008

Dose & Administration, Special Considerations and References updated 1/2009

Text updated 3/2008

Added 1/1995

Dose & Administration

Nitric oxide inhalation therapy (iNO) should be used only after mechanical ventilatory support has been optimized, including the use of surfactant.

Begin at 20 ppm.

If within 4 hours PaO_2 increases to at least 60 torr, decrease to 5 ppm. Continue at 5 ppm and wean $\text{fI}O_2$ as tolerated. When $\text{fI}O_2$ is less than 0.6 and ventilatory support has been decreased, wean iNO in 1 ppm increments at approximately 4 hour intervals as tolerated. Discontinue when stable on 1 ppm for 4 hours. The usual length of treatment is less than 4 days. Infants who cannot be weaned off after 4 days should undergo further diagnostic testing for other diseases.

Administer via an FDA/EMEA approved delivery system designed to accurately deliver NO uninterrupted into the ventilator system in parts-per-million concentrations that are constant throughout the respiratory cycle, while limiting NO_2 production (e.g., INOvent™).

Uses

Treatment of term and near-term infants (≥ 34 weeks GA) with hypoxic respiratory failure (Oxygenation Index > 25) associated with clinical or echocardiographic evidence of pulmonary hypertension. It is usually not effective in infants with congenital diaphragmatic hernia. Do not use in infants dependent on right-to-left cardiac blood flow. Use in preterm infants is controversial and should be done under the auspices of a research protocol.

Monitoring

Continuous monitoring of oxygenation, blood pressure and heart rate are mandatory. Measure blood methemoglobin concentration 4 hours after initiation of therapy and at 24 hour intervals thereafter. Monitoring of inspired gas must provide for continuous measurement of both NO and NO_2 concentrations, with a feedback mechanism that cuts off delivery if NO or NO_2 exceed acceptable limits.

Adverse Effects/Precautions

Abrupt discontinuation may result in worsening oxygenation and increased pulmonary artery pressures. The risks of methemoglobinemia and elevated NO_2 levels increase significantly at doses > 20 ppm. Methemoglobin has very high affinity for oxygen and has a profound effect on oxygen content. Small increases in methemoglobin cause significant decreases in available oxygen content. Normal methemoglobin levels are $< 1\%$. In most neonatal studies, methemoglobinemia was defined as levels of 5% to 7%. Cyanosis develops at levels of 10%, although the patients generally remain asymptomatic. At methemoglobin levels approaching 30%, patients begin to experience respiratory distress, and cardiac, gastrointestinal, and neurologic symptoms. A methemoglobin level greater than 50% is usually lethal. Avoid concomitant use of acetaminophen, metoclopramide, sulfa drugs, topical anesthetics (EMLA, benzocaine, lidocaine, prilocaine). Congenital deficiencies in the methemoglobin reductase enzyme system occur but are rare. The environmental exposure limit set by the Occupational Safety and Health Administration is 25 ppm for NO and 5 ppm for NO_2 .

continued...

Pharmacology

Inhaled nitric oxide (iNO) is a selective pulmonary vasodilator that decreases extrapulmonary right-to-left shunting. It activates guanyl cyclase by binding to its heme component leading to production of cyclic GMP, with subsequent relaxation of pulmonary vascular smooth muscle. Oxygenation is also improved due to the redirecting of blood from poorly aerated to better aerated distal air spaces. In addition, iNO appears to have both anti-oxidant and anti-inflammatory activities.

Special Considerations/Preparation

Nitric oxide for inhalation is supplied in medical grade gas cylinders. Store vertically in well-ventilated areas at room temperature. All cylinders should be returned to the supplier for disposal. Hospital personnel should receive specific training in the administration of iNO.

Selected References

- ◆ Barrington KJ, Finer NN: Inhaled nitric oxide for respiratory failure in preterm infants (Review). In: *The Cochrane Library*, Issue 1, 2008.
- ◆ Finer N, Barrington KJ: Nitric oxide for respiratory failure in infants born at term or near term (Cochrane Review). In: *The Cochrane Library*, Issue 4, 2006. Oxford. Update Software.
- ◆ Clark RH, Huckaby JL, Kueser TJ, et al. Low-dose nitric oxide therapy for persistent pulmonary hypertension: 1-year follow-up. *J Perinatol* 2003; 23(4):300-303.
- ◆ Lipkin PH, Davidson D, Spivak L, et al. Neurodevelopmental and medical outcomes of persistent pulmonary hypertension in term newborns treated with nitric oxide. *J Pediatr* 2002;140(3):306-310.
- ◆ Finer NN, Sun JW, Rich W, et al: Randomized, prospective study of low-dose versus high-dose inhaled nitric oxide in the neonate with hypoxic respiratory failure. *Pediatrics* 2001;108:948-55.
- ◆ Clark RH, Kueser TJ, Walker MW, et al: Low-dose nitric oxide therapy for persistent pulmonary hypertension of the newborn. *N Engl J Med* 2000;342:469-74.
- ◆ Kinsella JP, Abman SH: Clinical approach to inhaled nitric oxide therapy in the newborn with hypoxemia. *J Pediatr* 2000;136:717-26.
- ◆ The Neonatal Inhaled Nitric Oxide Study Group: Inhaled nitric oxide in term and near-term infants: Neurodevelopmental follow-up of the The Neonatal Inhaled Nitric Oxide Study Group (NINOS). *J Pediatr* 2000;136:611-17.
- ◆ Davidson D, Barefield ES, Kattwinkel J, et al: Safety of withdrawing inhaled nitric oxide therapy in persistent pulmonary hypertension of the newborn. *Pediatrics* 1999;104:231-36.
- ◆ The Neonatal Inhaled Nitric Oxide Study Group: Inhaled nitric oxide in full-term and nearly full-term infants with hypoxic respiratory failure. *N Engl J Med* 1997;336:597-604.
- ◆ Product Information, Ino, 2006

Uses and References updated 01/2009

Added 3/2004

Dose & Administration

See specific products (beractant, calfactant, or poractant alfa) for dosing and administration information.

Uses

Prophylaxis of infants at high risk for RDS (those < 29 weeks gestation).

Rescue treatment of infants with moderate to severe RDS.

Treatment of mature infants with respiratory failure due to meconium aspiration syndrome, pneumonia, or persistent pulmonary hypertension.

Monitoring

Assess ET tube patency and position. Oxygen saturation, EKG, and blood pressure should be monitored continuously during dosing. Assess for impairment of gas exchange caused by blockage of the airway. After dosing, frequent assessments of oxygenation and ventilation should be performed to prevent postdose hyperoxia, hypocarbia, and overventilation.

Adverse Effects/Precautions

Administration of exogenous surfactants should be restricted to highly supervised clinical settings, with immediate availability of clinicians experienced with intubation, ventilator management, and general care of premature infants. Reflux of exogenous surfactant up the ET tube and falls in oxygenation occur frequently. If the infant becomes dusky or agitated, heart rate slows, oxygen saturation falls more than 15%, or surfactant backs up in the ET tube, dosing should be slowed or halted. If necessary, ventilator settings and/or FiO_2 should be turned up. Pulmonary hemorrhage occurs in 2% to 4% of treated infants, primarily the smallest patients with untreated PDA. This may be due to hemorrhagic pulmonary edema caused by the rapid fall in pulmonary vascular resistance and resulting increased pulmonary blood flow.

Pharmacology

In infants with RDS, exogenous surfactant therapy reverses atelectasis and increases FRC, with rapid improvements in oxygenation. All preparations reduce mortality from RDS. Natural surfactants are more effective than synthetics in reducing pulmonary air leak. There are no significant differences between preparations in chronic lung disease or other long term outcomes. All commercially available preparations contain surfactant apoprotein C (SP-C), none contain SP-A. The lung-mince extracts Survanta® and Curosurf® contain less than 10% of the SP-B contained in the lung-wash extract Infasurf®.

Selected References

Review Articles

- ◆ Engle WA and the Committee on Fetus and Newborn: Surfactant-replacement therapy for respiratory distress in the preterm and term neonate. *Pediatrics* 2008;121:419-432.
- ◆ Suresh GK, Soll RF: Current surfactant use in premature infants. *Clin Perinatol* 2001;28:671-694.
- ◆ Rodriguez RJ, Martin RJ: Exogenous surfactant therapy in newborns. *Respir Care Clin North Am* 1999;5:595-616.
- ◆ Kattwinkel J: Surfactant: Evolving issues. *Clin Perinatol* 1998; 25:17-32.
- ◆ Morley CJ: Systematic review of prophylactic vs rescue surfactant. *Arch Dis Child* 1997;77:F70-F74.
- ◆ Halliday HL: Natural vs synthetic surfactants in neonatal respiratory distress syndrome. *Drugs* 1996;51:226-237.

Selected References for Non-RDS Indications

- ◆ Lotze A, Mitchell BR, Bulas DI, et al: Multicenter study of surfactant (Beractant) use in the treatment of term infants with severe respiratory failure. *J Pediatr* 1998;132:40.
- ◆ Findlay RD, Taeusch HW, Walther FJ: Surfactant replacement therapy for meconium aspiration syndrome. *Pediatrics* 1996;97:48.

References updated 1/2009

(Poractant alfa) Intratracheal Suspension**Dose & Administration**

Initial dose is 2.5 mL/kg per dose intratracheally, divided into 2 aliquots followed by up to two subsequent doses of 1.25 mL/kg per dose administered at 12-hour intervals if needed.

Clear the trachea of secretions. Shorten a 5F end-hole catheter so the tip of the catheter will protrude just beyond end of ET tube above infant's carina. Slowly withdraw entire contents of vial into a plastic syringe through a large (greater than 20 gauge) needle. **Do not filter or shake.**

Attach shortened catheter to syringe. Fill catheter with surfactant. Discard excess through catheter so only total dose to be given remains in syringe.

Administer in two to four aliquots with the infant in different positions to enhance distribution in the lungs. The catheter can be inserted into the infant's endotracheal tube without interrupting ventilation by passing the catheter through a neonatal suction valve attached to the endotracheal tube.

Alternatively, surfactant can be instilled through the catheter by briefly disconnecting the endotracheal tube from the ventilator. After administration of each aliquot, the dosing catheter is removed from the ET tube and the infant is ventilated for at least 30 seconds until stable.

Pharmacology

Pulmonary lung surfactants are essential for effective ventilation by modifying alveolar surface tension thereby stabilizing the alveoli. Curosurf® is a modified porcine-derived minced lung extract containing phospholipids, neutral lipids, fatty acids, and surfactant-associated proteins B and C. Each mL of surfactant contains 80 mg of total phospholipids (54 mg of phosphatidylcholine of which 30.5 mg dipalmitoyl phosphatidylcholine) and 1 mg of protein including 0.3 mg of SP-B.

Special Considerations/Preparation

Available in 1.5 mL (120 mg phospholipid) and 3 mL (240 mg phospholipid) vials. Refrigerate (2 °C to 8 °C [36 °F to 46 °F]) and protect from light. Inspect Curosurf® for discoloration; normal color is creamy white. If settling occurs during storage, gently turn vial upside-down in order to uniformly suspend. **Do not shake.** Used vials with residual drug should be discarded. Unopened vials that have been warmed to room temperature one time may be refrigerated within 24 hours and stored for future use. Should not be warmed and returned to the refrigerator more than once.

Selected References

- ◆ Collaborative European Multicenter Study Group: Surfactant replacement therapy for severe neonatal respiratory distress syndrome: A international randomized clinical trial. *Pediatrics* 1988;82:683-691.
- ◆ Bevilacqua G, Parmigiani S, Robertson B: Prophylaxis of respiratory distress syndrome by treatment with modified porcine surfactant at birth: a multicentre prospective randomized trial. *J Perinat Med* 1996;24:609-620.
- ◆ Egberts J, de Winter JP, Sedin G, et al: Comparison of prophylaxis and rescue treatment with Curosurf® in neonates less than 30 weeks' gestation: A randomized trial. *Pediatrics* 1993;92:768-774.
- ◆ Halliday HL, Tarnow-Mordi WO, Corcoran JD, et al: Multicentre randomised trial comparing high and low dose surfactant regimens for the treatment of respiratory distress syndrome (the Curosurf® 4 trials). *Arch Dis Child* 1993;69:276-280.
- ◆ Product Information, Dey, 2002

Added 3/2000

(Calfactant) Intratracheal Suspension**Dose & Administration**

Initial dose is 3 mL/kg per dose intratracheally, divided into 2 aliquots followed by up to three subsequent doses of 3 mL/kg per dose administered at 12-hour intervals if needed.

Clear the trachea of secretions. Shorten a 5F end-hole catheter so the tip of the catheter will protrude just beyond end of ET tube above infant's carina. Slowly withdraw entire contents of vial into a plastic syringe through a large (greater than 20 gauge) needle. Do not filter or shake.

Attach shortened catheter to syringe. Fill catheter with surfactant. Discard excess through catheter so only total dose to be given remains in syringe.

Administer in two to four aliquots with the infant in different positions to enhance distribution in the lungs. The catheter can be inserted into the infant's endotracheal tube without interrupting ventilation by passing the catheter through a neonatal suction valve attached to the endotracheal tube.

Alternatively, surfactant can be instilled through the catheter by briefly disconnecting the endotracheal tube from the ventilator. After administration of each aliquot, the dosing catheter is removed from the ET tube and the infant is ventilated for at least 30 seconds until stable.

Pharmacology

Pulmonary lung surfactants are essential for effective ventilation by modifying alveolar surface tension thereby stabilizing the alveoli. Infasurf® is a sterile, non-pyrogenic natural surfactant extracted from calf lungs containing phospholipids, neutral lipids, fatty acids, and surfactant-associated proteins B and C. Preservative free. Each mL of Infasurf® contains 35 mg of total phospholipids (26 mg of phosphatidylcholine of which 16 mg is disaturated phosphatidylcholine) and 0.65 mg of proteins including 0.26 mg of SP-B.

Special Considerations/Preparation

Available in 3-mL and 6-mL single-use vials. Refrigerate (2 °C to 8 °C [36 °F to 46 °F]) and protect from light. Inspect Infasurf® for discoloration; normal color is off-white. If settling occurs during storage, gently swirl vial in order to uniformly suspend. **Do not shake.** Used vials with residual drug should be discarded. Unopened vials that have been warmed to room temperature one time may be refrigerated within 24 hours and stored for future use. Should not be warmed and returned to the refrigerator more than once.

Selected References

- ◆ Bloom BT, Kattwinkel J, Hall RT, et al: Comparison of Infasurf® (calf lung surfactant extract) to Survanta (beractant) in the treatment and prevention of respiratory distress syndrome. *Pediatrics* 1997;100:31-38.
- ◆ Hudak ML, Farrell EE, Rosenberg AA, et al: A multicenter randomized, masked comparison trial of natural versus synthetic surfactant for the treatment of respiratory distress syndrome. *J Pediatr* 1996;128:396-406.
- ◆ Kendig JW, Ryan RM, Sinkin RA, et al: Comparison of two strategies for surfactant prophylaxis in very premature infants: A multicenter randomized trial. *Pediatrics* 1998;101:1006-1012.
- ◆ Product Information, Forest Pharmaceuticals, 2003

Added 3/2000

(Beractant) Intratracheal Suspension**Dose & Administration**

4 mL/kg per dose intratracheally, divided into 4 aliquots.

Prophylaxis: First dose is given as soon as possible after birth, with up to three additional doses in the first 48 hours of life, if indicated.

Rescue treatment of RDS: Up to four doses in first 48 hours of life, no more frequently than Q6 hours.

Before administration, allow to stand at room temperature for 20 minutes, or warm in the hand for at least 8 minutes. **Artificial warming methods should not be used.**

Shorten a 5F end-hole catheter so tip of catheter will protrude just beyond end of ET tube above infant's carina. Slowly withdraw entire contents of vial into a plastic syringe through a large (greater than 20 gauge) needle. Do not filter or shake. Attach shortened catheter to syringe. Fill catheter with Survanta. Discard excess Survanta through catheter so only total dose to be given remains in syringe.

Administer four quarter-doses with the infant in different positions to enhance distribution. The catheter can be inserted into the infant's endotracheal tube through a neonatal suction valve without interrupting ventilation. Alternatively, Survanta can be instilled through the catheter by briefly disconnecting the endotracheal tube from the ventilator. After administration of each quarter-dose, the dosing catheter is removed from the ET tube and the infant is ventilated for at least 30 seconds until stable.

Pharmacology

Survanta® is a modified natural bovine lung extract containing phospholipids, neutral lipids, fatty acids, and surfactant-associated proteins B and C, to which colfosceril palmitate (DPPC), palmitic acid, and tripalmitin are added. Resulting drug provides 25 mg/mL phospholipids (including 11 to 15.5 mg/mL DPPC), 0.5 to 1.75 mg/mL triglycerides, 1.4 to 3.5 mg/mL fatty acids, and less than 1 mg/mL protein. Survanta® is suspended in NS and heat sterilized. Animal metabolism studies show that most of a dose becomes lung-associated within hours of administration, and lipids enter endogenous surfactant pathways of reuse and recycling.

Special Considerations/Preparation

Available in 4- and 8-mL single-use vials. Refrigerate (2 °C to 8 °C [36 °F to 46 °F]) and protect from light. Inspect Survanta® for discoloration; normal color is off-white to light-brown. If settling occurs during storage, **swirl** vial gently. **Do not shake.** Vials should be entered only once. Used vials with residual drug should be discarded. Unopened vials that have been warmed to room temperature one time may be refrigerated within 24 hours and stored for future use. Should not be warmed and returned to the refrigerator more than once.

Selected References

- ◆ Zola EM, Overbach AM, Gunkel JH, et al: Treatment investigational new drug experience with Survanta (beractant). *Pediatrics* 1993;91:546.
- ◆ Hoekstra RE, Jackson JC, Myers TF, et al: Improved neonatal survival following multiple doses of bovine surfactant in very premature neonates at risk for respiratory distress syndrome. *Pediatrics* 1991;88:10.
- ◆ Liechty EA, Donovan E, Purohit D, et al: Reduction of neonatal mortality after multiple doses of bovine surfactant in low birth weight neonates with respiratory distress syndrome. *Pediatrics* 1991;88:19.
- ◆ Product Information, Abbott Laboratories, 2008

Updated 3/2008



MISCELLANEOUS DRUGS

Dose & Administration

1 or 2 drops instilled in the eye 10 to 30 minutes prior to funduscopic examination.

Use solutions containing concentrations of 0.5% or less in neonates.

May be used in conjunction with 1 drop of phenylephrine 2.5% ophthalmic solution.

Apply pressure to the lacrimal sac during and for 2 minutes after instillation to minimize systemic absorption.

Uses

Induction of mydriasis and cycloplegia for diagnostic and therapeutic ophthalmic procedures.

Monitoring

Monitor heart rate and assess for signs of ileus prior to feeding.

Adverse Effects/Precautions

Feedings should be withheld for 4 hours following procedure. Systemic effects are those of anticholinergic drugs: Fever, tachycardia, vasodilatation, dry mouth, restlessness, delayed gastric emptying and decreased gastrointestinal motility, and urinary retention. The use of solutions with concentrations of 1% or greater have caused systemic toxicity in infants.

Pharmacology

Anticholinergic drug that produces pupillary dilation by inhibiting the sphincter pupillae muscle, and paralysis of accommodation. Maximal mydriasis occurs 30 to 60 minutes following administration. Recovery of accommodation occurs in 6 to 24 hours. Without lacrimal sac occlusion, approximately 80% of each drop may pass through the nasolacrimal system and be available for rapid systemic absorption by the nasal mucosa.

Special Considerations/Preparation

Supplied as ophthalmic solution in 0.5%, 1% and 2% concentrations in 2- to 15-mL bottles. Store away from heat. **Do not refrigerate.** A preparation containing cyclopentolate 0.2% and phenylephrine 1% (Cyclomydril®) is commercially available in 2- and 8-mL Drop-tainers. A combination eye drop solution ("Caputo drops") may be prepared in a 15-mL bottle with 3.75 mL of cyclopentolate 2%, 7.5 mL of tropicamide 1%, and 3.75 mL of phenylephrine 10%. The final solution contains cyclopentolate 0.5%, tropicamide 0.5%, and phenylephrine 2.5%.

Selected References

- ◆ Bonthala S, Sparks JW, Musgrave KH, Berseth CL: Mydriatics slow gastric emptying in preterm infants. *J Pediatr* 2000;137:327-30.
- ◆ Wallace DK, Steinkuller PG: Ocular medications in children. *Clin Pediatr* 1998;37:645.
- ◆ Laws DE, Morton C, Weindling M, Clark D: Systemic effects of screening for retinopathy of prematurity. *Br J Ophthalmol* 1996;80:425-428.
- ◆ McGregor MLK: Anticholinergic agents, in Mauger TF, Craig EL (eds): *Havener's Ocular Pharmacology*, ed 6. St. Louis: Mosby-YearBook, 1994, pp 148-155.
- ◆ Caputo AR, Schnitzer RE, Lindquist TD, Sun S: Dilation in neonates: a protocol. *Pediatrics* 1982;69:77-80.
- ◆ Isenberg S, Everett S: Cardiovascular effects of mydriatics in low-birth-weight infants. *J Pediatr* 1984;105:111-112.
- ◆ Product Information, Falcon, 2004

References updated 3/2001

Dose & Administration

2 to 5 mg/kg per dose PO given Q8 hours. Begin therapy at the higher dosage and taper by response.

Uses

Treatment of persistent (more than a few days) or severe hypoglycemia due to hyperinsulinism. Positive responses are usually seen within 48 to 72 hours, and occur in less than 50% of neonates.

Monitoring

Periodic CBC and serum uric acid concentrations if treating long term.

Adverse Effects/Precautions

Sodium and fluid retention is common—consider concurrent treatment with chlorothiazide (which may also potentiate the hyperglycemic action of diazoxide). There are a few case reports of pulmonary hypertension and cardiac failure, perhaps due to a direct toxic vascular injury. Hyperuricemia, leukopenia, and neutropenia are rare complications. Excessive hair growth and coarse facial features develop with long term use. Ketoacidosis may occur during times of intercurrent illness.

Pharmacology

Diazoxide inhibits insulin release by opening ATP-sensitive potassium channels in normal pancreatic beta cells. The opening of these channels also occurs in cardiac and vascular smooth muscle, leading to decreases in blood pressure and the potential for other rare toxic cardiovascular effects. Diazoxide also reduces insulin release and counters the peripheral actions of insulin via catecholamine stimulation. The serum half-life is 10 to 24 hours in infants. Protein binding is more than 90% in adults, and it is primarily excreted unchanged by the kidneys.

Special Considerations/Preparation

Proglycem® is available as an oral suspension, 50 mg/mL concentration. Alcohol content is 7.25%. Shake well before use. Protect from light. Store at room temperature.

Selected References

- ◆ Nebesio TD, Hoover WC, Caldwell RL, et al: Development of pulmonary hypertension in an infant treated with diazoxide. *J Pediatr Endocrinol Metab* 2007;20:939-44.
- ◆ Hoe FM, Thornton PS, Wanner LA, et al. Clinical features and insulin regulation in infants with a syndrome of prolonged neonatal hyperinsulinism. *J Pediatr* 2006;148:207-212.
- ◆ Schwitzgebel VM, Gitelman SE: Neonatal hyperinsulinism. *Clin Perinatol* 1998;25:1015-1038.
- ◆ Kane C, Lindley KJ, Johnson PRV, et al: Therapy for persistent hyperinsulinemic hypoglycemia of infancy: understanding the responsiveness of beta cells to diazoxide and somatostatin. *J Clin Investig* 1997;100:1888-1893.
- ◆ Stanley CA: Hyperinsulinism in infants and children. *Pediatr Clin North Am* 1997;44:363-374.
- ◆ Product Information, Ivax, 2003

Pharmacology, Adverse Effects, and References updated 3/2008.

Dose & Administration

Apply 1 to 2 gm to distal half of the penis, then wrap with occlusive dressing. Allow dressing to remain intact for 60 to 90 minutes, remove and clean treated area completely prior to circumcision to avoid systemic absorption.

Uses

Topical analgesia for circumcision. Not effective for heel lancing.

Monitoring

Blood methemoglobin concentration if concerned about toxicity.

Adverse Effects/Precautions

Blanching and redness resolve without treatment. When measured, blood levels of methemoglobin in neonates after the application of 1 g of EMLA cream have been well below toxic levels. Two cases of methemoglobinemia in infants occurred after >3 g of EMLA cream was applied; in 1 of these cases, the infant also was receiving sulfamethoxazole. EMLA cream should not be used in neonates who are receiving other drugs known to induce methemoglobinemia: sulfonamides, acetaminophen, nitrates, nitroglycerin, nitroprusside, phenobarbital, and phenytoin.

Pharmacology

EMLA cream, containing 2.5% lidocaine and 2.5% prilocaine, attenuates the pain response to circumcision when applied 60 to 90 minutes before the procedure. The analgesic effect is limited during the phases associated with extensive tissue trauma such as during lysis of adhesions and tightening of the clamp. Stabilizes the neuronal membranes by inhibiting the ionic fluxes required for conduction and initiation of nerve impulses. There is a theoretic concern about the potential for neonates to develop methemoglobinemia after the application of EMLA cream, because a metabolite of prilocaine can oxidize hemoglobin to methemoglobin. Neonates are deficient in methemoglobin NADH cytochrome b_5 reductase. Lidocaine is metabolized rapidly by the liver to a number of active metabolites and then excreted renally.

Special Considerations/Preparation

Available in 5-gm and 30-gm tubes with Tegaderm dressing. Each gram of EMLA contains lidocaine 25 mg and prilocaine 25 mg in a eutectic mixture. pH of the product is 9. Contains no preservatives.

Selected References

- ◆ American Academy of Pediatrics, Task Force on Circumcision. Circumcision policy statement. *Pediatrics* 1999;103:686-693.
- ◆ Taddio A, Ohlsson A, Einarsen TR, et al: A systematic review of lidocaine-prilocaine cream (EMLA) in the treatment of acute pain in neonates. *Pediatrics* 1998;101:1-9.
- ◆ Lander J, Brady-Fryer B, Metcalfe JB, et al: Comparison of ringblock, dorsal penile nerve block, and topical anesthesia for neonatal circumcision: A randomized controlled trial. *JAMA* 1997;278:2157-2162.
- ◆ Taddio A, Stevens B, Craig K, et al: Efficacy and safety of lidocaine-prilocaine cream for pain during circumcision. *N Engl J Med* 1997;336:1197-1201.
- ◆ Product Information, AstraZeneca, 2005.

References updated 2004

Glucagon

Dose & Administration

200 mcg/kg per dose (0.2 mg/kg per dose) IV push, IM, or SC.

Maximum dose: 1 mg.

Continuous infusion: Begin with 10 to 20 mcg/kg per hour (0.5 to 1 mg per day). Rise in blood glucose should occur with one hour of starting infusion.

Uses

Treatment of hypoglycemia refractory to intravenous dextrose infusions, or when dextrose infusion is unavailable, or in cases of documented glucagon deficiency.

Monitoring

Follow blood glucose concentration closely. Watch for rebound hypoglycemia. Rise in blood glucose will last approximately 2 hours.

Adverse Effects/Precautions

Nausea and vomiting, tachycardia, and ileus. Hyponatremia and thrombocytopenia have also been reported.

Pharmacology

Glucagon stimulates synthesis of cyclic AMP, especially in liver and adipose tissue. Stimulates gluconeogenesis. In high doses, glucagon has a cardiac inotropic effect. Inhibits small-bowel motility and gastric-acid secretion.

Special Considerations/Preparation

Supplied in 1-mg single-dose vials. Dissolve the lyophilized product in the supplied diluent. Precipitates in chloride solutions. One unit of glucagon and 1 mg of glucagon are equivalent. Use immediately after reconstitution.

Solution Compatibility: No data are currently available on Dex/AA and other intravenous solutions.

Terminal Injection Site Compatibility: No data are currently available.

Selected References

- ◆ Charsha DS, McKinley PS, Whitfield JM: Glucagon infusion for treatment of hypoglycemia: efficacy and safety in sick, preterm neonates. *Pediatrics* 2003;111:220-1.
- ◆ Miralles RE, Lodha A, Perlman M, Moore AM: Experience with intravenous glucagon infusions as a treatment for resistant neonatal hypoglycemia. *Arch Pediatr Adolesc Med* 2002;156:99-1004.
- ◆ Hawdon JM, Aynsley-Green A, Ward Platt MP: Neonatal blood glucose concentrations: metabolic effect of intravenous glucagon and intragastric medium chain triglyceride. *Arch Dis Child* 1993;68:255.
- ◆ Mehta A, Wootton R, Cheng KN, et al: Effect of diazoxide or glucagon on hepatic production rate during extreme neonatal hypoglycemia. *Arch Dis Child* 1987;62:924.
- ◆ Davis SN, Granner DK: Insulin and oral hypoglycemic agents and the pharmacology of the endocrine pancreas, in Hardman JG, Limbird LE, Gilman AG (eds): *The Pharmacological Basis of Therapeutics*, ed 10. New York: Macmillan Co, 2001, pp 1707-08.
- ◆ Product Information, Eli Lilly, 2005

References Updated 3/2004

Dose & Administration

Inject 1 mL (150 units) as 5 separate 0.2-mL subcutaneous injections around the periphery of the extravasation site. Use 25- or 26-gauge needle and change after each injection.

The chances of therapeutic success may be increased by:

- 1) Initiating treatment within 1 hour of extravasation;
- 2) Subcutaneously flushing the affected area with up to 500 mL of normal saline after the hyaluronidase treatment;
- 3) Covering with a hydrogel dressing for 48 hours.

Uses

Prevention of tissue injury caused by IV extravasation. Suggested indications (some anecdotal) are for extravasations involving drugs that are irritating to veins because of hyperosmolarity or extreme pH (e.g. aminophylline, amphotericin B, calcium, diazepam, erythromycin, gentamicin, methicillin, nafcillin, oxacillin, phenytoin, potassium chloride, rifampin, sodium bicarbonate, tromethamine, vancomycin, and TPN, and concentrated IV solutions). Hyaluronidase is **not** indicated for treatment of extravasations of vasoconstrictive agents (e.g. dopamine, epinephrine, and norepinephrine).

Monitoring

No specific monitoring required.

Adverse Effects/Precautions

Not recommended for IV use.

Pharmacology

Hyaluronidase is a mucolytic enzyme that disrupts the normal intercellular barrier and allows rapid dispersion of extravasated fluids through tissues.

Special Considerations/Preparation

Amphadase® and Hydase™ are supplied as 150 USP units/mL in 2 mL glass vials. Store refrigerated. Do not freeze.

Solution Compatibility: D₅W, D₁₀W, and NS.

Terminal Injection Site Compatibility: Amikacin, pentobarbital, and sodium bicarbonate.

Incompatibility: Epinephrine, heparin, and phenytoin.

Selected References

- ◆ Ramasethu J: Prevention and management of extravasation injuries in neonates. *NeoReviews* 2004;5:e491-e497.
- ◆ Casanova D, Bardot J, Magalon G: Emergency treatment of accidental infusion leakage in the newborn: report of 14 cases. *Br J Plast Surg* 2001;54:396-399.
- ◆ Davies J, Gault D, Buchdahl: Preventing the scars of neonatal intensive care. *Arch Dis Child* 1994;70:F50-F51.
- ◆ Raszka WV, Kueser TK, Smith FR, Bass JW: The use of hyaluronidase in the treatment of intravenous extravasation injuries. *J Perinatol* 1990;10:146.
- ◆ Lehr VT, Lulic-Botica M, Lindblad WJ, et al: Management of infiltration injury in neonates using duoderm hydroactive gel. *Am J Perinatol* 2004;21:409-414.
- ◆ Product information, Amphastar Pharmaceuticals, Inc., 2005
- ◆ Product information, Akorn, 2007

Updated 3/2008

Compatibilities Updated 3/2005

NEOFAX® 2009

Dose & Administration

Physiologic replacement: 7 to 9 mg/m² per day IV or PO, in 2 or 3 doses.

Treatment of pressor- and volume-resistant hypotension (Stress doses): 20 to 30 mg/m² per day IV, in 2 or 3 doses, or approximately 1 mg/kg per dose every 8 hours.

Treatment of chorioamnionitis-exposed ELBW infants to decrease risk of CLD:

Initial dose: 0.5 mg/kg/dose IV Q12 hours for 12 days, followed by 0.25 mg/kg IV Q 12 hours for 3 days.

Body Surface Area

Weight (kg)	Surface Area (sq meters)
0.6	0.08
1	0.1
1.4	0.12
2	0.15
3	0.2
4	0.25

BSA (m²) = (0.05 x kg) + 0.05

Uses

Treatment of cortisol deficiency. Treatment of pressor-resistant hypotension. Adjunctive therapy for persistent hypoglycemia.

May improve survival and decrease CLD in ELBW infants exposed to chorioamnionitis.

Monitoring

Measure blood pressure and blood glucose frequently during acute illness.

Adverse Effects/Precautions

Hyperglycemia, hypertension, salt and water retention. There is an increased risk of GI perforations when treating concurrently with indomethacin. There is also an increased risk of disseminated *Candida* infections. Early, low-dose hydrocortisone treatment was not associated with increased cerebral palsy. Treated infants had indicators of improved developmental outcome.

Pharmacology

Hydrocortisone is the main adrenal corticosteroid, with primarily glucocorticoid effects. It increases the expression of adrenergic receptors in the vascular wall, thereby enhancing vascular reactivity to other vasoactive substances, such as norepinephrine and angiotensin II. Hypotensive babies who are cortisol deficient (< 15 mcg/dL) are most likely to respond, and blood pressure will increase within 2 hours of the first dose. Hydrocortisone also stimulates the liver to form glucose from amino acids and glycerol, and stimulates the deposition of glucose as glycogen. Peripheral glucose utilization is diminished, protein breakdown is increased, and lipolysis is activated. The net result is an increase in blood glucose levels. Renal effects include increased calcium excretion. The apparent half-life in premature infants is 9 hours.

continued...

NEOFAX® 2009

Hydrocortisone

Special Considerations/Preparation

Hydrocortisone sodium succinate is available as powder for injection in 2-mL vials containing 100 mg. Reconstitute using preservative-free sterile water for injection to 50 mg/mL (reconstituted solution contains 9 mg/mL benzyl alcohol). Also available in 2-, 4-, and 8-mL vials with a concentration of 125 mg/mL after reconstitution. Dilute with preservative-free normal saline or D5W to a final concentration of 1 mg/mL. Dilution stable for 3 days refrigerated.

Solution Compatibility: D₅W, D₁₀W, and NS.

Terminal Injection Site Compatibility: Dex/AA solutions, fat emulsion. Acyclovir, amikacin, aminophylline, amphotericin B, ampicillin, atropine, aztreonam, calcium chloride, calcium gluconate, cefepime, chloramphenicol, clindamycin, dexamethasone, digoxin, dopamine, enalaprilat, epinephrine, erythromycin lactobionate, esmolol, famotidine, fentanyl, furosemide, heparin, hydralazine, insulin, isoproterenol, lidocaine, linezolid, lorazepam, magnesium, methicillin, metoclopramide, metronidazole, morphine, neostigmine, netilmicin, nicardipine, oxacillin, pancuronium, penicillin G, piperacillin, piperacillin-tazobactam, potassium chloride, procainamide, propofol, propranolol, prostaglandin E₁, remifentanil, sodium bicarbonate, vecuronium and vitamin K₁.

Incompatibility: Ciprofloxacin, midazolam, nafcillin, pentobarbital, phenobarbital, and phenytoin.

Selected References

- ◆ Watterberg KL, Shaffer ML, Mishefske MJ, et al: Growth and neurodevelopmental outcomes after early low-dose hydrocortisone treatment in extremely low birth weight infants. *Pediatrics* 2007;120:40-48.
- ◆ Ng PC, Lee CH, Bnur FL, et al: A double-blind, randomized, controlled study of a "stress dose" of hydrocortisone for rescue treatment of refractory hypotension in preterm infants. *Pediatrics* 2006;117:367-375.
- ◆ Watterberg KL, Gerdes JS, Cole CH, et al: Prophylaxis of early adrenal insufficiency to prevent bronchopulmonary dysplasia: a multicenter trial. *Pediatrics* 2004;114:1649-1657.
- ◆ Fernandez E, Schrader R, Watterberg K: Prevalence of low cortisol values in term and near-term infants with vasopressor-resistant hypotension. *J Perinatol* 2004;25:114-118.
- ◆ Seri I, Tan R, Evans J: Cardiovascular effects of hydrocortisone in preterm infants with pressor-resistant hypotension. *Pediatrics* 2001;107:1070-1074.
- ◆ Botas CM, Kurlat I, Young SM, Sola A: Disseminated candidal infections and intravenous hydrocortisone in preterm infants. *Pediatrics* 1995;95:883.
- ◆ Briars GL, Bailey BJ: Surface area estimation: pocket calculator versus nomogram. *Arch Dis Child* 1994;70:246-247.
- ◆ Product Information, Pharmacia and Upjohn, 2003

Text and References updated 3/2008

Compatibilities updated 3/2007

Dose & Administration

Continuous IV infusion: 0.01 to 0.1 unit/kg per hour.

[Only regular insulin for injection may be administered intravenously.] To saturate plastic tubing binding sites, fill IV tubing with insulin solution and wait for at least 20 minutes before infusing. The use of higher insulin concentrations and longer wait times will shorten the time to steady-state.

Titrate using blood glucose concentration/reagent strips.

Intermittent dose: 0.1 to 0.2 unit/kg Q6 to 12 hours subQ.

Uses

Treatment of VLBW hyperglycemic infants with persistent glucose intolerance. Adjuvant therapy for hyperkalemia.

Monitoring

Follow blood glucose concentration frequently (Q15 to 30 minutes) after starting insulin infusion and after changes in infusion rate.

Adverse Effects/Precautions

May rapidly induce hypoglycemia. Insulin resistance may develop, causing a larger dose requirement. Euthyemic hyperinsulinemia due to exogenous insulin administration may cause metabolic acidosis. The most recent randomized controlled trial (Beardsall) and systematic review (Raney) concluded that routine use of insulin in VLBW infants to promote growth is not warranted.

Pharmacology

Degraded in liver and kidney. Enhances cellular uptake of glucose, conversion of glucose to glycogen, amino acid uptake by muscle tissue, synthesis of fat, and cellular uptake of potassium. Inhibits lipolysis and conversion of protein to glucose. Plasma half-life in adults is 9 minutes.

Special Considerations/Preparation

Regular human insulin [rDNA origin] is available as 100 units/mL concentration in 10-mL vials. For subcutaneous administration, dilute with sterile water or NS to a concentration of 0.5 or 1 unit/mL. For IV administration, make a 10 units/mL dilution with sterile water, then further dilute in compatible solution to a concentration of 0.05 to 1 unit/mL. **Keep refrigerated.**

Solution Compatibility: D₅W, and D₁₀W, and NS.

Terminal Injection Site Compatibility: Dex/AA solutions, fat emulsion. Amiodarone, ampicillin, aztreonam, cefazolin, cefoxitin, cimetidine, digoxin, dobutamine, esmolol, famotidine, gentamicin, heparin, hydrocortisone succinate, imipenem, indomethacin, lidocaine, meropenem, metoclopramide, midazolam, milrinone, morphine, nitroglycerin, pentobarbital, potassium chloride, propofol, ranitidine, sodium bicarbonate, sodium nitroprusside, ticarcillin/clavulanate, tobramycin, and vancomycin.

Incompatibility: Aminophylline, dopamine, micafungin, nafcillin, phenobarbital, and phenytoin.

continued...

Selected References

- ◆ Beardsall K, Vanhaesebrouck S, Ogilvy-Stuart AL, et al. Early insulin therapy in very-low-birth-weight infants. *N Engl J Med* 2008;359:1873-1884.
- ◆ Raney M, Donze A, Smith J: Insulin infusion for the treatment of hyperglycemia in low birth weight infants: examining the evidence. *Neonatal Netw* 2008;27:127-140.
- ◆ Mena P, Llanos A, Uauy R: Insulin homeostasis in the extremely low birth weight infant. *Semin Perinatol* 2001;25:436-446.
- ◆ Fuloria M, Friedberg MA, DuRant RH, Aschner JL: Effect of flow rate and insulin priming on the recovery of insulin from microbore infusion tubing. *Pediatrics* 1998;102:1401-1406.
- ◆ Poindexter BB, Karn CA, Denne SC: Exogenous insulin reduces proteolysis and protein synthesis in extremely low birth weight infants. *J Pediatr* 1998;132:948-953.
- ◆ Ostertag SG, Jovanovic L, Lewis B, Auld PAM: Insulin pump therapy in the very low birth weight infant. *Pediatrics* 1986;78:625.
- ◆ Product Information, Novo Nordisk, 2005

Adverse Effects/Precautions and References updated 1/2009
Compatibilities updated 3/2004

Dose & Administration

Initial oral dose: 10 to 14 mcg/kg per dose PO Q24 hours.

(37.5 to 50 mcg/dose for an average term infant).

Dosage is adjusted in 12.5-mcg increments. Always round upward.

Initial IV dose: 5 to 8 mcg/kg per dose Q24 hours.

Uses

Treatment of hypothyroidism.

Monitoring

After 2 weeks of treatment, serum levothyroxine (T₄) concentration should be in the high normal range—10 to 16 mcg/dL—and should be maintained in this range for the first year of life. Serum triiodothyronine (T₃) concentration should be normal (70 to 220 ng/dL), and TSH should have declined from initial value. After 12 weeks of treatment, serum TSH concentration should be in the normal range, less than 15 mU/L. Serum T₄ and TSH concentrations should be measured at two weeks of age, then every 1 to 2 months, or 2 weeks after any change in dosage. Assess for signs of hypothyroidism: Lethargy, poor feeding, constipation, intermittent cyanosis, and prolonged neonatal jaundice. Assess for signs of thyrotoxicosis: hyperreactivity, altered sleep pattern, tachycardia, tachypnea, fever, exophthalmos, and goiter. Periodically assess growth, development, and bone-age advancement.

Adverse Effects/Precautions

Prolonged overtreatment can produce premature craniosynostosis and acceleration of bone age.

Pharmacology

Tissue deiodination converts T₄ to T₃, the active metabolite. Elimination of both T₄ and T₃ is equally in the urine and feces. Clinical effects will persist for 1 week after discontinuation of the drug. Levothyroxine prepared as an oral suspension is 50% to 80% bioavailable. Oral dosing produces effects within 3 to 5 days, while IV dosing produces effects in 6 to 8 hours.

Special Considerations/Preparation

Oral suspension is not commercially available. Available as scored tablets ranging from 25 to 300 mcg per tablet. Prepare oral dosage form by crushing tablet(s) and suspending in a small amount of sterile water, breast milk, or non-soy formula. **Use immediately.** Monitor patients closely when switching brand of drug, due to some differences in bioavailability.

The injectable form should not be given orally, as it crystallizes when exposed to acid. Injectable form is available as lyophilized powder in vials containing 200 or 500 mcg. **Use only NS for reconstitution.** Manufacturer's suggested final concentrations are 40 mcg/mL or 100 mcg/mL; however, suggested dilution is a final concentration of 20 mcg/mL.

Use immediately. Do not add to any other IV solution.

Selected References

- ◆ Selva KA, Mandel SH, Rien L, et al: Initial treatment of L-thyroxine in congenital hypothyroidism. *J Pediatr* 2002;141:786-92.
- ◆ AAP Section on Endocrinology and Committee on Genetics, and Committee on Public Health, American Thyroid Association: Newborn screening for congenital hypothyroidism: Recommended guidelines. *Pediatrics* 1993;91:1203-1209.
- ◆ Germak JA, Foley TP: Longitudinal assessment of L-thyroxine therapy for congenital hypothyroidism. *J Pediatr* 1990;117:211.
- ◆ Product Information, Bedford, 2003

Updated 3/2003

Dose & Administration**Treatment of hyperinsulinemic hypoglycemia:**

Initial dose: 1 mcg/kg per dose Q6h subQ or IV. Titrate upward to desired effect. Initial response should occur within 8 hours; tachyphylaxis may occur within several days.

Maximum dose: 10 mcg/kg per dose Q6h.

Treatment of chylothorax: Begin at 1 mcg/kg per hour continuous infusion, subQ or IV. Titrate upward as necessary; chyle production should significantly decrease within 24 hours.

Maximum dose: 7 mcg/kg per hour.

Uses

Treatment of refractory hyperinsulinemic hypoglycemia. Adjunctive treatment of congenital and post-operative chylothorax.

Monitoring

Monitor blood glucose closely.

Adverse Effects/Precautions

Vomiting, diarrhea, abdominal distention and steatorrhea may occur. Pulmonary hypertension has been reported in treated former premature infants with chronic lung disease. Hyperglycemia may occur in patients being treated for chylothorax.

Pharmacology

Octreotide is a long-acting analog of the natural hormone somatostatin. It is an even more potent inhibitor of growth hormone, glucagon, and insulin than somatostatin. Like somatostatin, it also suppresses LH response to GnRH, decreases splanchnic blood flow, and inhibits release of serotonin, gastrin, vasoactive intestinal peptide, secretin, motilin, and pancreatic polypeptide. After subcutaneous injection, octreotide is absorbed rapidly and completely from the injection site. The elimination half-life of octreotide from plasma is approximately 1.7 hours in adults, compared with 1 to 3 minutes for the natural hormone. Excreted unchanged into the urine.

Special Considerations/Preparation

Available in 1-mL single-dose ampules for injection containing 50-, 100-, or 500-mcg, and in 5-mL multiple-dose vials in concentrations of 200 and 1000 mcg/mL. pH 3.9 to 4.5. Osmolarity is 279 mOsm/kg. Refrigerate and protect from light. Do not warm artificially. After initial use, multiple dose vials should be discarded within 14 days. Ampuls should be opened just prior to administration and the unused portion discarded.

For SC injection use undiluted drug unless dose volume is not accurately measurable. For continuous IV administration consider making a dilution of 10 to 25 mcg/mL using D₅W or NS.

Octreotide

Solution Compatibility: D₅W and NS.

Solution Incompatibility: Do not add directly to Dex/AA bag because of the formation of glycosyl octreotide conjugate.

Terminal Injection Site Compatibility: Dex/AA and heparin.

Incompatibility: Fat emulsion and micafungin.

Selected References

- ◆ Young S, Dalglish S, Eccleston A, et al: Severe congenital chylothorax treated with octreotide. *J Perinatol* 2004;24:200-202.
- ◆ de Lonlay P, Touati G, Robert J-J, Saudubray J-M: Persistent hyperinsulinemic hypoglycaemia. *Semin Neonatol* 2002;7:95-100.
- ◆ Schwitzgebel VM, Gitelman SE: Neonatal hyperinsulinism. *Clin Perinatol* 1998;25:1015-38.
- ◆ Cheung Y-F, Leung MP, Yip M-M: Octreotide for treatment of postoperative chylothorax. *J Pediatr* 2001;139:157-59.
- ◆ Product Information, Novartis, 2005

Updated 3/2005

Dose & Administration

1 drop instilled in the eye at least 10 minutes prior to funduscopic procedures.

Use **only** the 2.5% ophthalmic solution in neonates.

Apply pressure to the lacrimal sac during and for 2 minutes after instillation to minimize systemic absorption.

Uses

Induction of mydriasis and cycloplegia for diagnostic and therapeutic ophthalmic procedures.

Monitoring

Monitor heart rate and oxygen saturation in babies with BPD.

Adverse Effects/Precautions

May cause decreased pulmonary compliance, tidal volume, and peak airflow in babies with BPD. Do not use in patients receiving beta-blocker medications (e.g. propranolol). The use of 10% solutions has caused systemic hypertension and tachycardia in infants.

Pharmacology

Alpha-adrenergic. Mydriasis begins within 5 minutes of instillation and lasts for 60 minutes. Without lacrimal sac occlusion, approximately 80% of each drop may pass through the nasolacrimal system and be available for rapid systemic absorption by the nasal mucosa.

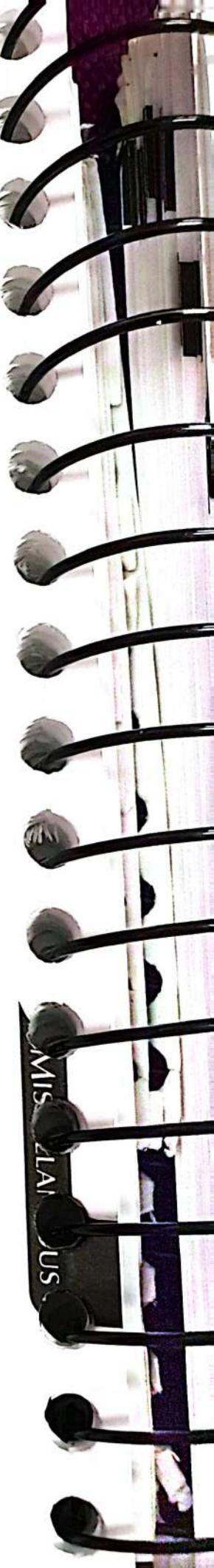
Special Considerations/Preparation

Supplied as ophthalmic solution in 0.12%, 2.5%, and 10% concentrations in 2 to 15 mL quantities. Do not use solution that becomes discolored or contains precipitate. Refer to specific product or manufacturer's recommendation for storage. A preparation containing cyclopentolate 0.2% and phenylephrine 1% (Cyclomydril®) is commercially available in 2- and 8-mL Drop-tainers. A combination eye drop solution ("Caputo drops") may be prepared in a 15-mL bottle with 3.75 mL of cyclopentolate 2%, 7.5 mL of tropicamide 1%, and 3.75 mL of phenylephrine 10%. The final solution contains cyclopentolate 0.5%, tropicamide 0.5%, and phenylephrine 2.5%. Use within 24 hours, as the solution contains no preservatives.

Selected References

- ◆ Wallace DK, Steinkuller PG: Ocular medications in children. *Clin Pediatr* 1998;37:645-652.
- ◆ Laws DE, Morton C, Weindling M, Clark D: Systemic effects of screening for retinopathy of prematurity. *Br J Ophthalmol* 1996;80:425-428.
- ◆ McGregor MLK: Adrenergic agonists, in Mauger TF, Craig EL (eds): *Havener's Ocular Pharmacology*, ed 6. St. Louis: Mosby-YearBook, 1994, pp 70-72.
- ◆ Mirmanesh SJ, Abbasi S, Bhutani VK: Alpha-adrenergic bronchoprovocation in neonates with bronchopulmonary dysplasia. *J Pediatr* 1992;121:622-625.
- ◆ Isenberg S, Everett S: Cardiovascular effects of mydriatics in low-birth-weight infants. *J Pediatr* 1984;105:111-112
- ◆ Caputo AR, Schnitzer RE, Lindquist TD, Sun S: Dilation in neonates: a protocol. *Pediatrics* 1982;69:77-80.
- ◆ Borromeo-McGrall V, Bordiuk JM, Keitel H: Systemic hypertension following ocular administration of 10% phenylephrine in the neonate. *Pediatrics* 1973;51:1032-1036.
- ◆ Product Information, Alcon, 2005

Added 3/99



Dose & Administration**Dosage based on base deficit:**

$\text{HCO}_3 \text{ needed (mEq)} = \text{HCO}_3 \text{ deficit (mEq/L)} \times (0.3 \times \text{body wt [kg]})$
 Administer half of calculated dose, then assess need for remainder.

Usual dosage: 1 to 2 mEq/kg IV over at least 30 minutes.

Recommended dilution: 0.25 mEq/mL.

Maximum concentration: 0.5 Eq/mL.

Can also be administered by continuous IV infusion or PO.

Uses

Treatment of normal anion gap metabolic acidosis caused by renal or GI losses.

Sodium bicarbonate is not a recommended therapy in neonatal resuscitation guidelines. Administration during brief CPR may be detrimental. Administration during prolonged resuscitation remains controversial - use only after adequate ventilation is established and there is no response to other therapies.

Monitoring

Follow ABGs, acid/base status, serum calcium and potassium.

Adverse Effects/Precautions

Bicarbonate administered during inadequate ventilation increases PCO_2 , thereby decreasing pH. Rapid infusion of hypertonic solution is linked to IVH. Local tissue necrosis at IV site. Hypocalcemia, hypokalemia, and hypernatremia.

Pharmacology

When bicarbonate is administered, buffering of hydrogen ions occurs, leading to increased production of carbon dioxide and water. Animal studies of resuscitation demonstrate poor coronary perfusion leads to carbon dioxide accumulation within the myocardium, leading to decreased myocardial contractility.

Special Considerations/Preparation

Supplied by many manufacturers in multiple concentrations: 4% (0.48 mEq/mL), 4.2% (0.5 mEq/mL), 7.5% (0.9 mEq/mL) and 8.4% (1 mEq/mL). Maximum concentration used in neonates is 0.5 mEq/mL. May dilute with sterile water for injection. Do not infuse with calcium or phosphate containing solutions - precipitation will occur.

Osmolarity

Concentration (%)	Concentration (mEq/mL)	Approximate Osmolarity (mOsm/L)
8.4	1	1800
4.2	0.5	900
2.8	0.33	600
2.1	0.25	450

Solution Compatibility: D₅W, D₁₀W, and NS.

Terminal Injection Site Compatibility: Fat emulsion. Acyclovir, amikacin, aminophylline, amphotericin B, ampicillin, atropine, aztreonam, cefepime, cefoxitin, ceftazidime, ceftriaxone, chloramphenicol, cimetidine, clindamycin, dexamethasone, erythromycin lactobionate, esmolol, famotidine, fentanyl, furosemide, heparin, hyaluronidase, hydrocortisone succinate, indomethacin, insulin, lidocaine, linezolid, meropenem, milrinone, morphine, nafcillin, netilmicin, penicillin G, pentobarbital, phenobarbital, phenytoin, piperacillin-tazobactam, potassium chloride, propofol, remifentanil, vancomycin, and vitamin K₁.

Incompatibility: Dex/AA. Amiodarone, calcium chloride, calcium gluconate, cefotaxime, ciprofloxacin, dobutamine, dopamine, epinephrine, glycopyrrolate, imipenem/cilastatin, isoproterenol, magnesium sulfate, methadone, methicillin, metoclopramide, midazolam, mivacurium, nicardipine, norepinephrine, oxacillin, ticarcillin/clavulanate, and vecuronium.

Selected References

- ◆ Aschner JL, Poland RL: Sodium bicarbonate: basically useless therapy. *Pediatrics* 2008;122:831-835.
- ◆ van Alfen-van der Velden AA, Hopman JC, Klaessens JH, et al: Effects of rapid versus slow infusion of sodium bicarbonate on cerebral hemodynamics and oxygenation in preterm infants. *Biol Neonate* 2006;90:122-127.
- ◆ Lokesh L, Kumar P, Murki S, Narang A. A randomized controlled trial of sodium bicarbonate in neonatal resuscitation - effect on immediate outcome. *Resuscitation* 2004;60:219-23.
- ◆ Murki M, Kumar P, Lingappa L, Narang A. Effect of a single dose of sodium bicarbonate given during neonatal resuscitation at birth on the acid-base status on first day of life. *Journal of Perinatology* 2004;24:696-9.
- ◆ Ammari AN, Schulze KF: Uses and abuses of sodium bicarbonate in the neonatal intensive care unit. *Curr Opin Pediatr* 2002;14:151-156.
- ◆ Wyckoff MH, Perlman J, Niermeyer S: Medications during resuscitation - what is the evidence? *Semin Neonatol* 2001;6:251-259.
- ◆ Howell JH: Sodium bicarbonate in the perinatal setting—revisited. *Clin Perinatol* 1987;14:807.

Dose & Administration, Uses, Monitoring, Adverse Effects/Precautions, Pharmacology, and References updated 1/2009
Compatibilities updated 3/2005

Dose & Administration (Tromethamine)

1 to 2 mmol/kg (3.3 to 6.6 mL/kg) per dose IV.

Infuse in a large vein over at least 30 minutes.

Dose (of the 0.3 M solution) may be calculated from the following formula:

$$\text{Dose (mL)} = \text{Weight (kg)} \times \text{Base deficit (mEq/L)}$$

Maximum dose in neonates with normal renal function is approximately 5 to 7 mmol/kg per 24 hours. Clinical studies support only short term use.

Uses

Treatment of metabolic acidosis, primarily in mechanically ventilated patients with significant hypercarbia or hypernatremia. **Do not use in patients who are anuric or uremic.** THAM is not indicated for treatment of metabolic acidosis caused by bicarbonate deficiency.

Monitoring

Observe IV site closely for signs of extravasation. Follow blood-gas results to assess therapeutic efficacy. Follow urine output. Monitor for respiratory depression, hypoglycemia, and hyperkalemia when using several doses.

Adverse Effects/Precautions

Most reports of toxicity in neonates (hypoglycemia, hyperkalemia, liver necrosis) were related to rapid umbilical venous infusion of high doses of THAM base solutions that were more alkaline and hypertonic than the THAM acetate solution currently available from Abbott (pH 8.6; osmolarity 380 mOsm/L). **Irritating to veins.**

Pharmacology

THAM (Tris-Hydroxymethyl Aminomethane) is a proton acceptor that generates NH_3^+ and HCO_3^- without generating CO_2 . The protonated R-NH_3^+ is eliminated by the kidneys. Unlike bicarbonate, THAM does not require an open system for CO_2 elimination in order to exert its buffering effect.

Special Considerations/Preparation

Supplied as a 0.3-M solution (1 mmol = 3.3 mL) in a 500-mL single-dose container with no bacteriostatic agent. Intended for single-dose use and unused portion should be discarded.

Compatibilities: No data are currently available on solutions and additives.

Selected References

- ◆ Holmdahl MH, Wiklund L, Wetterberg T, et al: The place of THAM in the management of acidemia in clinical practice. *Acta Anaesthesiol Scand* 2000;44:524-527.
- ◆ Nahas GG, Sutin KM, Fermon C, et al: Guidelines for the treatment of acidemia with THAM. *Drugs* 1998;55:191-224. (Errata published 1998;55:517).
- ◆ Baum JD, Robertson NRC: Immediate effects of alkaline infusion in infants with respiratory distress syndrome. *J Pediatr* 1975;87:255.
- ◆ Strauss J: Tris (hydroxymethyl amino-methane [THAM]): A pediatric evaluation. *Pediatrics* 1968;41:667.
- ◆ Gupta JM, Dahlenburg GW, Davis JW: Changes in blood gas tensions following administration of amine buffer THAM to infants with respiratory distress syndrome. *Arch Dis Child* 1967;42:416-427.
- ◆ Product Information, Hospira, 2006

Text and references updated 3/2001

Dose & Administration

1 drop instilled in the eye at least 10 minutes prior funduscopic procedures.

Use **only** the 0.5% ophthalmic solution in neonates.

Apply pressure to the lacrimal sac during and for 2 minutes after instillation to minimize systemic absorption.

Uses

Induction of mydriasis and cycloplegia for diagnostic and therapeutic ophthalmic procedures.

Monitoring

Monitor heart rate and assess for signs of ileus prior to feeding.

Adverse Effects/Precautions

Feedings should be withheld for 4 hours following procedure. Systemic effects are those of anticholinergic drugs: Fever, tachycardia, vasodilatation, dry mouth, restlessness, decreased gastrointestinal motility, and urinary retention. The use of solutions with concentrations of 1% or greater have caused systemic toxicity in infants.

Pharmacology

Anticholinergic drug that produces pupillary dilation by inhibiting the sphincter pupillae muscle, and paralysis of accommodation. Mydriasis begins within 5 minutes of instillation, cycloplegia occurs in 20 to 40 minutes. Recovery of accommodation occurs in 6 hours. Without lacrimal sac occlusion, approximately 80% of each drop may pass through the nasolacrimal system and be available for rapid systemic absorption by the nasal mucosa.

Special Considerations/Preparation

Supplied as ophthalmic solution in 0.5%, and 1% concentrations in 2-, 3-, and 15-mL dropper bottles. Store away from heat. **Do not refrigerate.**

A combination eye drop solution ("Caputo drops") may be prepared in a 15-mL bottle with 3.75 mL of cyclopentolate 2%, 7.5 mL of tropicamide 1%, and 3.75 mL of phenylephrine 10%. The final solution contains cyclopentolate 0.5%, tropicamide 0.5%, and phenylephrine 2.5%.

Use within 24 hours, as the solution contains no preservatives.

Selected References

- ◆ Wallace DK, Steinkuller PG: Ocular medications in children. *Clin Pediatr* 1998;37:645-652.
- ◆ Laws DE, Morton C, Weindling M, Clark D: Systemic effects of screening for retinopathy of prematurity. *Br J Ophthalmol* 1996;80:425-428.
- ◆ McGregor MLK: Anticholinergic agents, in Mauger TF, Craig EL (eds): *Havener's Ocular Pharmacology*, ed 6. St. Louis: Mosby-YearBook, 1994, pp 148-155.
- ◆ Caputo AR, Schnitzer RE, Lindquist TD, Sun S: Dilation in neonates: a protocol. *Pediatrics* 1982;69:77-80.
- ◆ Product Information, Alcon, 2004

Added 3/99

VITAMINS/MINERALS

Dose & Administration

Usual dosage: 1 dropperful (1 mL) orally Q24 hours.

Percentages of the Reference Daily Intakes (%RDIs) listed in the table below are for healthy infants 0 to 6 months of age.

AquADEKs™ Pediatric Liquid

	Vitamins	% Daily value
-	Amount per mL	0-6 months
A (IU)	5751	432
C (mg)	45	113
D3 (IU)	400	200
E (IU)	50	839
E (mg)	15	*
K1 (mcg)	400	20,000
B1 (mg)	0.6	300
B2 (mg)	0.6	200
Niacin (mg)	6	300
B6 (mg)	0.6	600
Biotin (mcg)	15	300
Pantothenic acid (mg)	3	176
Zinc (mg)	5	250
Selenium (mcg)	10	67
Beta-carotene (mg)	3	*
Coenzyme Q (mg)	2	*

*Daily value not established.

Uses

Multivitamin supplement for infants with cholestasis and other conditions associated with malabsorption of fat soluble vitamins.

Calcium - Oral

Dose & Administration

20 to 80 mg/kg elemental calcium per day PO in divided doses.

Calcium gluconate 10% IV formulation (9.3 mg/mL elemental calcium): 2 to 8 mL/kg per day.

Calcium carbonate 250 mg/mL suspension (100 mg/mL elemental calcium): 0.2 to 0.8 mL/kg per day.

Calcium glubionate syrup (23 mg/mL elemental calcium): 1 to 3.5 mL/kg per day.

Uses

Treatment of non-acute hypocalcemia in babies able to tolerate oral medications.

Monitoring

Periodically measure serum calcium concentrations. Assess GI tolerance. Assess serum phosphorus and vitamin D levels when indicated.

Adverse Effects/Precautions

Oral calcium preparations are hypertonic, especially calcium glubionate syrup. Gastric irritation and diarrhea occur often. Use with caution in infants who are at risk for necrotizing enterocolitis.

Pharmacology

Absorption of calcium administered orally is approximately 50%. Absorption takes place throughout the small intestine, and is primarily regulated by 1,25-dihydroxy Vitamin D. Calcium carbonate significantly interferes with the absorption of levothyroxine. The osmolarity of calcium glubionate syrup is 2500 mOsm/L, and of calcium gluconate is 700 mOsm/L.

Special Considerations/Preparation

Calcium carbonate (Roxane) is available as a 250 mg/mL suspension (equivalent to 100 mg/mL elemental calcium) in 5-mL unit dose cups. Calcium glubionate 6.5% syrup (Rugby/Watson) yields 23 mg/mL elemental calcium (1.16 mEq/mL) and is available in 473 mL bottles. Osmolarity is 2500 mOsm/L.

Selected References

- ◆ Hsu SC, Levine MA: Perinatal calcium metabolism: physiology and pathophysiology. *Semin Neonat* 2004;9:23-36.
- ◆ Singh N, Weisler SL, Hershman JM: The acute effect of calcium carbonate on the intestinal absorption of levothyroxine. *Thyroid* 2001;11:967-71.
- ◆ Product information, Roxane, 1996.

Text updated 3/2008

Dose & Administration

Symptomatic hypocalcemia - acute treatment: 35 to 70 mg/kg per dose (0.35 to 0.7 mL/kg per dose, equivalent to 10 to 20 mg/kg elemental calcium).

Dilute in appropriate fluid, then infuse in IV over 10 to 30 minutes while monitoring for bradycardia. Stop infusion if heart rate is less than 100 beats per minute.

Do not give intra-arterially.

Maintenance treatment: 75 to 300 mg/kg per day (0.75 to 3 mL/kg per day, equivalent to 20 to 80 mg/kg elemental calcium). Administer by continuous IV infusion. Treat for 3 to 5 days, and follow serum concentrations periodically.

Exchange transfusion: 33 mg per 100 mL citrated blood exchanged (equals 0.33 mL per 100 mL blood exchanged). Infuse IV over 10 to 30 minutes.

Uses

Treatment and prevention of hypocalcemia, usually defined as a serum ionized calcium concentration less than approximately 4 mg/dL (or total serum calcium less than approximately 8 mg/dL).

Monitoring

If possible, measure ionized calcium directly. Avoid hypercalcemia during treatment. Correct hypomagnesemia if present. Observe IV infusion site closely for extravasation. Observe IV tubing for precipitates. Monitor continuously for bradycardia when giving bolus doses.

Adverse Effects/Precautions

Rapid administration is associated with bradycardia or cardiac standstill. Cutaneous necrosis or calcium deposition occurs with extravasation. Bolus infusions by UAC have been associated with intestinal bleeding and lower-extremity tissue necrosis.

Pharmacology

Calcium chloride may be more bioavailable than calcium gluconate, but it also is more likely to cause metabolic acidosis. Administration by continuous infusion is more efficacious than intermittent bolus dosing due to less renal calcium loss. Ionized calcium is the physiologically active fraction, accounting for approximately 50% of total blood calcium. The remainder is bound to albumin (40%) or complexed (10%) with citrate, phosphate, and bicarbonate. Early hypocalcemia is common in asphyxiated infants, premature infants, and infants of diabetic mothers. Significant decreases in ionized calcium may occur during acute alkalosis and following exchange transfusions with citrated blood. Clinical signs suggestive of hypocalcemia in neonates include muscle twitching, jitteriness, generalized seizures, and QTc above 0.4 second.

Special Considerations/Preparation

Calcium chloride 10% injection yields 27 mg/mL elemental calcium (1.36 mEq/mL). Osmolarity is 2040 mOsm/L. Injectable calcium salts should be stored at room temperature and are stable indefinitely.

Solution Compatibility: D₅W, D₁₀W, and NS.

Terminal Injection Site Compatibility: Dex/AA solutions, fat emulsion. Amikacin, amiodarone, chloramphenicol, dobutamine, dopamine, epinephrine, esmolol, hydrocortisone, isoproterenol, lidocaine, methicillin, milrinone, morphine, penicillin G, pentobarbital, phenobarbital, potassium chloride, prostaglandin E₁, and sodium nitroprusside.

Incompatibility: Amphotericin B, ceftriaxone, methylprednisolone, metoclopramide, sodium bicarbonate, and phosphate and magnesium salts when mixed directly.

Selected References

- ◆ Rigo J, DeCurtis M: Disorders of calcium, phosphorus, and magnesium metabolism. In: Martin RJ, Fanaroff AA, Walsh MC (eds): *Neonatal-Perinatal Medicine: Diseases of the Fetus and Newborn*, ed 8. St. Louis: Mosby, 2005, pp 1508-1514.
- ◆ Mimouni F, Tsang RC: Neonatal hypocalcemia: to treat or not to treat? (A review). *J Am Coll Nutr* 1994;13:408-15.
- ◆ Broner CW, Stidham GL, Westernkirchner DF, Watson DC: A prospective, randomized, double-blind comparison of calcium chloride and calcium gluconate therapies for hypocalcemia in critically ill children. *J Pediatr* 1990;117:986.
- ◆ Scott SM, Ladenson JH, Aguanna JJ, et al: Effect of calcium therapy in sick premature infants with early neonatal hypocalcemia. *J Pediatr* 1984;104:747.
- ◆ Roberts RJ: *Drug Therapy in Infants*. Philadelphia: WB Saunders Co, 1984, p 294.
- ◆ Product Information, Abbott, 2002

Compatibilities updated 7/2007

References updated 3/2007

Dose & Administration

Symptomatic hypocalcemia - acute treatment: 100 to 200 mg/kg per dose (1 to 2 mL/kg per dose, equivalent to 10 to 20 mg/kg elemental calcium).

Dilute in appropriate fluid, then infuse in IV over 10 to 30 minutes while monitoring for bradycardia. Stop infusion if heart rate is less than 100 beats per minute.

Do not give intra-arterially.

Maintenance treatment: 200 to 800 mg/kg per day (2 to 8 mL/kg per day, equivalent to 20 to 80 mg/kg elemental calcium).

Administer by continuous IV infusion. Treat for 3 to 5 days, and follow serum concentrations periodically.

May also be give orally in the same dose.

Exchange transfusion: 100 mg per 100 mL citrated blood exchanged (equals 1 mL per 100 mL blood exchanged). Infuse IV over 10 minutes.

Uses

Treatment and prevention of hypocalcemia, usually defined as a serum ionized calcium concentration less than approximately 4 mg/dL (or total serum calcium less than approximately 8 mg/dL).

Treatment of asymptomatic infants is controversial.

Monitoring

If possible, measure ionized calcium directly. Avoid hypercalcemia during treatment. Correct hypomagnesemia if present. Observe IV infusion site closely for extravasation. Observe IV tubing for precipitates. Monitor continuously for bradycardia when giving bolus doses. Assess for GI intolerance when treating PO.

Pharmacology

Ionized calcium is the physiologically active fraction, accounting for approximately 50% of total blood calcium. The remainder is bound to albumin (40%) or complexed (10%) with citrate, phosphate, and bicarbonate. Early hypocalcemia is common in asphyxiated infants, premature infants, and infants of diabetic mothers. Significant decreases in ionized calcium may occur during acute alkalosis and following exchange transfusions with citrated blood. Clinical signs suggestive of hypocalcemia in neonates include muscle twitching, jitteriness, generalized seizures, and QT_c above 0.4 second. Calcium chloride may be more bioavailable than calcium gluconate, but it also is more likely to cause metabolic acidosis. Administration by continuous infusion is more efficacious than intermittent bolus dosing due to less renal calcium loss.

Special Considerations/Preparation

Calcium gluconate 10% injection yields 9.3 mg/mL elemental calcium (0.46 mEq/mL). Osmolarity is 700 mOsm/L. Injectable calcium salts should be stored at room temperature and are stable indefinitely.

Solution Compatibility: D₅W, D₁₀W, and NS.

Terminal Injection Site Compatibility: Dex/AA solutions, fat emulsion. Amikacin, aminophylline, amiodarone, ampicillin, aztreonam, caffeine citrate, cefazolin, cefepime, chloramphenicol, dobutamine, enalaprilat, epinephrine, famotidine, furosemide, heparin, hydrocortisone, isoproterenol, lidocaine, linezolid, meropenem, methicillin, midazolam, milrinone, netilmicin, nicardipine, penicillin G, phenobarbital, piperacillin-tazobactam, potassium chloride, propofol, remifentanil, tobramycin, and vancomycin.

Incompatibility: Amphotericin B, ceftriaxone, clindamycin, esmolol, fluconazole, indomethacin, methylprednisolone, metoclopramide, sodium bicarbonate, and phosphate and magnesium salts when mixed directly.

Selected References

- ◆ Rigo J, DeCurtis M: Disorders of calcium, phosphorus, and magnesium metabolism. In: Martin RJ, Fanaroff AA, Walsh MC (eds). *Neonatal-Perinatal Medicine: Diseases of the Fetus and Newborn*, ed 8. St. Louis: Mosby, 2005, pp 1508-1514.
- ◆ Porcelli PJ, Oh W: Effects of single dose calcium gluconate infusion in hypocalcemic preterm infants. *Am J Perinatol* 1995;12:18-21.
- ◆ Mimouni F, Tsang RC: Neonatal hypocalcemia: to treat or not to treat? (A review). *J Am Coll Nutr* 1994;13:408-15.
- ◆ Broner CW, Stidham GL, Westernkirchner DF, Watson DC: A prospective, randomized, double-blind comparison of calcium chloride and calcium gluconate therapies for hypocalcemia in critically ill children. *J Pediatr* 1990;117:986.
- ◆ Scott SM, Ladenson JH, Aguanna JJ, et al: Effect of calcium therapy in sick premature infants with early neonatal hypocalcemia. *J Pediatr* 1984;104:747.
- ◆ Roberts RJ: *Drug Therapy in Infants*. Philadelphia: WB Saunders Co, 1984, p 294.
- ◆ Product Information, APP, 2002

Compatibilities updated 7/2007

References updated 3/2007

Dose & Administration

2 mg/kg per day of elemental iron for growing premature infants. (Maximum of 15 mg/day). Begin therapy after 2 weeks of age. Infants with birthweights less than 1000 grams may need 4 mg/kg per day. 6 mg/kg per day of elemental iron for patients receiving erythropoietin. Administer PO in 1 or 2 divided doses, preferably diluted in formula.

Uses

Iron supplementation for prevention and treatment of anemia.

Monitoring

Monitor hemoglobin and reticulocyte counts during therapy. Observe stools, check for constipation.

Adverse Effects/Precautions

In growing premature infants, iron supplementation should not be started until adequate vitamin E is supplied in the diet; otherwise, iron may increase hemolysis. Nausea, constipation, black stools, lethargy, hypotension, and erosion of gastric mucosa.

Pharmacology

Well absorbed from stomach.

Special Considerations/Preparation

Drops: Fer-In-Sol® drops now available as 15 mg elemental iron per 1 mL (0.2% alcohol) while other manufacturers FeSO₄ drops remain 15 mg elemental iron per 0.6 mL. Confirm product concentration.

Elixir: Contains 44 mg elemental iron per 5 mL (some with 5% alcohol).

Selected References

- ◆ Rao R, Georgieff M: Microminerals. In: Tsang R, Uauy R, Koletzko B, Zlotkin S. *Nutrition of the Preterm Infant. Scientific Basis and Practical Guidelines*. Cincinnati, Ohio: Digital Publishing Inc; 2005: pp 277-288.
- ◆ Rao R, Georgieff MK: Neonatal iron nutrition. *Semin Neonatol* 2001;6:425-35.
- ◆ Siimes MA, Järvenpää A-L: Prevention of anemia and iron deficiency in very low-birth-weight infants. *J Pediatr* 1982;101:277-280.
- ◆ Oski FA: Iron requirements of the premature infant, in Tsang R (ed): *Vitamin and Mineral Requirements in Preterm Infants*. New York: Marcel Dekker, 1985, p 18.
- ◆ Product Information, Mead Johnson, 2009

Special Considerations updated 1/2009
References updated 3/2007

the first time, the author has been able to identify the species of the genus *Leptothrix* occurring in India. The author wishes to thank Dr. S. K. Srivastava, Director, Botanical Survey of India, for his permission to publish the results. The author also thanks Dr. P. C. Srivastava, Head, Department of Botany, Banaras Hindu University, Varanasi, for his help in identification of the species.

Dose & Administration

IV administration: Infuvite® Pediatric is a sterile product consisting of two vials: a 4 mL vial labeled **Vial 1** and a 1 mL vial labeled **Vial 2**. The daily dose is a function of infant weight as indicated in the following table.

Do not exceed this daily dose.

Infuvite Dosing

	< 1 kg	≥ 1 kg and < 3 kg	≥ 3 kg
Vial 1	1.2 mL	2.6 mL	4 mL
Vial 2	0.3 mL	0.65 mL	1 mL

Adverse Effects/Precautions

Warnings: INFUVITE® Pediatric is administered in intravenous solutions, which may contain aluminum that may be toxic. Aluminum may reach toxic levels with prolonged parenteral administration if kidney function is impaired. Premature neonates are particularly at risk because their kidneys are immature, and they require large amounts of calcium and phosphate solution, which contain aluminum.

Research indicates that patients with impaired kidney function, including premature neonates who receive parenteral levels of aluminum at greater than 4 to 5 mcg/kg per day accumulate aluminum at levels associated with central nervous system and bone toxicity. Tissue loading may occur at even lower rates of administration.

Pharmacology

INFUVITE® Pediatric

Vial 1 (4 mL)	Amt*
Vitamin A** (as palmitate)	2300 IU (0.7 mg)
Vitamin D** (IU) (cholecalciferol)	400 IU (10 mcg)
Ascorbic Acid (vitamin C)	80 mg
Vitamin E** (dl-alpha tocopheryl acetate)	7 IU (7 mg)
Thiamine (as hydrochloride) B ₁	1.2 mg
Riboflavin (as phosphate) B ₂	1.4 mg
Niacinamide B ₃	17 mg
Pyridoxine hydrochloride B ₆	1 mg
d-Panthenol	5 mg
Vitamin K ₁ **	0.2 mg

Vial 2 (1 mL)
Biotin
Folic Acid
Vitamin B ₁₂ (cyanocobalamin)

Biotin	20 mcg
Folic Acid	140 mcg
Vitamin B ₁₂ (cyanocobalamin)	1 mcg

* Amounts based upon guidelines published by the American Medical Association Department of Foods and Nutrition, JPEN 3(4);25862:1979.

Vial 1 (4 mL) Inactive ingredients: 50 mg polysorbate 80, sodium hydroxide and/or hydrochloric acid for pH adjustment and water for injection.

** Polysorbate 80 is used to water solubilize the oil-soluble vitamins A, D, E, and K.

Vial 2 (1 mL) Inactive ingredients: 75 mg mannitol, citric acid and/or sodium citrate for pH adjustment and water for injection.

continued...

Special Considerations/Preparation

After INFUVITE® *Pediatric* is diluted in an intravenous infusion, the resulting solution is ready for immediate use. Inspect visually for particulate matter and discoloration prior to administration, whenever solution and container permit. Exposure to light should be minimized. Discard any unused portion. **Store between 2-8 °C (36-46 °F).**

Incompatibility: Alkaline solutions or moderately alkaline drugs: acetazolamide, aminophylline, ampicillin, and chlorothiazide. Direct addition to intravenous fat emulsions is not recommended.

Selected References

- ◆ Product Information, Baxter Clinitec 2001

Added 3/2002

Dose & Administration

0.4 to 1 mg/kg (400 to 1000 mcg/kg) per day IV continuous infusion in Dex/AA solutions containing at least 2% amino acids.

Uses

Iron supplementation in patients unable to tolerate oral iron, especially those also being treated with erythropoietin.

Monitoring

Periodic CBC and reticulocyte count. Observe Dex/AA solution for rust-colored precipitates.

Adverse Effects/Precautions

No adverse effects have been observed in patients who have received low doses infused continuously. Large (50 mg) intramuscular doses administered to infants were associated with increased risk of infection. Retrospective reviews of adult patients who received larger doses injected over a few minutes report a 0.7% risk of immediate serious allergic reactions, and a 5% risk of delayed such as myalgia, arthralgia, phlebitis, and lymphadenopathy.

Pharmacology

Iron dextran for intravenous use is a complex of ferric hydroxide and low molecular mass dextran. The dextran serves as a protective lipophilic colloid. Radiolabeled iron dextran injected into adult subjects localized to the liver and spleen before being incorporated into RBC hemoglobin. Complete clearance occurred by 3 days. Approximately 40% of the labeled iron was bound to transferrin within 11 hours. The addition of iron dextran to Dex/AA solutions inhibits the spontaneous generation of peroxides.

Special Considerations/Preparation

Available as a 50 mg/mL concentration in 2-mL single-dose vials. Store at room temperature.

*****Mix only in Dex/AA solutions containing at least 2% amino acids.**

Selected References

- ◆ Mayhew SL, Quick MW: Compatibility of iron dextran with neonatal parenteral nutrition solutions. *Am J Health-Syst Pharm* 1997;54:570-1.
- ◆ Lavoie J-C, Chessex P: Bound iron admixture prevents the spontaneous generation of peroxides in total parenteral nutrition solutions. *J Pediatr Gastroenterol Nutr* 1997;25:307-11.
- ◆ Friel JK, Andrews WL, Hall MS, et al: Intravenous iron administration to very-low-birth-weight newborns receiving total and partial parenteral nutrition. *JPEN* 1995;19:114-18.
- ◆ Burns DL, Mascioli EA, Bistrian BR: Parenteral iron dextran therapy: a review. *Nutrition* 1995;11:163-68.
- ◆ Kanakakorn K, Cavill I, Jacobs A: The metabolism of intravenously administered iron-dextran. *Br J Haematol* 1973;25:637-43.
- ◆ Product Information, Watson, 2006

Added 3/98

Potassium chloride

Dose & Administration

Initial oral replacement therapy: 0.5 to 1 mEq/kg per day divided and administered with feedings (small, more frequent aliquots preferred). Adjust dosage based on monitoring of serum potassium concentrations.

$$1 \text{ g KCl} = 13.4 \text{ mEq K}^+ \quad 1 \text{ mEq K}^+ = 74.6 \text{ mg KCl}$$

Acute treatment of symptomatic hypokalemia: Begin with 0.5 to 1 mEq/kg IV over 1 hour, then reassess. Maximum concentration: 40 mEq/L for peripheral, 80 mEq/L for central venous infusions.

Monitoring

Continuous EKG monitoring is mandatory if administering by the IV route, especially for central infusions. Observe IV site closely for signs of extravasation when using concentrated solutions. Monitor serum potassium concentration. Assess for GI intolerance.

Adverse Effects/Precautions

Rapid IV infusions, especially those through central lines, may cause arrhythmias including heart block and cardiac arrest. Peripheral IV administration of concentrated potassium solutions is associated with thrombophlebitis and pain at the injection site. GI irritation is common—most commonly diarrhea, vomiting, and bleeding—minimized by dividing oral doses and administering with feedings. Use with caution (if at all) in patients receiving potassium-sparing diuretics, e.g. spironolactone.

Pharmacology

Potassium is the major intracellular cation. Hypokalemia in critically ill neonates is usually the result of diuretic (furosemide, thiazides) therapy or diarrhea. Other causes include congenital adrenal hyperplasia and renal disorders. Alkalosis, as well as insulin infusions, will lower serum potassium concentrations by driving the ion intracellularly. Symptoms of hypokalemia include neuromuscular weakness and paralysis, ileus, urine retention, and EKG changes (ST segment depression, low-voltage T wave, and appearance of U wave). Hypokalemia increases digitalis toxicity. Oral potassium preparations are completely absorbed.

Special Considerations/Preparation

Potassium chloride for injection is supplied as 2-mEq/mL solution. **Always dilute before administration.** Hyperosmolar - 4355 mOsm/kg determined by freezing-point depression. pH ranges from 4 to 8 depending on buffering. Various oral solutions are available, with concentrations ranging from 10 to 40 mEq per 15 mL. Other oral forms available include powder packets, tablets, and sustained-release capsules.

Solution Compatibility: Most standard IV solutions.

Terminal Injection Site Compatibility: Most drugs.

Incompatibility: Amphotericin B, diazepam, and phenytoin.

Selected References

- ◆ Satlin LM, Schwartz GI: Disorders of potassium metabolism, in Ichikawa I (ed): *Pediatric Textbook of Fluids and Electrolytes*. Baltimore: Williams & Wilkins, 1990, p 227.
 - ◆ Morgan BC: Rapidly infused potassium chloride therapy in a child. *JAMA* 1981;245:2446.
 - ◆ DeFronzo RA, Bia M: Intravenous potassium chloride therapy. *JAMA* 1981;245:2446.
- Updated 3/97 Compatibilities updated 3/2007

Dose & Administration

Initial diagnostic dose: 50 to 100 mg IV push, or IM.

Maintenance dose: 50 to 100 mg PO Q24 hours. High doses may be required during periods of intercurrent illness.

Uses

Diagnosis and treatment of pyridoxine-dependent seizures.

Monitoring

When possible, initial administration of pyridoxine should be accompanied by EEG monitoring.

Adverse Effects/Precautions

Risk of profound sedation. Ventilator support may be necessary.

Pharmacology

Pyridoxine-dependent seizures are a result of defective binding of pyridoxine in the formation of GABA (an inhibitory neurotransmitter). Administration of pharmacologic doses of pyridoxine will correct this GABA deficiency.

Special Considerations/Preparation

Injectable form available in concentration of 100 mg/mL (1 mL in 2-mL vial). May use injectable form orally; mix in simple syrup if desired.

Protect from light.

Solution Incompatibility: Alkaline solutions. No data are currently available on Dex/AA.

Terminal Injection Site Compatibility: Fat emulsion.

Incompatibility: Iron salts and oxidizing agents. No data are currently available on heparin and potassium chloride.

Selected References

- ◆ Gospe SM: Current perspectives on pyridoxine-dependent seizures. *J Pediatr* 1998;132:919-923.
- ◆ Gordon N: Pyridoxine dependency: An update. *Dev Med Child Neurol* 1997;39:63.
- ◆ Mikati MA, Trevathan E, Krishnamoorthy KS, Lombroso CT: Pyridoxine-dependent epilepsy: Investigations and long-term followup. *Electroencephalogr Clin Neurophysiol* 1991;78:215
- ◆ Kroll JS: Pyridoxine for neonatal seizures: An unexpected danger. *Dev Med Child Neurol* 1985;27:369.
- ◆ Bankier A, Turner M, Hopkins IJ: Pyridoxine-dependent seizures: A wider clinical spectrum. *Arch Dis Child* 1983;58:415.
- ◆ Product Information, Abraxis, 2006

Updated 3/99

Compatibilities updated 3/99

(Retinyl Palmitate)

Dose & Administration

Parenteral treatment of Vitamin A deficiency: 5000 units IM 3 times weekly for 4 weeks.

Administer using 29-g needle and insulin syringe.

DO NOT ADMINISTER IV.

Uses

To reduce the risk of Chronic Lung Disease in high risk premature neonates with Vitamin A deficiency. In the NICHD-sponsored trial, 14 infants needed to be treated to prevent 1 case of Chronic Lung Disease.

Monitoring

Assess regularly for signs of toxicity: full fontanel, lethargy, irritability, hepatomegaly, edema, mucocutaneous lesions, and bony tenderness. Consider measuring plasma retinol concentrations if available, especially if patient is also receiving glucocorticoid therapy. Desired concentrations are approximately 30 to 60 mcg/dL.

Concentrations < 20 mcg/dL indicate deficiency, while those > 100 mcg/dL are potentially toxic.

Adverse Effects/Precautions

See monitoring section. Coincident treatment with glucocorticoids should be avoided, as it significantly raises plasma vitamin A concentrations.

Pharmacology

The pulmonary histopathologic changes of BPD and Vitamin A deficiency are remarkably similar. Vitamin A is the generic name for a group of fat soluble compounds which have the biological activity of the primary alcohol, retinol. Retinol metabolites exhibit potent and site-specific effects on gene expression and on lung growth and development. Retinol is supplied in the diet as retinyl esters.

Special Considerations/Preparation

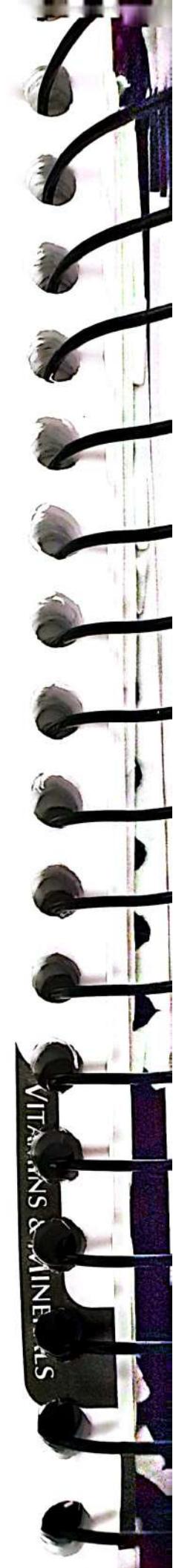
Available as Aquasol A® Parenteral (water-miscible vitamin A palmitate) 50,000 units per mL, equivalent to 15 mg retinol per mL, in 2 mL vials.

Protect from light. Store refrigerated at 36 to 46 °F (2 to 8 °C). Do not freeze.

Selected References

- ◆ Tyson JE, Wright LL, Oh W, Kennedy K, et al: Vitamin A supplementation for extremely-low-birth-weight infants. *N Engl J Med* 1999;340:1962-68.
- ◆ Darlow BA, Graham PJ. Vitamin A supplementation for preventing morbidity and mortality in very low birthweight infants (Cochrane Review). In: *The Cochrane Library*, Issue 1, 2004. Chichester, UK: John Wiley & Sons, Ltd.
- ◆ Shenai JP: Vitamin A supplementation in very low birthweight neonates: rationale and evidence. *Pediatrics* 1999;104:1369-74.
- ◆ Product information, Mayne, 2005

References updated 3/2003



Dose & Administration

Supplementation: 400 units per day PO.

Treatment of vitamin D deficiency: 1000 units per day PO.

Uses

Prevention and treatment of vitamin D deficiency. For breastfed infants, the AAP recommends that supplementation should begin within the first few days of life, regardless of whether the infant is exclusively breastfed or supplemented with infant formula. Exclusively formula-fed infants receiving at least 1000 mL/day of formula receive adequate amounts of vitamin D without supplementation. Recent data indicate that administration of high doses of vitamin D (4000 to 6400 units daily) to breastfeeding mothers is capable of raising 25(OH)-D levels in the infant to levels similar to those seen with infant supplementation without causing hypervitaminosis D in the mother.

Monitoring

Signs of vitamin D deficiency include symptomatic hypocalcemia (including seizures), growth failure, irritability, lethargy, and increased susceptibility for respiratory infections. A 25-hydroxyvitamin D (25(OH)-D) concentration of less than 50 nmol/L is thought to be indicative of vitamin D deficiency in infants.

Adverse Effects/Precautions

Signs of vitamin D toxicity include hypercalcemia, azotemia, vomiting, and nephrocalcinosis. A 25(OH)-D concentration greater than 250 nmol/L may be associated with a risk for vitamin D intoxication.

Pharmacology

The main source of vitamin D is vitamin D₃, which is synthesized in the skin through exposure to ultraviolet B (UV-B) radiation. UV-B in the range of 290 to 315 nm initiates the synthesis of vitamin D₃ by converting 7-dehydrocholesterol into previtamin D₃, which is further converted to vitamin D₃. Vitamin D₃ binds to vitamin D-binding protein and is transported to the liver for 25-hydroxylation to 25(OH)-D (calcidiol). Calcidiol undergoes further hydroxylation in the kidney and other tissues to calcitriol (1,25-dihydroxyvitamin D) (1,25-OH₂-D), the active form of vitamin D. Calcitriol stimulates the intestinal absorption of calcium and phosphorous, renal reabsorption of filtered calcium, and mobilization of calcium and phosphorous from bone. As a supplement, vitamin D₃ has been shown to be more effective in raising 25(OH)-D levels when compared with vitamin D₂.

Special Considerations/Preparation

Vitamin D supplements are available as vitamin D₂ (ergocalciferol; plant derived) and vitamin D₃ (cholecalciferol; animal derived).

Drisdol® (ergocalciferol oral solution) contains 200 units (5 mcg) vitamin D₂ per drop. The inactive ingredient is propylene glycol.

Baby Ddrops™ (cholecalciferol liquid vitamin supplement) is supplied as 400 units vitamin D₃ per drop. The inactive ingredient is purified palm-kernel oil.

Bio-D-Mulsion™ (cholecalciferol; emulsified vitamin D₃) is supplied as 400 units per drop. Inactive ingredients include water, sesame oil and acacia.

Just D (cholecalciferol) is supplied as 400 units vitamin D₃ per mL. The inactive ingredient is corn oil.

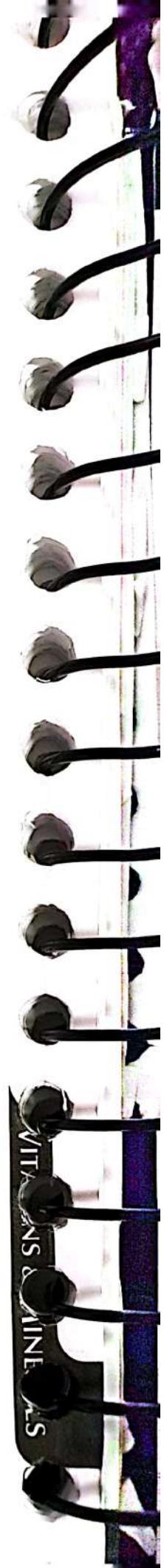
The vitamin D₃ content of Vi-Daylin® and Vi-Sol® products is 400 units per mL.

The vitamin D₃ content of AquADEKs™ drops is 400 units per mL.

Selected References

- ◆ American Academy of Pediatrics Committee on Nutrition: Vitamins. In: *Pediatric Nutrition Handbook*. 6th ed. Elk Grove Village, IL: American Academy of Pediatrics 2009: pp 458, 464-466.
- ◆ Wagner CL, Greer FR and the Section on Breastfeeding and Committee on Nutrition: Prevention of rickets and vitamin D deficiency in infants, children, and adolescents. *Pediatrics* 2008;122:1142-1152.
- ◆ Misra M, Pacaud D, Petryk A et al: Vitamin D deficiency in children and its management: Review of current knowledge and recommendations. *Pediatrics* 2008;122:398-417.

Added 3/2009



(dl-alpha-tocopherol acetate)**Dose & Administration**

5 to 25 units per day PO. Dilute with feedings. Do not administer simultaneously with iron—iron absorption is impaired.

Uses

Prevention of vitamin E deficiency. May be indicated in babies receiving erythropoietin and high iron dosages. Higher doses used to reduce oxidant-induced injury (ROP, BPD, IVH) remain controversial.

Monitoring

Assess feeding tolerance. Signs of vitamin E deficiency include hemolytic anemia and thrombocytosis. Physiologic serum vitamin E concentrations are between 0.8 and 3.5 mg/dL.

Adverse Effects/Precautions

Feeding intolerance may occur due to hyperosmolarity of preparation. Pharmacologic doses of alpha tocopherol have been associated with increased rates of sepsis (antioxidant effect of drug) and NEC (osmolarity of oral formulation).

Pharmacology

Alpha-tocopherol is the most active antioxidant of the group of tocopherols known as Vitamin E. The amount required by the body is primarily dependent upon the dietary intake of fat, especially polyunsaturated fatty acids (PUFA). Human milk and currently available infant formulas contain adequate Vitamin E and have appropriate E:PUFA ratios to prevent hemolytic anemia. Infants receiving supplemental iron amounts above 2 mg/kg/day may also require additional Vitamin E. Oral absorption of vitamin E is dependent upon hydrolysis that requires bile salts and pancreatic esterases. This can be quite variable in very immature infants and those with fat malabsorption. Free tocopherol is absorbed in the small intestine, taken via chylomicrons into the gastrointestinal lymphatics, then carried via low-density lipoproteins to be incorporated into cell membranes. Significant tissue accumulation may occur with pharmacologic doses.

Special Considerations/Preparation

Available as liquid drops: Aquavit E® (Cypress Pharmaceutical), 15 units (=15 mg) per 0.3 mL. Water solubilized with polysorbate 80. Also contains propylene glycol. Hyperosmolar (3620 mOsm/kg H₂O). Store at controlled room temperature.

Selected References

- ◆ Gross SJ: Vitamin E. In Tsang RC, Lucas A, Uauy R, Zlotkin S (eds): *Nutritional Needs of the Preterm Infant: Scientific Basis and Practical Guidelines*. Pauling, New York: Caduceus Medical Publishers, 1993, pp 101-109.
- ◆ Roberts RJ, Knight ME: Pharmacology of vitamin E in the newborn. *Clin Perinatol* 1987;14:843-855.
- ◆ Raju TNK, Langenberg P, Bhutani V, Quinn GE: Vitamin E prophylaxis to reduce retinopathy of prematurity: A reappraisal of published trials. *J Pediatr* 1997;131:844-850.

Added 3/2001

Dose & Administration

Recommended Prophylaxis: 0.5 to 1 mg IM at birth.

Preterm infants <32 weeks gestation:

BW <1000 grams: 0.5 mg IM.

BW <1000 grams: 0.3 mg/kg IM.

Alternate strategy for healthy, term, exclusively breast-fed infants:

1 to 2 mg PO at birth, at 1 to 2 weeks of age, and at 4 weeks of age.

Oral prophylaxis is contraindicated in infants who are premature, ill, on antibiotics, have cholestasis, or have diarrhea. There has been an increased number of cases of hemorrhagic disease of the newborn in countries that have changed to oral prophylaxis, primarily in patients who received only a single oral dose.

Also: Maternal daily intake of 5 mg/day of phylloquinone significantly increases Vitamin K concentrations in breastmilk and infant plasma.

Treatment of severe hemorrhagic disease: 1 to 10 mg IV slow push.

(See Adverse Effects/Precautions for rate of administration.)

Uses

Prophylaxis and therapy of hemorrhagic disease of the newborn. Treatment of hypoprothrombinemia secondary to factors limiting absorption or synthesis of vitamin K₁.

Monitoring

Check prothrombin time when treating clotting abnormalities.

(A minimum of 2 to 4 hours is needed for measurable improvement.)

Adverse Effects/Precautions

Severe reactions, including death, have been reported with IV administration in adults. These reactions are extremely rare, and have resembled anaphylaxis and included shock and cardiac/respiratory arrest.

With IV administration, give very slowly, not exceeding 1 mg per minute, with physician present. Pain and swelling may occur at IM injection site. Efficacy of treatment with vitamin K₁ is decreased in patients with liver disease. The risk of childhood cancer is not increased by IM administration of vitamin K₁.

Note: A box warning statement in the AquaMEPHYTON® product information states that intramuscular administration "should be restricted to those situations where the subcutaneous route is not feasible and the serious risk is considered justified". However, this does not apply to newborns, and the American Academy of Pediatrics recommends the single intramuscular dose at birth as above. The product information labeling reflects this recommended newborn dosing.

Pharmacology

Vitamin K₁ (phytonadione) promotes formation of the following clotting factors in the liver: active prothrombin (factor II), proconvertin (factor VII), plasma thromboplastin component (factor IX), and Stuart factor (factor X). Vitamin K₁ does **not** counteract the anticoagulant action of heparin.

Vitamin K₁

Special Considerations/Preparation

Available as a 2 mg/mL aqueous dispersion in 0.5-mL ampules and 10 mg/mL aqueous dispersion in 1-mL ampules and 2.5- and 5-mL vials. Contains 0.9% (9 mg/mL) benzyl alcohol as a preservative.

***** Efficacy with giving this preparation orally is uncertain. *****

Protect from light.

An extemporaneous oral suspension can be made by triturating six 5-mg tablets in a mortar. While mixing, add 5 mL purified water, USP and 5 mL 1% methylcellulose. Transfer to a graduate and qs to 30 mL with 70% sorbitol solution. Final concentration is 1 mg/mL and suspension is stable for 3 days refrigerated. Shake well before using.

Solution Compatibility: D₅W, D₁₀W, and NS.

Terminal Injection Site Compatibility: Dex/AA. Amikacin, ampicillin, dobutamine, chloramphenicol, cimetidine, epinephrine, famotidine, heparin, hydrocortisone succinate, netilmicin, potassium chloride, ranitidine, and sodium bicarbonate.

Incompatibility: Phenytoin.

Selected References

- ◆ American Academy of Pediatrics Committee on Nutrition: Vitamins. In: *Pediatric Nutrition Handbook*. 6th ed. Elk Grove Village, IL: American Academy of Pediatrics 2009: pp 93, 468-471.
- ◆ Nahata MC, Pai VB, Hippel TF, eds. *Pediatric Drug Formulations*. 5th ed. Cincinnati, OH: Harvey Whitney Books Company; 2004:219.
- ◆ Costakos DT, Greer FR, Love LA, et al: Vitamin K prophylaxis for premature infants: 1 mg versus 0.5 mg. *Am J Perinatol* 2003;20:485-90.
- ◆ American Academy of Pediatrics, Committee on Fetus and Newborn: Controversies concerning vitamin K and the newborn. *Pediatrics* 2003;112:191-92.
- ◆ Kumar D, Greer FR, Super DM, et al: Vitamin K status of premature infants: implications for current recommendations. *Pediatrics* 2001;108:1117-1122.
- ◆ Fiore LD, Scola MA, Cantillon CE, Brophy MT: Anaphylactoid reactions to Vitamin K. *J Thromb Thrombolysis* 2001;11:175-188.
- ◆ Zipursky AL: Prevention of vitamin K deficiency bleeding in newborns. *Br J Haematol* 1999;104:430-437.
- ◆ Greer FR: Vitamin K deficiency and hemorrhage in infancy. *Clin Perinatol* 1995;22:759.
- ◆ Greer FR, Marshall SP, Foley AL, Suttie JW: Improving the vitamin K status of breastfeeding infants with maternal vitamin K supplements. *Pediatrics* 1997;99:88.
- ◆ Product Information, Hospira, 2004.
- ◆ Product Information, Aton Pharma, 2007.

Dosing and References updated 01/2009

Special Considerations updated 12/2008

Compatibilities updated 3/2001

Dose & Administration

1 dropperful (1 mL) Q24 hours, or as directed by physician. Percentages of the Reference Daily Intakes (%RDIs) listed in the table below are for infants.

Vi-Daylin® Multivitamin Products

	Vi-Daylin® ADC Vitamin Drops	Vi-Daylin® ADC Vitamins + Iron Drops	Vi-Daylin® Multivitamin Drops	Vi-Daylin® Multivitamin + Iron Drops
	Amt (%) RDI	Amt (%) RDI	Amt (%) RDI	Amt (%) RDI
Vitamins				
A (IU)	1350 (90)	1350 (90)	1350 (90)	1350 (90)
D (IU)	400 (100)	400 (100)	360 (90)	360 (90)
C (mg)	32 (90)	32 (90)	32 (90)	32 (90)
E (IU)			5 (90)	5 (90)
Thiamine (B ₁) (mg)			0.4 (80)	0.5 (89)
Riboflavin (B ₂) (mg)			0.5 (90)	0.5 (90)
Niacin (mg)			7 (90)	7 (90)
B ₆ (mg)			0.4 (90)	0.4 (90)
B ₁₂ (mcg)			1.4 (68)	
Minerals				
Iron (mg)		9 (60)		9 (60)

Dose & Administration

1 dropperful (1 mL) Q24 hours, or as directed by physician. Percentages of the Reference Daily Intakes (%RDIs) listed in the table below are for infants.

Vi-Sol® Products

	Tri-Vi-Sol® Multivitamin Drops	Tri-Vi-Sol® Multivitamin with Iron Drops	Poly-Vi-Sol® Multivitamin Drops	Poly-Vi-Sol® Multivitamin with Iron Drops
	Amt (%RDI)	Amt (%RDI)	Amt (%RDI)	Amt (%RDI)
Vitamins				
A (IU)	1500 (100)	1500 (100)	1500 (100)	1500 (100)
D (IU)	400 (100)	400 (100)	400 (100)	400 (100)
C (mg)	35 (100)	35 (100)	35 (100)	35 (100)
E (IU)			5 (100)	5 (100)
Thiamine (B ₁) (mg)			0.5 (100)	0.5 (100)
Riboflavin(B ₂) (mg)			0.6 (100)	0.6 (100)
Niacin (mg)			8 (100)	8 (100)
B ₆ (mg)			0.4 (100)	0.4 (100)
B ₁₂ (mcg)			2 (100)	2 (100)
Minerals				
Iron (mg)		10 (67)		10 (67)

NUTRITIONALS

The following information, although accurate at the time of publication, is subject to change. The most current information may be obtained by referring to product packaging.

Potential renal solute load is estimated as follows:

$$[\text{Protein (g)} \times 5.714] + [\text{Na(mOsm)} + \text{K(mOsm)} + \text{Cl(mOsm)} + \text{P(mOsm)}]$$

Dilution Table

Use the Powder-20 Dilution Table to reconstitute the following infant formulas from powder:

Similac® Advance®	Enfamil® LactoFree® LIPIL® 20
Similac® Alimentum®	Enfamil® Gentlease™ LIPIL®
Similac® Isomil® Advance®	Enfamil® LIPIL® with Iron 20
Similac Sensitive™ (Lactose Free)	Pregestimil® LIPIL® Powder 20 **
Similac® PM 60/40	Enfamil® ProSobee® LIPIL® 20
Similac® Organic	Nutramigen® LIPIL® 20 **

Dilution Table Powder-20

Caloric Density (Cal/fl oz)	Water (fl oz)	Level Unpacked (Scoopful)	Approximate Yield (fl oz)
20*	2	1	2
22	3.5	2	4
24	5	3	6
27	4.25	3	5

* Standard mixture

** Packed Level Scoopful

NOTE: Refer to 'Dilution Table Liquid-20' under 'Nutritionals' when mixing 40 Cal/fl oz concentrate.

Use the Powder-22 Dilution Table to reconstitute the following infant formulas from powder:

Similac® NeoSure®

Enfamil® EnfaCare® LIPIL® 22

Dilution Table Powder-22

Caloric Density (Cal/fl oz)	Water (fl oz)	Level Unpacked (Scoopful)	Approximate Yield (fl oz)
20	4.5	2	5
22*	2	1	2
24	5.5	3	6.5
27	8	5	9

* Standard mixture

Use the Liquid-20 Dilution Table to reconstitute the following infant formulas from (40 Cal/fl oz) liquid concentrate:

Similac® Advance®
Similac Sensitive™
Similac® Isomil® Advance®
Enfamil® LIPIL® with Iron 20

Enfamil® LactoFree® LIPIL® 20
Enfamil® ProSobee® LIPIL® 20
Nutramigen® LIPIL® 20

Dilution Table Liquid-20

Caloric Density (Cal/fl oz)	Water (fl oz)	Concentrated Liquid (fl oz)	Approximate Yield (fl oz)
20*	1	1	2
22	2.5	3	5.5
24	2	3	5
27	1	2	3

* Standard mixture

Human Milk (Mature)

Nutrient per Liter	Term*	Preterm
Energy, Cal	680	671
Volume, mL	1000	1000
Protein, g	10.48	14.09
% of total calories †	6	8
Fat, g	39.05	38.93
% of total calories ‡	52	52
Linoleic acid, mg	3741	3691
Carbohydrate, g	72	66.4
% of total calories §	42	40
Water, g	898	879
Minerals		
Calcium, mg (mEq)	279 (13.9)	248 (12.4)
Phosphorus, mg (mEq)	143	128
Magnesium, mg	34.7	30.9
Iron, mg	0.27	1.21
Zinc, mg	1.22	3.42
Manganese, mcg	7	6
Copper, mcg	252	644
Molybdenum, mcg	—	—
Iodine, mcg	109	107
Selenium, mcg	15.0	14.8
Sodium, mg (mEq)	177 (7.7)	248 (10.8)
Potassium, mg (mEq)	531 (13.6)	570 (14.6)
Chloride, mg (mEq)	422 (11.9)	550 (15.5)
Vitamins		
Vitamin A, IU	2252	3899
Vitamin D, IU	20	20
Vitamin E, IU	4.1	10.7
Vitamin K, mcg	2	2
Thiamine (B ₁), mcg	211	208
Riboflavin (B ₂), mcg	347	483
Vitamin B ₆ , mcg	204	148
Vitamin B ₁₂ , mcg	0.48	0.47
Niacin, mcg	1803	1503
Folic acid (Folacin), mcg	48	33
Pantothenic acid, mcg	1803	1805
Biotin, mcg	4.1	4.0
Vitamin C (Ascorbic acid), mg	41	107
Choline, mg	95	94
Inositol, mg	149.7	147.7
L-Carnitine, mg	—	—
Taurine, mg	—	—
Nucleotide fortification, mg	—	—
Renal Solute Load, mOsm	97.6	125.6
Osmolality, mOsm/kg H₂O	286	290
Osmolarity, mOsm/L	257	255

* Composition of human milk varies with maternal diet, stage of lactation, within feedings, diurnally, and among mothers^{1,2}. Values represent mature term milk (not colostrum or transitional milk). Total potentially available nucleotides = 72 mg/L³. The extent of bioavailability of all sources of nucleotides has not been determined.

¹ American Academy of Pediatrics Committee on Nutrition: Pediatric Nutrition Handbook, 4th ed. Elk Grove Village: American Academy of Pediatrics, 1998:40, 132-135, 217, 258, 655-658.

² Lawrence RA: Breastfeeding: A Guide for the Medical Profession, 5th ed. St. Louis: Mosby Inc, 1999:136, 737.

³ Leach JL, Baxter JH, Molitor BE, et al: Total potentially available nucleotides of human milk by stage of lactation. Am J Clin Nutr 1995;61:1224-1230.

† Protein Source: Mother's milk

‡ Fat Source: Mother's milk

§ Carbohydrate Source: Lactose

Preterm Human Milk + Similac® Human Milk Fortifier

1 pk/50 mL (adds an additional 2 Cal/fl oz)

1 pk/25 mL (adds an additional 4 Cal/fl oz)

Nutrient per Liter	1 pk/50 mL	1 pk/25 mL
Energy, Cal	731	790
Volume, mL	1000	1000
Protein, g	18.84	23.46
% of total calories [†]	10	12
Fat, g	40.18	41.41
% of total calories ⁺⁺	49	47
Linoleic acid, mg	3642	3594
Carbohydrate, g	74.4	82.2
% of total calories [§]	41	42
Water, g	867	856
Minerals		
Calcium, mg (mEq)	822 (41)	1381 (68.9)
Phosphorus, mg (mEq)	456	777
Magnesium, mg	65	98.2
Iron, mg	2.92*	4.58*
Zinc, mg	8.31	13.07
Manganese, mcg	41	76
Copper, mcg	1474	2283
Molybdenum, mcg	—	—
Iodine, mcg	106	105
Selenium, mcg	17	19.2
Sodium, mg (mEq)	319 (13.9)	388 (16.9)
Potassium, mg (mEq)	874 (22.3)	1169 (29.9)
Chloride, mg (mEq)	730 (20.6)	906 (25.5)
Vitamins		
Vitamin A, IU	6906	9834
Vitamin D, IU	612	1188
Vitamin E, IU	26.4	41.6
Vitamin K, mcg	42.9	82.8
Thiamine (B ₁), mcg	1355	2471
Riboflavin (B ₂), mcg	2534	4531
Vitamin B ₆ , mcg	1187	2198
Vitamin B ₁₂ , mcg	3.62	6.69
Niacin, mcg	19096	36225
Folic acid (Folacin), mcg	146	256
Pantothenic acid, mcg	9181	16364
Biotin, mcg	132.2	257.1
Vitamin C (Ascorbic acid), mg	229	348
Choline, mg	102	109
Inositol, mg	164.7	181.3
L-Carnitine, mg	—	—
Taurine, mg	—	—
Nucleotide fortification, mg	—	—
Renal Solute Load, mOsm	179.2	231.5
Osmolality, mOsm/kg H ₂ O	343 (est.)	385 (est.)
Osmolarity, mOsm/L	297	329

* Additional iron may be supplied from other sources as necessary.

† Protein Source: Preterm human milk, nonfat milk and whey protein concentrate.

++ Fat Source: Preterm human milk and MCT oil.

§ Carbohydrate Source: Lactose and corn syrup solids.

Precaution: Tolerance to enteral feedings should be confirmed by offering small volumes of unfortified human milk. Once enteral feeding is well established, Similac Human Milk Fortifier can be added to human milk.

Preterm Human Milk + Enfamil® Human Milk Fortifier

1 pk/50 mL (22 Cal/fl oz)
1 pk/25 mL (24 Cal/fl oz)

Nutrient per Liter	1 pk/50 mL	1 pk/25 mL
Energy, Cal	739	803
Volume, mL	1000	1000
Protein, g	19.6	25
% of total calories [†]	11	12
Fat, g	43.9	48.7
% of total calories ^{††}	54	55
Linoleic acid, mg	4391	5070
Carbohydrate, g	68.4	70
% of total calories [§]	37	35
Water, g	879	874
Minerals		
Calcium, mg (mEq)	698 (34.8)	1147 (57.2)
Phosphorus, mg (mEq)	378	627
Magnesium, mg	36	41
Iron, mg	8.41*	15.6*
Zinc, mg	7.02	10.6
Manganese, mcg	56	106
Copper, mcg	864	1080
Molybdenum, mcg	—	—
Iodine, mcg	—	—
Selenium, mcg	—	—
Sodium, mg (mEq)	328 (14.3)	407 (17.7)
Potassium, mg (mEq)	715 (18.3)	857 (21.9)
Chloride, mg (mEq)	615 (17.3)	677 (19.1)
Vitamins		
Vitamin A, IU	8649	13377
Vitamin D, IU	770	1520
Vitamin E, IU	33.7	56.6
Vitamin K, mcg	24	46
Thiamine (B ₁), mcg	958	1707
Riboflavin (B ₂), mcg	1583	2680
Vitamin B ₆ , mcg	723	1297
Vitamin B ₁₂ , mcg	1.37	2.27
Niacin, mcg	16503	31494
Folic acid (Folacin), mcg	158	283
Pantothenic acid, mcg	5455	9095
Biotin, mcg	19.5	33
Vitamin C (Ascorbic acid), mg	170	229
Choline, mg	—	—
Inositol, mg	—	—
L-Carnitine, mg	—	—
Taurine, mg	—	—
Nucleotide fortification, mg	—	—
Renal Solute Load, mOsm	174	221.8
Osmolality, mOsm/kg H₂O	308	325
Osmolarity, mOsm/L	270	284

* Additional iron may be supplied from other sources as necessary.

† Protein Source: Mature preterm human milk, whey protein concentrate, sodium caseinate.

†† Fat Source: Preterm human milk and corn syrup solids.

§ Carbohydrate Source: Lactose.

Precautions: Tolerance to enteral feedings should be confirmed by offering small volumes of unfortified human milk. Once enteral feeding is well established, Enfamil Human Milk Fortifier can be added to human milk.

Preparation:

24 Cal/fl oz = 2 pks + 48 mL Mature Preterm Human Milk (yield 1.6 fl oz)

24 Cal/fl oz = 2 pks + 60 mL Term Human Milk (yield 2.0 fl oz)

Preterm Human Milk + Prolact+ H²MF™ Human Milk Fortifier

Prolact+ 4 H²MF™ formulated to meet target of 4 Cal/fl oz. Fortifies breast milk up to 2.3 g of protein in 100 mL of nutrition.

Prolact+ 6 H²MF™ formulated to meet target of 6 Cal/fl oz. Fortifies breast milk up to 2.8 g of protein in 100 mL of nutrition.

Prolact+ 8 H²MF™ formulated to meet target of 8 Cal/fl oz. Fortifies breast milk up to 3.2 g of protein in 100 mL of nutrition.

Prolact+ 10 H²MF™ formulated to meet target of 10 Cal/fl oz. Fortifies breast milk up to 3.7 g of protein in 100 mL of nutrition.

Nutrient per 100 mL	Preterm Milk	Prolact+4	Prolact+6	Prolact+8	Prolact+10
Mixing ratios BM:H ² MF	n/a	4:1	7:3	3:2	1:1
Energy, cal	67	83	91	98	104
Protein (human), g	1.4	2.3	2.8	3.2	3.7
Carbohydrate, g	6.6	7.3	7.6	8	7.8
Fat (human), g	3.9	4.9	5.4	5.9	6.5
Minerals					
Sodium, mg	25	54	54	54	61
Potassium, mg	57	71	71	71	75
Calcium, mg	25	128	128	128	154
Phosphorus, mg	12.8	70	70	70	86
Magnesium, mg	3.1	8	8	8	9
Chloride, mg	55	83	83	83	91
Manganese, mcg	0.7	2.4	2.4	2.4	2.8
Copper, mcg	64	67	67	67	68
Zinc, mg	0.34	0.74	0.74	0.74	0.84
Iron, mg	0.12	0.2	0.2	0.2	0.2
Osmolality, mOsm/kg H₂O	~290	<335	<360	<325	<350
Fatty Acids*					
Linoleic acid, mg		250	375	500	625
Linolenic acid, mg		2	3	4	5
Arachadonic acid, mg		6.6	9.8	13.1	16.5
Docosahexaenoic acid, mg		2	3	4	5

* Fatty acid data for preterm human milk is not available. Values shown represent levels of nutrients found in Prolact+ fortifiers.

Enfamil® Human Milk Fortifier

Enfamil® Human Milk Fortifier

Nutrient	per 1 pk	per 4 pk
Energy, Cal	3.38	13.53
Protein, g	0.28	1.1
Fat, g	0.25	1
Linoleic acid, mg	35	140
Carbohydrate, g	<0.1	<0.4
Minerals		
Calcium, mg (mEq)	23 (1.12)	90 (4.49)
Phosphorus, mg (mEq)	12.5 (0.40)	50 (1.61)
Magnesium, mg	0.25	1
Iron, mg	0.36	1.44
Zinc, mg	0.18	0.72
Manganese, mcg	2.5	10
Copper, mcg	11	44
Iodine, mcg	-	-
Selenium, mcg	-	-
Sodium, mg (mEq)	4 (0.17)	16 (0.7)
Potassium, mg (mEq)	7.3 (0.19)	29 (0.74)
Chloride, mg (mEq)	3.3 (0.09)	13 (0.37)
Vitamins		
Vitamin A, IU	238	950
Vitamin D, IU	38	150
Vitamin E, IU	1.15	4.6
Vitamin K, mcg	1.1	4.4
Thiamine (B ₁), mcg	38	150
Riboflavin (B ₂), mcg	55	220
Vitamin B ₆ , mcg	29	115
Vitamin B ₁₂ , mcg	0.05	0.18
Niacin, mcg	750	3000
Folic acid (Folacin), mcg	6.3	25
Pantothenic acid, mcg	183	730
Biotin, mcg	0.68	2.7
Vitamin C (Ascorbic acid), mg	3	12
Renal Solute Load, mOsm	2.4	9.7

* Additional iron should be supplied from other sources.

Precautions: Nutritionally incomplete. Tolerance to enteral feedings should be confirmed by offering small volumes of unfortified human milk. Once enteral feeding is well established, Enfamil Human Milk Fortifier can be added.

Similac® Human Milk Fortifier

Nutrient	per 1 pk	per 4 pks
Energy, Cal	3.5	14.4
Protein, g	0.25	1
Fat, g	0.09	0.36
Linoleic acid, mg	-	-
Carbohydrate, g	0.45	1.8
Minerals		
Calcium, mg (mEq)	29.25 (1.46)	117 (5.84)
Phosphorus, mg (mEq)	16.8 (0.54)	67 (2.16)
Magnesium, mg	1.75	7
Iron, mg	0.08*	0.35*
Zinc, mg	0.26	1
Manganese, mcg	1.8	7.2
Copper, mcg	42.5	170
Iodine, mcg	-	-
Selenium, mcg	0.13	0.5
Sodium, mg (mEq)	3.75 (0.16)	15 (0.65)
Potassium, mg (mEq)	15.75 (0.4)	63 (1.61)
Chloride, mg (mEq)	9.5 (0.27)	38 (1.07)
Vitamins		
Vitamin A, IU	155	620
Vitamin D, IU	30	120
Vitamin E, IU	0.8	3.2
Vitamin K, mcg	2.07	8.3
Thiamine (B ₁), mcg	58.3	233
Riboflavin (B ₂), mcg	104	417
Vitamin B ₆ , mcg	53	211
Vitamin B ₁₂ , mcg	0.16	0.64
Niacin, mcg	893	3570
Folic acid (Folacin), mcg	5.75	23
Pantothenic acid, mcg	375	1500
Biotin, mcg	6.6	26
Vitamin C (Ascorbic acid), mg	6.3	25
Choline, mg	0.5	2
Inositol, mg	0.96	3.9
Renal Solute Load, mOsm	2.8	11.2

* Additional iron should be supplied from other sources.

Precautions: Nutritionally incomplete. Tolerance to enteral feedings should be confirmed by offering small volumes of unfortified human milk. Once enteral feeding is well established, Similac Human Milk Fortifier can be added.

Prolact+ H²MF™ Human Milk Fortifier 327

Prolact+ H²MF™ Human Milk Fortifier (Human, Pasteurized)

Prolact+ 4 H²MF™ formulated to meet target of 4 Cal/fl oz. Fortifies breast milk up to 2.3 g of protein in 100 mL of nutrition.

Prolact+ 6 H²MF™ formulated to meet target of 6 Cal/fl oz. Fortifies breast milk up to 2.8 g of protein in 100 mL of nutrition.

Prolact+ 8 H²MF™ formulated to meet target of 8 Cal/fl oz. Fortifies breast milk up to 3.2 g of protein in 100 mL of nutrition.

Prolact+ 10 H²MF™ formulated to meet target of 10 Cal/fl oz. Fortifies breast milk up to 3.7 g of protein in 100 mL of nutrition.

Nutrient	Prolact+4	Prolact+6	Prolact+8	Prolact+10
Energy, kcal¹	141	141	141	141
Volume, mL	100	100	100	100
Protein, g²	6	6	6	6
% of total kcal ³	17%	17%	17%	17%
Fat, g²	9	9	9	9
% of total calories ³	57%	57%	57%	57%
Carbohydrate, g⁴	9.1	9.1	9.1	9.1
% of total calories ³	26%	26%	26%	26%
Minerals				
Calcium, mg ²	588	400	306	250
Phosphorus, mg ²	348	236	181	147
Magnesium, mg ²	25.6	18.1	14.4	12.1
Iron, mg ⁴	0.5	0.5	0.5	0.5
Zinc, mg ²	2.7	1.9	1.5	1.3
Manganese, mcg ⁴	<60	<60	<60	<60
Copper, mcg ²	304	224	184	160
Sodium, mg ²	185	132	105	89
Potassium, mg ²	172	134	115	103
Chloride, mg ²	193	147	124	110
Vitamins				
Vitamin A, IU ⁴	298	298	298	298
Vitamin D, IU ⁵	130	130	130	130
Vitamin E, IU ⁵	2	2	2	2
Vitamin K, mcg ⁵	<1	<1	<1	<1
Thiamine B ₁ , mcg ⁵	20	20	20	20
Riboflavin B ₂ , mcg ⁵	75	75	75	75
Niacin, mcg ⁵	262	262	262	262
Folic acid, mcg ⁵	27	27	27	27
Pantothenic Acid, mcg ⁵	374	374	374	374
Biotin, mcg ⁵	0.9	0.9	0.9	0.9
Vitamin C, mg ⁴	<1	<1	<1	<1

¹ Derived from protein, carbohydrate, and fat [Atwater factors].

² Manufacturing target for Prolact+ fortifiers.

³ Calories from component divided by total energy.

⁴ Based on historical data of Prolact+ fortifier lots.

⁵ Naturally occurring in milk after pasteurization. Based on specific testing from three lots.

Preterm Human Milk + Similac® Special Care® 30 (1:1 ratio)

25 Cal/fl oz (approximate)

Based on mean nutrient concentrations in human milk.

Nutrient	per 100 Cal	per 100 mL
Energy, Cal	100	84.3
Volume, mL	119	100
Protein, g	2.64	2.23
% of total calories [†]	—	—
Fat, g	6.29	5.3
% of total calories ⁺⁺	—	—
Linoleic acid, mg	640	540
Carbohydrate, g	8.6	7.24
% of total calories [§]	—	—
Water, g	—	—
Minerals		
Calcium, mg (mEq)	123	103.7
Phosphorus, mg (mEq)	68	57.1
Magnesium, mg	9.1	7.6
Iron, mg	1.15	0.97
Zinc, mg	1.11	0.93
Manganese, mcg	8	6.4
Copper, mcg	189	159
Molybdenum, mcg	—	—
Iodine, mcg	10	8
Selenium, mcg	—	—
Sodium, mg (mEq)	41	34
Potassium, mg (mEq)	111	94
Chloride, mg (mEq)	81	69
Vitamins		
Vitamin A, IU	984	829
Vitamin D, IU	91	77
Vitamin E, IU	3	2.6
Vitamin K, mcg	7.3	6.2
Thiamine (B ₁), mcg	163	137
Riboflavin (B ₂), mcg	402	339
Vitamin B ₆ , mcg	159	134
Vitamin B ₁₂ , mcg	0.36	0.3
Niacin, mcg	3098	2611
Folic acid (Folacin), mcg	24	20.4
Pantothenic acid, mcg	1251	1054
Biotin, mcg	22.5	19
Vitamin C (Ascorbic acid), mg	29	24.1
Choline, mg	12	9.8
Inositol, mg	33	27.7
L-Carnitine, mg	—	—
Taurine, mg	—	—
Nucleotide fortification, mg	—	—
Renal Solute Load, mOsm	24.2	20.4
Osmolality, mOsm/kg H₂O		310
Osmolarity, mOsm/L	310 (est.)	

[†] Protein Source: Preterm human milk, nonfat milk and whey protein concentrate.

⁺⁺ Fat Source: Preterm human milk, medium chain triglycerides, soy and coconut oils.

[§] Carbohydrate Source: Preterm human milk, corn syrup solids, lactose.

When combined with human milk, does not increase concentrations of nutrients to levels achieved with Similac® Human Milk Fortifier.

Similac® Special Care® 30 with Iron

329

Similac® Special Care® 30 with Iron Premature Infant Formula 30 Cal/fl oz

Nutrient	per 100 Cal	per Liter
Energy, Cal	100	1014
Volume, mL	99	1000
Protein, g	3	30.4
% of total calories [†]	12	12
Fat, g	6.61	67.1
% of total calories ^{††}	57	57
Linoleic acid, mg	700	7101
Carbohydrate, g	7.73	78.4
% of total calories [§]	31	31
Water, g	84	852
Minerals		
Calcium, mg (mEq)	180 (9)	1826 (91.3)
Phosphorus, mg (mEq)	100	1014
Magnesium, mg	12	122
Iron, mg	1.8	18.3
Zinc, mg	1.5	15.22
Manganese, mcg	12	122
Copper, mcg	250	2536
Molybdenum, mcg	—	—
Iodine, mcg	6	61
Selenium, mcg	1.8	18.3
Sodium, mg (mEq)	43 (1.9)	436 (19)
Potassium, mg (mEq)	129 (3.3)	1308 (33.5)
Chloride, mg (mEq)	81 (2.3)	821 (23.2)
Vitamins		
Vitamin A, IU	1250	12681
Vitamin D, IU	150	1522
Vitamin E, IU	4	40.6
Vitamin K, mcg	12	122
Thiamine (B ₁), mcg	250	2536
Riboflavin (B ₂), mcg	620	6290
Vitamin B ₆ , mcg	250	2536
Vitamin B ₁₂ , mcg	0.55	5.58
Niacin, mcg	5000	50722
Folic acid (Folinic), mcg	37	375
Pantothenic acid, mcg	1900	19274
Biotin, mcg	37	375.3
Vitamin C (Ascorbic acid), mg	37	375
Choline, mg	10	101
Inositol, mg	40	406
L-Carnitine, mg		
Taurine, mg		
Nucleotide fortification, mg		
Renal Solute Load, mOsm	27.8	282.3
Osmolality, mOsm/kg H₂O	325	325
Osmolarity, mOsm/L		

[†] Protein Source: Nonfat Milk, Whey protein concentrate

^{††} Fat Source: Medium Chain Triglycerides, Soy Oil, Coconut Oil (0.21% DHA; 0.33% ARA)

[§] Carbohydrate Source: Corn Syrup Solids, Lactose

Term Human Milk + Similac® NeoSure® Powder

Term Human Milk + Similac® NeoSure® Powder *

Nutrient per 100 mL	22 Cal/fl oz	24 Cal/fl oz	27 Cal/fl oz
Energy, Cal	76	83	93
Protein, g	1.27	1.45	1.73
% of total calories [†]	6.7	7	7.4
Fat, g	4.33	4.7	5.27
% of total calories ^{††}	51.4	51.2	51
Linoleic acid, mg	435	486	567
Carbohydrate, g	8.01	8.69	9.77
% of total calories [§]	42.2	42.1	42
Water, g	87	86	87
Minerals			
Calcium, mg	37	44	56
Phosphorus, mg (mEq)	19	24	31
Magnesium, mg (mEq)	4.2	4.9	5.9
Iron, mg	0.19	0.32	0.53
Zinc, mg	0.22	0.31	0.45
Manganese, mcg	1	2	3
Copper, mcg	35	44	57
Molybdenum, mcg	-	-	-
Iodine, mcg	12	13	15
Selenium, mcg	1.7	1.8	2.1
Sodium, mg (mEq)	21	23	26
Potassium, mg (mEq)	65	74	90
Chloride, mg (mEq)	48	53	61
Vitamins			
Vitamin A, IU	263	294	344
Vitamin D, IU	8	13	21
Vitamin E, IU	0.7	1	1.4
Vitamin K, mcg	1.2	2	3.3
Thiamine (B ₁), mcg	40	56	81
Riboflavin (B ₂), mcg	48	58	75
Vitamin B ₆ , mcg	29	36	47
Vitamin B ₁₂ , mcg	0.08	0.11	0.16
Niacin, mcg	320	461	685
Folic acid, mcg	7.1	8.9	11.7
Pantothenic acid, mcg	248	305	395
Biotin, mcg	1.2	1.8	2.9
Vitamin C, mg	5	6	8
Choline, mg	10	12	13
Inositol, mg	18	20	24
L-Carnitine, mg	-	-	-
Taurine, mg	-	-	-
Nucleotide fortification, mg	-	-	-
Renal Solute Load, mOsm	11.9	13.6	16.3
Osmolality, mOsm/kg H₂O	-	-	-
Osmolarity, mOsm/L	-	-	-

* Nutrient needs of small premature infants may not be met by this fortification strategy.
Compare nutrient profile to fortification with Similac Human Milk Fortifier.

† Protein Source: Term human milk, nonfat milk and whey protein concentrate.

†† Fat Source: High-oleic safflower, soy, MCT, coconut, Term human milk, and C.cohnii¹ and M. alpina² oils.

¹ A source of docosahexaenoic acid (DHA).

² A source of arachidonic acid (ARA).

§ Carbohydrate Source: Lactose, maltodextrin.

WARNING: Powdered infant formulas are not sterile and should not be fed to premature infants or infants who might have immune problems.

Preparation:

22 Calorie = 1 tsp level powder + 130 mL Term Human Milk

24 Calorie = 1 tsp level powder + 70 mL Term Human Milk

27 Calorie = 1 tsp level powder + 40 mL Term Human Milk

Term Human Milk + EnfaCare® LIPIL® Powder

Term Human Milk + EnfaCare® LIPIL® Powder *

Nutrient per 100 mL	22 Cal/fl oz	24 Cal/fl oz	27 Cal/fl oz
Energy, Cal	74	81	91
Protein, g	1.34	1.54	1.85
% of total calories †	6.6	7.1	7.6
Fat, g	4.24	4.6	5.13
% of total calories ‡‡	51.3	51	50.6
Linoleic acid, mg	438	505	606
Carbohydrate, g	8.3	9	10.1
% of total calories §	42.3	42.2	42.1
Water, g	89	88	86
Minerals			
Calcium, mg (mEq)	35 (1.8)	43 (2.2)	57 (2.9)
Phosphorus, mg (mEq)	17.1 (0.5)	22 (0.7)	29 (0.9)
Magnesium, mg	4	4.6	5.4
Iron, mg	0.15	0.29	0.49
Zinc, mg	0.21	0.3	0.44
Manganese, mcg	1.8	2.9	4.5
Copper, mcg	33	42	55
Molybdenum, mcg	-	-	-
Iodine, mcg	12	14	16
Selenium, mcg	1.7	1.9	2.2
Sodium, mg (mEq)	17.5 (0.8)	20 (0.9)	24 (1.1)
Potassium, mg (mEq)	58 (1.5)	65 (1.6)	76 (1.9)
Chloride, mg (mEq)	47 (1.3)	53 (1.5)	61 (1.7)
Vitamins			
Vitamin A, IU	255	286	333
Vitamin D, IU	7.6	13.6	22.6
Vitamin E, IU	0.69	0.98	1.43
Vitamin K, mcg	0.76	1.36	2.26
Thiamine (B ₁), mcg	35	50	72
Riboflavin (B ₂), mcg	49	63	85
Vitamin B ₆ , mcg	27	35	45
Vitamin B ₁₂ , mcg	0.07	0.09	0.12
Niacin, mcg	290	439	661
Folic acid (Folacin), mcg	6.6	8.5	11.3
Pantothenic acid, mcg	239	300	393
Biotin, mcg	0.83	1.28	1.94
Vitamin C (Ascorbic acid), mg	5.2	6.3	8.1
Choline, mg	11	13	15
Inositol, mg	17	19	22
L-Carnitine, mg	-	-	-
Taurine, mg	-	-	-
Nucleotide fortification, mg	0.3	0.61	1.08
Renal Solute Load, mOsm	11.4	13.1	15.7
Osmolality, mOsm/kg H₂O	308	332	368
Osmolarity, mOsm/L	274	292	319

* Nutrient needs of small premature infants may not be met by this fortification strategy.
Compare nutrient profile to fortification with Enfamil Human Milk Fortifier.

† Protein Source: Term human milk, nonfat milk and whey protein concentrate.

‡‡ Fat Source: High-oleic vegetable, soy, MCT, coconut, and C. cohnii¹ and M. alpina² oils.

¹ A source of docosahexaenoic acid (DHA).

² A source of arachidonic acid (ARA).

§ Carbohydrate Source: Lactose, maltodextrin.

WARNING: Powdered infant formulas are not sterile and should not be fed to premature infants or infants who might have immune problems.

Preparation:

22 Calorie = 1/4 tsp packed powder + 45 mL Human Milk

24 Calorie = 1/2 tsp packed powder + 45 mL Human Milk

27 Calorie = 1 tsp packed powder + 45 mL Human Milk

Similac® Special Care® 20 with Iron Premature Infant Formula *

Similac® Special Care® 20 Low Iron Premature Infant Formula **

20 Cal/fl oz (Ready to Feed)

Nutrient	per 100 Cal	per Liter
Energy, Cal	100	676
Volume, mL	148	1000
Protein, g	3	20.29
% of total calories †	12	12
Fat, g	5.43	36.72
% of total calories ‡‡	47	47
Linoleic acid, mg	700	4734
Carbohydrate, g	10.3	69.7
% of total calories §	41	41
Water, g	133	899
Minerals		
Calcium, mg (mEq)	180 (9)	1217 (60.7)
Phosphorus, mg (mEq)	100	676
Magnesium, mg	12	81.2
Iron, mg	1.8* (0.37)**	12.17* (2.5)**
Zinc, mg	1.5	10.14
Manganese, mcg	12	81
Copper, mcg	250	1691
Molybdenum, mcg	—	—
Iodine, mcg	6	41
Selenium, mcg	1.8	12.2
Sodium, mg (mEq)	43 (1.9)	291 (12.6)
Potassium, mg (mEq)	129 (3.3)	872 (22.3)
Chloride, mg (mEq)	81 (2.3)	548 (15.5)
Vitamins		
Vitamin A, IU	1250	8454
Vitamin D, IU	150	1014
Vitamin E, IU	4	27.1
Vitamin K, mcg	12	81
Thiamine (B ₁), mcg	250	1691
Riboflavin (B ₂), mcg	620	4193
Vitamin B ₆ , mcg	250	1691
Vitamin B ₁₂ , mcg	0.55	3.72
Niacin, mcg	5000	33815
Folic acid (Folacin), mcg	37	250
Pantothenic acid, mcg	1900	12849
Biotin, mcg	37	250
Vitamin C (Ascorbic acid), mg	37	250
Choline, mg	10	68
Inositol, mg	40	271
L-Carnitine, mg	—	—
Taurine, mg	—	—
Nucleotide fortification, mg	10.7	72.4
Renal Solute Load, mOsm	27.8	188.2
Osmolality, mOsm/kg H₂O	235	235
Osmolarity, mOsm/L	211	211

* The addition of iron to this formula conforms to the recommendation of the Committee on Nutrition of the American Academy of Pediatrics.

** Low-Iron: additional iron should be supplied from other sources.

† Protein Source: Nonfat milk and whey protein concentrate.

‡‡ Fat Source: Medium chain triglyceride, soy, and coconut oils (0.25% DHA; 0.4% ARA).

§ Carbohydrate Source: Corn syrup solids and lactose.

Precautions: Tolerance to enteral feedings should be confirmed by initially offering small volumes of hypocaloric formula followed by cautious progression to higher caloric feedings. Spitting up, excessive gastric residuals, abdominal distention, abnormal stools or stool patterns, or other signs of intestinal dysfunction have been associated with enteral feeding before the intestinal tract is ready to accommodate the regimen. At the first sign of these problems, enteral feeding should be slowed or discontinued.

Similac® Special Care® 24

Similac® Special Care® 24 with Iron Premature Infant Formula *
Similac® Special Care® 24 Low Iron Premature Infant Formula **
24 Cal/fl oz (Ready to Feed)

Nutrient	per 100 Cal	per Liter
Energy, Cal	100	812
Volume, mL	124	1000
Protein, g	3	24.34
% of total calories †	12	12
Fat, g	5.43	44.07
% of total calories ‡‡	47	47
Linoleic acid, mg	700	5681
Carbohydrate, g	10.3	83.6
% of total calories §	41	41
Water, g	109	885
Minerals		
Calcium, mg (mEq)	180 (9)	1461 (72.9)
Phosphorus, mg (mEq)	100	812
Magnesium, mg	12	97.4
Iron, mg	1.8* (0.37)**	14.61* (3)**
Zinc, mg	1.5	12.17
Manganese, mcg	12	97
Copper, mcg	250	2029
Molybdenum, mcg	—	—
Iodine, mcg	6	49
Selenium, mcg	1.8	14.6
Sodium, mg (mEq)	43 (1.9)	349 (15.2)
Potassium, mg (mEq)	129 (3.3)	1047 (26.8)
Chloride, mg (mEq)	81 (2.3)	657 (18.6)
Vitamins		
Vitamin A, IU	1250	10144
Vitamin D, IU	150	1217
Vitamin E, IU	4	32.5
Vitamin K, mcg	12	97
Thiamine (B ₁), mcg	250	2029
Riboflavin (B ₂), mcg	620	5032
Vitamin B ₆ , mcg	250	2029
Vitamin B ₁₂ , mcg	0.55	4.46
Niacin, mcg	5000	40578
Folic acid (Folacin), mcg	37	300
Pantothenic acid, mcg	1900	15419
Biotin, mcg	37	300
Vitamin C (Ascorbic acid), mg	37	300
Choline, mg	10	81
Inositol, mg	40	325
L-Carnitine, mg	—	—
Taurine, mg	—	—
Nucleotide fortification, mg	8.9	72.2
Renal Solute Load, mOsm	27.8	225.8
Osmolality, mOsm/kg H₂O	280	280
Osmolarity, mOsm/L	246	246

* The addition of iron to this formula conforms to the recommendation of the Committee on Nutrition of the American Academy of Pediatrics.

** Low-Iron: additional iron should be supplied from other sources.

† Protein Source: Nonfat milk and whey protein concentrate.

‡‡ Fat Source: Medium chain triglyceride, soy, and coconut oils (0.25% DHA; 0.4% ARA).

§ Carbohydrate Source: Corn syrup solids and lactose.

Precautions: Tolerance to enteral feedings should be confirmed by initially offering small volumes of hypocaloric formula followed by cautious progression to higher caloric feedings. Spitting up, excessive gastric residuals, abdominal distention, abnormal stools or stool patterns, or other signs of intestinal dysfunction have been associated with enteral feeding before the intestinal tract is ready to accommodate the regimen. At the first sign of these problems, enteral feeding should be slowed or discontinued.

334 Similac® Special Care® with Iron 24 + Similac® Special Care® with Iron 30

Similac® Special Care® with Iron 24 + Similac® Special Care® with Iron 30
Similac® Special Care® with Iron 24 mixed with Similac® Special Care® with
Iron 30

Nutrient per 100 mL	2:1 ratio 26 Cal/fl oz	1:1 ratio 27 Cal/fl oz	1:2 ratio 28 Cal/fl oz
Energy, Cal	88	91	95
Protein, g	2.64	2.74	2.84
Fat, g	5.17	5.56	5.94
Carbohydrate, g	8.2	8.1	8
Minerals			
Calcium, mg	158	164	170
Phosphorus, mg	88	91	95
Magnesium, mg	10.6	11	11.4
Iron, mg	1.58	1.64	1.7
Zinc, mg	1.32	1.37	1.42
Manganese, mcg	11	11	11
Copper, mcg	220	228	237
Iodine, mcg	5	5	6
Sodium, mg	38	39	41
Potassium, mg	113	118	122
Chloride, mg	71	74	77
Vitamins			
Vitamin A, IU	1099	1141	1184
Vitamin D, IU	132	137	142
Vitamin E, IU	3.5	3.7	3.8
Vitamin K, mcg	10.6	11	11.4
Thiamine (B1), mcg	220	228	237
Riboflavin (B2), mcg	545	566	587
Vitamin B6, mcg	220	228	237
Vitamin B12, mcg	0.48	0.5	0.52
Niacin, mcg	4396	4565	4734
Folic acid (Folacin), mcg	32.5	33.8	35
Pantothenic acid, mcg	1670	1735	1799
Biotin, mcg	32.5	33.8	35
Vitamin C (Ascorbic acid), mg	33	34	35
Choline, mg	9	9	9
Inositol, mg	35	37	38
Renal Solute Load, mOsm	24.5	25.4	26.3
Approx. Osmolality, mOsm/kg H₂O	295	305	310

Similac® Special Care® 24 High Protein with Iron Premature Infant Formula
24 Cal/fl oz (Ready to Feed)

Nutrient	per 100 Cal	per Liter
Energy, Cal	100	810
Volume, mL	123	1000
Protein, g	3.3	26.8
% of total calories †	13	13
Fat, g	5.43	44.1
% of total calories ‡‡	47	47
Carbohydrate, g	10	81
% of total calories §	40	40
Minerals		
Calcium, mg	180	1460
Phosphorus, mg	100	810
Magnesium, mg	12	97
Iron, mg	1.8	14.6
Zinc, mg	1.5	12.2
Manganese, mcg	12	100
Copper, mcg	250	2030
Iodine, mcg	6	50
Selenium, mcg	1.8	15
Sodium, mg (mEq)	43 (1.9)	350 (15)
Potassium, mg (mEq)	129 (3.3)	1050 (27)
Chloride, mg (mEq)	81 (2.3)	660 (19)
Vitamins		
Vitamin A, IU	1250	10140
Vitamin D, IU	150	1220
Vitamin E, IU	4	32
Vitamin K, mcg	12	97
Thiamin B ₁ , mcg	250	2030
Riboflavin B ₂ , mcg	620	5030
Vitamin B ₆ , mcg	250	2030
Vitamin B ₁₂ , mcg	0.55	4.5
Niacin, mcg	5000	40580
Folic Acid, mcg	37	300
Pantothenic Acid, mcg	1900	15420
Biotin, mcg	37	300
Vitamin C, mg	37	300
Choline, mg	10	80
Inositol, mg	40	320
Linoleic Acid, mg	700	5680
Renal Solute Load, mOsm	29.5	240
Osmolality, mOsm/kg H₂O	280	280

† Protein Source: Nonfat milk and whey protein concentrate.

‡‡ Fat Source: Medium chain triglyceride, soy and coconut oils (0.25% DHA; 0.4% ARA).

§ Carbohydrate source: Corn syrup solids and lactose.

336 Similac® Special Care® 24 High Protein + Similac® Special Care® with Iron 30

Similac® Special Care® 24 High Protein with Iron mixed with
Similac® Special Care® with Iron 30

Nutrient per 100 mL	2:1 ratio 26 Cal/fl oz	1:1 ratio 27 Cal/fl oz	1:2 ratio 28 Cal/fl oz
Energy, Cal	88	91	95
Volume, mL	100	100	100
Protein, g	2.8	2.86	2.92
Fat, g	5.17	5.56	5.94
Carbohydrate, g	8	8	7.9
Minerals			
Calcium, mg	158	164	170
Phosphorus, mg	88	91	95
Magnesium, mg	10.6	11	11.4
Iron, mg	1.58	1.64	1.7
Zinc, mg	1.32	1.37	1.42
Manganese, mcg	11	11	11
Copper, mcg	220	228	237
Iodine, mcg	5	5	6
Selenium, mcg	1.6	1.6	1.7
Sodium, mg (mEq)	38 (1.6)	39 (1.7)	41 (1.8)
Potassium, mg (mEq)	113 (2.9)	118 (3)	122 (3.1)
Chloride, mg (mEq)	71 (2)	74 (2.1)	77 (2.2)
Vitamins			
Vitamin A, IU	1099	1141	1184
Vitamin D, IU	132	137	142
Vitamin E, IU	3.5	3.7	3.8
Vitamin K, mcg	10.6	11	11.4
Thiamin B ₁ , mcg	220	228	237
Riboflavin B ₂ , mcg	545	566	587
Vitamin B ₆ , mcg	220	228	237
Vitamin B ₁₂ , mcg	0.48	0.5	0.52
Niacin, mcg	4396	4565	4734
Folic Acid, mcg	32.5	33.8	35
Pantothenic Acid, mcg	1670	1735	1799
Biotin, mcg	32.5	33.8	35
Vitamin C, mg	33	34	35
Choline, mg	9	9	9
Inositol, mg	35	37	38
Linoleic Acid, mg	615	639	663
Renal Solute Load, mOsm	25.4	26.1	26.8
Osmolality, mOsm/kg H₂O	295	305	310

NAT

UTR

Infant Formula with Iron

20 Cal/fl oz

Nutrient	per 100 Cal	per Liter
Energy, Cal	100	676
Volume, mL	148	1000
Protein, g	2.07	14
% of total calories [†]	8	8
Fat, g	5.4	36.5
% of total calories ^{††}	49	49
Linoleic acid, mg	1000	6757
Carbohydrate, g	11.2	75.7
% of total calories [§]	43	43
Water, g	133	899
Minerals		
Calcium, mg (mEq)	78 (3.9)	528 (26.4)
Phosphorus, mg (mEq)	42	284
Magnesium, mg	6	41
Iron, mg	1.8*	12*
Zinc, mg	0.75	5.07
Manganese, mcg	5	34
Copper, mcg	90	609
Molybdenum, mcg	—	—
Iodine, mcg	6	41
Selenium, mcg	1.8	12.2
Sodium, mg (mEq)	24 (1)	162 (7.1)
Potassium, mg (mEq)	105 (2.7)	710 (18.2)
Chloride, mg (mEq)	65 (1.8)	440 (12.4)
Vitamins		
Vitamin A, IU	300	2029
Vitamin D, IU	60	406
Vitamin E, IU	1.5	10.1
Vitamin K, mcg	8	54
Thiamine (B ₁), mcg	100	676
Riboflavin (B ₂), mcg	150	1014
Vitamin B ₆ , mcg	60	406
Vitamin B ₁₂ , mcg	0.25	1.69
Niacin, mcg	1050	7101
Folic acid (Folacin), mcg	15	101
Pantothenic acid, mcg	450	3043
Biotin, mcg	4.4	29.8
Vitamin C (Ascorbic acid), mg	9	61
Choline, mg	16	108
Inositol, mg	4.7	31.8
L-Carnitine, mg	1.5	10
Taurine, mg	6.5	44
Nucleotide fortification, mg	10.7	72
Renal Solute Load, mOsm	18.7	126.7
Osmolality, mOsm/kg H₂O	310	310
Osmolarity, mOsm/L	270	270

* The addition of iron to this formula conforms to the recommendation of the Committee on Nutrition of the American Academy of Pediatrics.

† Protein Source: Nonfat milk and whey protein concentrate.

†† Fat Source: High oleic safflower, soy, and coconut oils (0.15% DHA; 0.4% ARA).

§ Carbohydrate Source: Lactose and galacto-oligosaccharides (GOS)**.

** GOS (prebiotic) is approximately 5% of the total carbohydrate and provides approximately 1.3 Cal/g.

WARNING: Powdered infant formulas are not sterile and should not be fed to premature infants or infants who might have immune problems.

Similac® PM 60/40 Low Iron Infant Formula *
20 Cal/fl oz

Nutrient	per 100 Cal	per Liter
Energy, Cal	100	676
Volume, mL	148	1000
Protein, g	2.22	15.01
% of total calories †	9	9
Fat, g	5.6	37.9
% of total calories ‡	50	50
Linoleic acid, mg	1000	6763
Carbohydrate, g	10.2	69
% of total calories §	41	41
Water, g	134	899
Minerals		
Calcium, mg (mEq)	56 (2.8)	379 (18.9)
Phosphorus, mg (mEq)	28	189
Magnesium, mg	6	40.6
Iron, mg	0.7*	4.7*
Zinc, mg	0.8	5.1
Manganese, mcg	5	34
Copper, mcg	90	609
Molybdenum, mcg	—	—
Iodine, mcg	6	41
Selenium, mcg	1.8	12.2
Sodium, mg (mEq)	24 (1)	162 (7.1)
Potassium, mg (mEq)	80 (2.1)	541 (13.8)
Chloride, mg (mEq)	59 (1.7)	399 (11.3)
Vitamins		
Vitamin A, IU	300	2029
Vitamin D, IU	60	406
Vitamin E, IU	1.5	10.1
Vitamin K, mcg	8	54
Thiamine (B ₁), mcg	100	676
Riboflavin (B ₂), mcg	150	1014
Vitamin B ₆ , mcg	60	406
Vitamin B ₁₂ , mcg	0.3	1.7
Niacin, mcg	1050	7101
Folic acid (Folacin), mcg	15	101
Pantothenic acid, mcg	450	3043
Biotin, mcg	5	30.4
Vitamin C (Ascorbic acid), mg	9	61
Choline, mg	12	81
Inositol, mg	24	162
L-Carnitine, mg	—	—
Taurine, mg	—	—
Nucleotide fortification, mg	—	—
Renal Solute Load, mOsm	18.3	124.1
Osmolality, mOsm/kg H₂O	280	280
Osmolarity, mOsm/L	254	254

* Additional iron should be supplied from other sources.

† Protein Source: Whey protein concentrate and sodium caseinate.

‡ Fat Source: High oleic safflower, coconut, and soy oils.

§ Carbohydrate Source: Lactose.

Precautions: In conditions where the infant is losing abnormal quantities of one or more electrolytes, it may be necessary to supply electrolytes from sources other than the formula. It may be necessary to supply low-birth-weight infants weighing less than 1500 g at birth additional calcium, phosphorus, and sodium during periods of rapid growth.

WARNING: Powdered infant formulas are not sterile and should not be fed to premature infants or infants who might have immune problems.

Similac Sensitive™ Infant Formula with Iron (Formerly Similac® Lactose Free)
 20 Cal/fl oz

Nutrient	per 100 Cal	per Liter
Energy, Cal	100	676
Volume, mL	148	1000
Protein, g	2.14	14.47
% of total calories [†]	9	9
Fat, g	5.4	36.52
% of total calories ^{††}	49	49
Linoleic acid, mg	1000	6763
Carbohydrate, g	10.7	72.4
% of total calories [§]	43	43
Water, g	133	899
Minerals		
Calcium, mg (mEq)	84 (4.2)	568 (28.3)
Phosphorus, mg (mEq)	56	379
Magnesium, mg	6	40.6
Iron, mg	1.8*	12.2*
Zinc, mg	0.75	5.07
Manganese, mcg	5	34
Copper, mcg	90	609
Molybdenum, mcg	—	—
Iodine, mcg	9	61
Selenium, mcg	1.8	12.2
Sodium, mg (mEq)	30 (1.3)	203 (8.8)
Potassium, mg (mEq)	107 (2.7)	724 (18.5)
Chloride, mg (mEq)	65 (1.8)	440 (12.4)
Vitamins		
Vitamin A, IU	300	2029
Vitamin D, IU	60	406
Vitamin E, IU	3	20.3
Vitamin K, mcg	8	54
Thiamine (B ₁), mcg	100	676
Riboflavin (B ₂), mcg	150	1014
Vitamin B ₆ , mcg	60	406
Vitamin B ₁₂ , mcg	0.25	1.69
Niacin, mcg	1050	7101
Folic acid (Folacin), mcg	15	101
Pantothenic acid, mcg	450	3043
Biotin, mcg	4.4	29.8
Vitamin C (Ascorbic acid), mg	9	61
Choline, mg	16	108
Inositol, mg	4.3	29.1
L-Carnitine, mg	—	—
Taurine, mg	—	—
Nucleotide fortification, mg	—	—
Renal Solute Load, mOsm	19.9	134.7
Osmolality, mOsm/kg H₂O	200	200
Osmolarity, mOsm/L	180	180

* The addition of iron to this formula conforms to the recommendation of the Committee on Nutrition of the American Academy of Pediatrics.

† Protein Source: Milk protein isolate.

†† Fat Source: High oleic safflower, soy, and coconut oils (0.15% DHA, 0.40% ARA).

§ Carbohydrate Source: Corn maltodextrin and sucrose.

WARNING: Powdered infant formulas are not sterile and should not be fed to premature infants or infants who might have immune problems.

Similac Sensitive R.S.TM Infant Formula with Iron

Nutrient	per 100 Cal	per Liter
Energy, Cal	100	676
Volume, mL	148	1000
Protein, g	2.14	14.47
% of total calories [†]	9	9
Fat, g	5.4	36.5
% of total calories ^{††}	49	49
Linoleic acid, mg	1000	6760
Carbohydrate, g	10.7	72.4
% of total calories [§]	43	43
Water, g	133	899
Minerals		
Calcium, mg (mEq)	84 (4.2)	568 (28.3)
Phosphorus, mg (mEq)	56	379
Magnesium, mg	6	40.6
Iron, mg	1.8	12.2
Zinc, mg	0.75	5.1
Manganese, mcg	5	34
Copper, mcg	90	609
Molybdenum, mcg		
Iodine, mcg	9	61
Selenium, mcg	1.8	12.2
Sodium, mg (mEq)	30 (1.3)	203 (8.8)
Potassium, mg (mEq)	107 (2.7)	724 (18.5)
Chloride, mg (mEq)	65 (1.8)	440 (12.4)
Vitamins		
Vitamin A, IU	300	2029
Vitamin D, IU	60	406
Vitamin E, IU	3	20.3
Vitamin K, mcg	8	54
Thiamine (B ₁), mcg	100	676
Riboflavin (B ₂), mcg	150	1014
Vitamin B ₆ , mcg	60	406
Vitamin B ₁₂ , mcg	0.25	1.7
Niacin, mcg	1050	7101
Folic acid (Folacin), mcg	15	101
Pantothenic acid, mcg	450	3043
Biotin, mcg	4.4	29.8
Vitamin C (Ascorbic acid), mg	9	61
Choline, mg	16	108
Inositol, mg	4.3	29.1
L-Carnitine, mg		
Taurine, mg		
Nucleotide fortification, mg		
Renal Solute Load, mOsm	19.9	134.7
Osmolality, mOsm/kg H₂O	200	200
Osmolarity, mOsm/L	180	180

[†] Protein Source: Milk protein isolate^{††} Fat Source: High oleic safflower, soy, and coconut oils (0.15% DHA; 0.4% ARA)[§] Carbohydrate Source: Corn syrup, rice starch, sugar

Infant Formula made with Organic Milk

Nutrient	per 100 Cal	per Liter
Energy, Cal	100	676
Volume, mL	148	1000
Protein, g	2.07	14
% of total calories ⁺	8	8
Fat, g	5.49	37.1
% of total calories ⁺⁺	49	49
Linoleic acid, mg	860	5816
Carbohydrate, g	10.56	71.4
% of total calories [§]	42	42
Water, g	133	899
Minerals		
Calcium, mg (mEq)	78 (3.9)	528 (26.3)
Phosphorus, mg (mEq)	42	284
Magnesium, mg	6	41
Iron, mg	1.8	12.2
Zinc, mg	0.75	5.07
Manganese, mcg	5	34
Copper, mcg	90	609
Molybdenum, mcg	—	—
Iodine, mcg	6	41
Selenium, mcg	1.8	12.2
Sodium, mg (mEq)	24 (1)	162 (7.1)
Potassium, mg (mEq)	105 (2.7)	710 (18.2)
Chloride, mg (mEq)	65 (1.8)	439 (12.4)
Vitamins		
Vitamin A, IU	300	2029
Vitamin D, IU	60	406
Vitamin E, IU	1.5	10.1
Vitamin K, mcg	8	54
Thiamine (B ₁), mcg	100	676
Riboflavin (B ₂), mcg	150	1014
Vitamin B ₆ , mcg	60	406
Vitamin B ₁₂ , mcg	0.25	1.69
Niacin, mcg	1050	7101
Folic acid (Folacin), mcg	15	101
Pantothenic acid, mcg	450	3043
Biotin, mcg	4.4	29.8
Vitamin C (Ascorbic acid), mg	9	61
Choline, mg	16	108
Inositol, mg	4.7	31.8
L-Carnitine, mg	—	—
Taurine, mg	—	—
Nucleotide fortification, mg	*	*
Renal Solute Load, mOsm	18.8	126.8
Osmolality, mOsm/kg H₂O	225	225
Osmolarity, mOsm/L		

* The addition of iron to this formula conforms to the recommendation of the Committee on Nutrition of the American Academy of Pediatrics.

[†] Protein Source: Organic nonfat dry milk.

⁺⁺ Fat Source: Organic high oleic sunflower, organic soy, and organic coconut oils (0.15% DHA; 0.4% ARA).

[§] Carbohydrate Source: Organic corn maltodextrin, organic lactose and organic sugar from evaporated cane juice.

⁺ Contains C. Cohnii oil, a source of docosahexaenoic acid (DHA), and M. Alpina oil, a source of arachidonic acid (ARA).

Nutritionally Complete Amino Acid-Based Medical Food and Infant Formula with Iron *

20 Cal/fl oz

Nutrient	per 100 Cal	per Liter
Energy, Cal	100	676
Volume, mL	148	1000
Protein, g	3.1	20.6
% of total calories [†]	15	15
Fat, g	4.8	32.7
% of total calories ^{††}	42	42
Linoleic acid, mg	840	5680
Carbohydrate, g	10.7	72.4
% of total calories [§]	43	43
Water, g	132.5	895
Minerals		
Calcium, mg (mEq)	116 (5.8)	784 (39.2)
Phosphorus, mg (mEq)	84.2	569
Magnesium, mg	8.4	57
Iron, mg	1.5*	10.1*
Zinc, mg	0.8	5.4
Manganese, mcg	84	568
Copper, mcg	105	710
Molybdenum, mcg	2.5	16.9
Iodine, mcg	8.4	57
Selenium, mcg	2.3	15.5
Sodium, mg (mEq)	45 (2)	304 (13.2)
Potassium, mg (mEq)	150 (3.9)	1014 (26)
Chloride, mg (mEq)	60 (1.7)	406 (11.4)
Vitamins		
Vitamin A, IU	273	1845
Vitamin D, IU	42	284
Vitamin E, IU	2.1	14.2
Vitamin K, mcg	6	40.6
Thiamine (B ₁), mcg	210	1420
Riboflavin (B ₂), mcg	105	710
Vitamin B ₆ , mcg	84.2	569
Vitamin B ₁₂ , mcg	0.4	2.7
Niacin, mcg	1680	11357
Folic acid (Folacin), mcg	29.5	199
Pantothenic acid, mcg	421	2846
Biotin, mcg	4.2	28.4
Vitamin C (Ascorbic acid), mg	9	61
Choline, mg	9.5	64
Inositol, mg	5.1	34
L-Carnitine, mg	5.5	37
Taurine, mg	11.4	77
Nucleotide fortification, mg	—	—
Renal Solute Load, mOsm	28	187
Osmolality, mOsm/kg H₂O	350	350
Osmolarity, mOsm/L	309	309

* The addition of iron to this formula conforms to the recommendation of the Committee on Nutrition of the American Academy of Pediatrics.

† Protein Source: Free L-amino acids.

†† Fat Source: High oleic safflower, medium chain triglyceride, and soy oils.

§ Carbohydrate Source: Corn syrup solids.

WARNING: Powdered infant formulas are not sterile and should not be fed to premature infants or infants who might have immune problems.

Dilution Table - EleCare® Powder

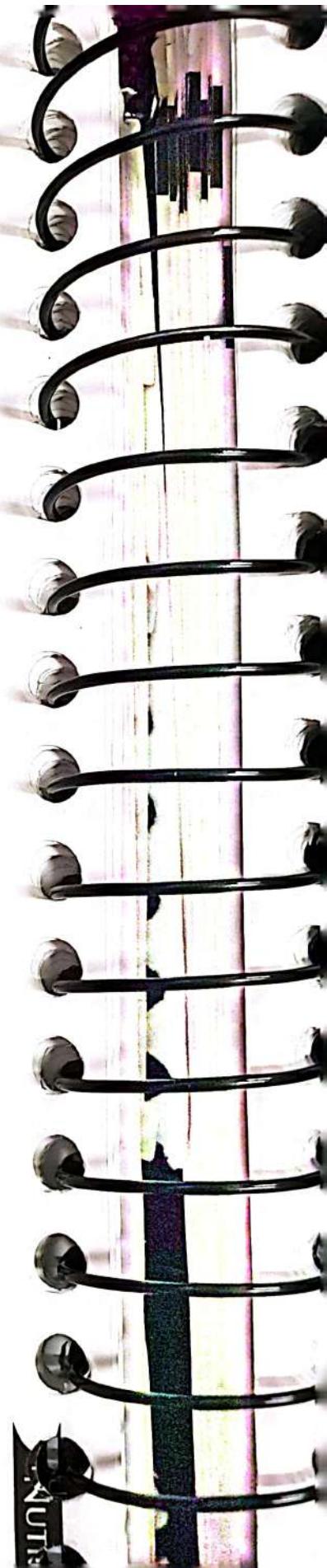
343

Dilution Table - EleCare® Powder

Caloric Density (Cal/fl oz)	Water (fl oz)	Level Unpacked Scoopful	Approximate Yield (fl oz)
20*	2	1	2
22	3.5	2	4
24	8	5	9
27	7	5	8
30**	5	4	6

* Standard infant mixture.

** Standard pediatric mixture.



Similac® Isomil® Advance® Soy Formula with Iron *

20 Cal/fl oz

Nutrient	per 100 Cal	per Liter
Energy, Cal	100	676
Volume, mL	148	1000
Protein, g	2.45	16.57
% of total calories †	10	10
Fat, g	5.46	36.93
% of total calories ‡	49	49
Linoleic acid, mg	1000	6763
Carbohydrate, g	10.3	69.7
% of total calories §	41	41
Water, g	133	899
Minerals		
Calcium, mg (mEq)	105 (5.2)	710 (35.4)
Phosphorus, mg (mEq)	75	507
Magnesium, mg	7.5	50.7
Iron, mg	1.8*	12.2*
Zinc, mg	0.75	5.07
Manganese, mcg	25	169
Copper, mcg	75	507
Molybdenum, mcg	—	—
Iodine, mcg	15	101
Selenium, mcg	1.8	12.2
Sodium, mg (mEq)	44 (1.9)	298 (12.9)
Potassium, mg (mEq)	108 (2.8)	730 (18.7)
Chloride, mg (mEq)	62 (1.8)	419 (11.8)
Vitamins		
Vitamin A, IU	300	2029
Vitamin D, IU	60	406
Vitamin E, IU	1.5	10.1
Vitamin K, mcg	11	74
Thiamine (B ₁), mcg	60	406
Riboflavin (B ₂), mcg	90	609
Vitamin B ₆ , mcg	60	406
Vitamin B ₁₂ , mcg	0.45	3.04
Niacin, mcg	1350	9130
Folic acid (Folacin), mcg	15	101
Pantothenic acid, mcg	750	5072
Biotin, mcg	4.5	30.4
Vitamin C (Ascorbic acid), mg	9	61
Choline, mg	12	81
Inositol, mg	5	33.8
L-Carnitine, mg	2.1	14
Taurine, mg	8	54
Nucleotide fortification, mg	—	—
Renal Solute Load, mOsm	22.8	154.5
Osmolality, mOsm/kg H₂O	200	200
Osmolarity, mOsm/L	180	180

* The addition of iron to this formula conforms to the recommendation of the Committee on Nutrition of the American Academy of Pediatrics.

† Protein Source: Soy protein isolate and L-methionine.

‡ Fat Source: High oleic safflower, soy, and coconut oils (0.15% DHA; 0.4% ARA).

§ Carbohydrate Source: Corn syrup and sucrose.

Precautions: This formula is not recommended for preterm infants who weigh less than 1800 g.

WARNING: Powdered infant formulas are not sterile and should not be fed to premature infants or infants who might have immune problems.

**Similac® Alimentum® Hypoallergenic Formula with Iron * Ready-to-Feed and Powder
20 Cal/fl oz**

Nutrient	per 100 Cal	per Liter
Energy, Cal	100	676
Volume, mL	148	1000
Protein, g	2.75	18.6
% of total calories †	11	11
Fat, g	5.54	37.47
% of total calories ‡‡	48	48
Linoleic acid, mg	1900	12850
Carbohydrate, g	10.2	69
% of total calories §	41	41
Water, g	133	899
Minerals		
Calcium, mg (mEq)	105 (5.2)	710 (35.4)
Phosphorus, mg (mEq)	75	507
Magnesium, mg	7.5	50.7
Iron, mg	1.8*	12.17*
Zinc, mg	0.75	5.07
Manganese, mcg	8	54
Copper, mcg	75	507
Molybdenum, mcg	—	—
Iodine, mcg	15	101
Selenium, mcg	1.8	12.2
Sodium, mg (mEq)	44 (1.9)	298 (12.9)
Potassium, mg (mEq)	118 (3)	798 (20.5)
Chloride, mg (mEq)	80 (2.3)	541 (15.2)
Vitamins		
Vitamin A, IU	300	2029
Vitamin D, IU	45	304
Vitamin E, IU	3	20.3
Vitamin K, mcg	15	101
Thiamine (B ₁), mcg	60	406
Riboflavin (B ₂), mcg	90	609
Vitamin B ₆ , mcg	60	406
Vitamin B ₁₂ , mcg	0.45	3.04
Niacin, mcg	1350	9130
Folic acid (Folacin), mcg	15	101
Pantothenic acid, mcg	750	5072
Biotin, mcg	4.5	30.4
Vitamin C (Ascorbic acid), mg	9	61
Choline, mg	12	81
Inositol, mg	5	33.8
L-Carnitine, mg	—	—
Taurine, mg	—	—
Nucleotide fortification, mg	—	—
Renal Solute Load, mOsm	25.3	171.3
Osmolality, mOsm/kg H₂O	370	370
Osmolarity, mOsm/L	333	333

* The addition of iron to this formula conforms to the recommendation of the Committee on Nutrition of the American Academy of Pediatrics.

† Protein Source: Casein hydrolysate, L-cystine, L-tyrosine, and L-tryptophan.

‡‡ Fat Source: Safflower oil, medium chain triglyceride, and soy oil (0.15% DHA; 0.4% ARA).

§ Carbohydrate Source: Sucrose and modified tapioca starch.

WARNING: Powdered infant formulas are not sterile and should not be fed to premature infants or infants who might have immune problems.

Similac® NeoSure® Infant Formula with Iron *

22 Cal/fl oz

Nutrient	per 100 Cal	per Liter
Energy, Cal	100	744
Volume, mL	134	1000
Protein, g	2.8	20.83
% of total calories †	11	11
Fat, g	5.5	40.92
% of total calories ‡	49	49
Linoleic acid, mg	750	5579
Carbohydrate, g	10.1	75.1
% of total calories §	40	40
Water, g	120	893
Minerals		
Calcium, mg (mEq)	105 (5.2)	781 (39)
Phosphorus, mg (mEq)	62	461
Magnesium, mg	9	67
Iron, mg	1.8*	13.4*
Zinc, mg	1.2	8.9
Manganese, mcg	10	74
Copper, mcg	120	893
Molybdenum, mcg	—	—
Iodine, mcg	15	112
Selenium, mcg	2.3	17.1
Sodium, mg (mEq)	33 (1.4)	245 (10.7)
Potassium, mg (mEq)	142 (3.6)	1056 (27)
Chloride, mg (mEq)	75 (2.1)	558 (15.7)
Vitamins		
Vitamin A, IU	460	3422
Vitamin D, IU	70	521
Vitamin E, IU	3.6	26.8
Vitamin K, mcg	11	81.8
Thiamine (B ₁), mcg	220	1637
Riboflavin (B ₂), mcg	150	1116
Vitamin B ₆ , mcg	100	744
Vitamin B ₁₂ , mcg	0.4	2.98
Niacin, mcg	1950	14506
Folic acid (Folacin), mcg	25	186
Pantothenic acid, mcg	800	5951
Biotin, mcg	9	67
Vitamin C (Ascorbic acid), mg	15	112
Choline, mg	16	119
Inositol, mg	35	260
L-Carnitine, mg	—	—
Taurine, mg	—	—
Nucleotide fortification, mg	9.7	72.2
Renal Solute Load, mOsm	25.2	187.4
Osmolality, mOsm/kg H₂O	250	250
Osmolarity, mOsm/L	223	223

* The addition of iron to this formula conforms to the recommendation of the Committee on Nutrition of the American Academy of Pediatrics.

† Protein Source: Nonfat milk and whey protein concentrate.

‡ Fat Source: Soy oil, coconut oil, and medium chain triglycerides (0.15% DHA; 0.4% ARA).

§ Carbohydrate Source: Corn syrup solids and lactose.

WARNING: Powdered infant formulas are not sterile and should not be fed to premature infants or infants who might have immune problems.

PediaSure® Complete, Balanced Nutrition®
30 Cal/fl oz (Ready to Use)

Nutrient	per 100 Cal	per Liter
Energy, Cal	100	1000
Volume, mL	100	1000
Protein, g	3	30
% of total calories [†]	12	12
Fat, g	3.8	38
% of total calories ⁺⁺	35	35
Linoleic acid, mg	—	—
Carbohydrate, g	13.1	131
% of total calories [§]	53	53
Water, g	84.5	845
Minerals		
Calcium, mg (mEq)	97.2 (4.9)	972 (49)
Phosphorus, mg (mEq)	84.5	845
Magnesium, mg	19.9	199
Iron, mg	1.4	14
Zinc, mg	0.59	5.9
Manganese, mcg	150	1500
Copper, mcg	100	1000
Molybdenum, mcg	3.6	36
Iodine, mcg	9.7	97
Selenium, mcg	3.2	32
Sodium, mg (mEq)	38 (1.7)	380 (17)
Potassium, mg (mEq)	131 (3.4)	1310 (34)
Chloride, mg (mEq)	101.4 (2.9)	1014 (29)
Vitamins		
Vitamin A, IU	160.6	1606
Vitamin D, IU	51	507
Vitamin E, IU	2.3	23
Vitamin K, mcg	5.9	59
Thiamine (B ₁), mcg	270	2700
Riboflavin (B ₂), mcg	210	2100
Vitamin B ₆ , mcg	260	2600
Vitamin B ₁₂ , mcg	0.59	5.9
Niacin, mcg	1000	10000
Folic acid (Folacin), mcg	30	300
Pantothenic acid, mcg	1000	10000
Biotin, mcg	19	190
Vitamin C (Ascorbic acid), mg	10.1	101
Choline, mg	30	300
Inositol, mg	8	80
L-Carnitine, mg	1.7	17
Taurine, mg	7.2	72
Nucleotide fortification, mg	—	—
Renal Solute Load, mOsm	27.5	275
Osmolality, mOsm/kg H₂O*	480	480
Osmolarity, mOsm/L	364	364

[†] Protein Source: Milk protein concentrate, whey Protein Concentrate, and soy protein isolate

⁺⁺ Fat Source: High Oleic Safflower, Soy and Medium-Chain Triglyceride Oils

[§] Carbohydrate Source: Sucrose and Corn Maltodextrin

* Vanilla, Strawberry, Banana Cream; Chocolate = 540 mOsm/kg water; Orange Cream = 560 mOsm/kg water.

Chocolate Pediasure does not contain whey protein concentrate.

Precaution: Not for children with galactosemia.

PediaSure® Complete, Balanced Nutrition®
 30 Cal/fl oz (Ready to Use)

Nutrient	per 100 Cal	per Liter
Energy, Cal	100	1000
Volume, mL	100	1000
Protein, g	3	30
% of total calories [†]	12	12
Fat, g	3.8	38
% of total calories ^{††}	35	35
Linoleic acid, mg	—	—
Carbohydrate, g	13.1	131
% of total calories [§]	53	53
Water, g	84.5	845
Minerals		
Calcium, mg (mEq)	97.2 (4.9)	972 (49)
Phosphorus, mg (mEq)	84.5	845
Magnesium, mg	19.9	199
Iron, mg	1.4	14
Zinc, mg	0.59	5.9
Manganese, mcg	150	1500
Copper, mcg	100	1000
Molybdenum, mcg	3.6	36
Iodine, mcg	9.7	97
Selenium, mcg	3.2	32
Sodium, mg (mEq)	38 (1.7)	380 (17)
Potassium, mg (mEq)	131 (3.4)	1310 (34)
Chloride, mg (mEq)	101.4 (2.9)	1014 (29)
Vitamins		
Vitamin A, IU	160.6	1606
Vitamin D, IU	51	507
Vitamin E, IU	2.3	23
Vitamin K, mcg	5.9	59
Thiamine (B ₁), mcg	270	2700
Riboflavin (B ₂), mcg	210	2100
Vitamin B ₆ , mcg	260	2600
Vitamin B ₁₂ , mcg	0.59	5.9
Niacin, mcg	1000	10000
Folic acid (Folacin), mcg	30	300
Pantothenic acid, mcg	1000	10000
Biotin, mcg	19	190
Vitamin C (Ascorbic acid), mg	10.1	101
Choline, mg	30	300
Inositol, mg	8	80
L-Carnitine, mg	1.7	17
Taurine, mg	7.2	72
Nucleotide fortification, mg	—	—
Renal Solute Load, mOsm	27.5	275
Osmolality, mOsm/kg H₂O*	480	480
Osmolarity, mOsm/L	364	364

[†] Protein Source: Milk protein concentrate, whey Protein Concentrate, and soy protein isolate
^{††} Fat Source: High Oleic Safflower, Soy and Medium-Chain Triglyceride Oils

[§] Carbohydrate Source: Sucrose and Corn Maltodextrin

* Vanilla, Strawberry, Banana Cream; Chocolate = 540 mOsm/kg water; Orange Cream = 560 mOsm/kg water.

Chocolate PediaSure does not contain whey protein concentrate.

Precaution: Not for children with galactosemia.

PediaSure® Enteral
Complete, Balanced Nutrition®
30 Cal/fl oz (Ready to Use)

Nutrient	per 100 Cal	per Liter
Energy, Cal	100	1000
Volume, mL	100	1000
Protein, g	3	30
% of total calories [†]	12	12
Fat, g	4	40
% of total calories ^{††}	35	35
Linoleic acid, mg	—	—
Carbohydrate, g	13.3	133
% of total calories [§]	53	53
Water, g	85.4	854
Minerals		
Calcium, mg (mEq)	97.2 (4.9)	972 (49)
Phosphorus, mg (mEq)	84.5	845
Magnesium, mg	19.9	199
Iron, mg	1.4	14
Zinc, mg	0.59	5.9
Manganese, mcg	150	1500
Copper, mcg	100	1000
Molybdenum, mcg	3.6	36
Iodine, mcg	9.7	97
Selenium, mcg	3.2	32
Sodium, mg (mEq)	38 (1.7)	380 (17)
Potassium, mg (mEq)	131 (3.4)	1310 (34)
Chloride, mg (mEq)	101.4 (2.9)	1014 (29)
Vitamins		
Vitamin A, IU	160.6	1606
Vitamin D, IU	50.7	507
Vitamin E, IU	2.3	23
Vitamin K, mcg	5.9	59
Thiamine (B ₁), mcg	270	2700
Riboflavin (B ₂), mcg	210	2100
Vitamin B ₆ , mcg	260	2600
Vitamin B ₁₂ , mcg	0.59	5.9
Niacin, mcg	1000	10000
Folic acid (Folacin), mcg	30	300
Pantothenic acid, mcg	1000	10000
Biotin, mcg	19	190
Vitamin C (Ascorbic acid), mg	10.1	101
Choline, mg	30	300
Inositol, mg	8	80
L-Carnitine, mg	1.7	17
Taurine, mg	7.2	72
Nucleotide fortification, mg	—	—
Renal Solute Load, mOsm	27.7	277
Osmolality, mOsm/kg H₂O	335	335
Osmolarity, mOsm/L	—	—

[†] Protein Source: Milk protein concentrate.

^{††} Fat Source: High Oleic Safflower, Soy and Medium-Chain Triglyceride Oils.

[§] Carbohydrate Source: Sucrose and Corn Maltodextrin.
Kosher. Gluten-free. Lactose-free.

Precaution: Not for children with galactosemia

Enfamil® EnfaCare® LIPIL® powder

Enfamil® EnfaCare® LIPIL® ready to use

22 Cal/fl oz (see dilution tables for mixing instructions)

Nutrient	per 100 Cal	per Liter
Energy, Cal	100	746
Volume, mL	134	1000
Protein, g	2.8	20.8
% of total calories ⁺	11	11
Fat, g	5.3	39.5
% of total calories ⁺⁺	47	47
Linoleic acid, mg	950	7087
Carbohydrate, g	10.4	77.6
% of total calories [§]	42	42
Water, g	120	895
Minerals		
Calcium, mg (mEq)	120 (6)	895 (44.8)
Phosphorus, mg (mEq)	66 (2.1)	492 (15.7)
Magnesium, mg	8	60
Iron, mg	1.8*	13.4*
Zinc, mg	1.25	9.3
Manganese, mcg	15	112
Copper, mcg	120	895
Molybdenum, mcg	—	—
Iodine, mcg	21	156
Selenium, mcg	2.8	20.8
Sodium, mg (mEq)	35 (1.5)	261 (11.3)
Potassium, mg (mEq)	105 (2.7)	783 (20)
Chloride, mg (mEq)	78 (2.2)	581 (16.4)
Vitamins		
Vitamin A, IU	450	3357
Vitamin D, IU	80 (P) 70 (L)	597 (P) 522 (L)
Vitamin E, IU	4	30
Vitamin K, mcg	8	60
Thiamine (B ₁), mcg	200	1492
Riboflavin (B ₂), mcg	200	1492
Vitamin B ₆ , mcg	100	746
Vitamin B ₁₂ , mcg	0.3	2.2
Niacin, mcg	2000	14920
Folic acid (Folacin), mcg	26	194
Pantothenic acid, mcg	850	6341
Biotin, mcg	6	45
Vitamin C (Ascorbic acid), mg	16	119
Choline, mg	24	179
Inositol, mg	30	224
L-Carnitine, mg	2	14.9
Taurine, mg	6	45
Nucleotide fortification, mg	4	31
Renal Solute Load, mOsm	24	182.5
Osmolality, mOsm/kg H₂O	250 (L) 300 (P)	250 (L) 300 (P)
Osmolarity, mOsm/L	220 (L) 270 (P)	220 (L) 270 (P)

* The addition of iron to this formula conforms to the recommendation of the Committee on Nutrition of the American Academy of Pediatrics.

† Protein Source: Whey protein concentrate 60%, nonfat milk 40%.

++ Fat Source: High oleic vegetable oil 34%, soy oil 29%, MCT oil 20%, coconut oil 14%, and single-cell oil blend rich in DHA and ARA.

§ Carbohydrate Source: Powder—lactose 70%, corn syrup solids 30%. Liquid—maltodextrin 60%, lactose 40%.

WARNING: Powdered infant formulas are not sterile and should not be fed to premature infants or infants who might have immune problems.

Enfamil® EnfaCare® LIPIL® + Enfamil® LIPIL® Concentrate 24

Enfamil® EnfaCare® LIPIL® + Enfamil® LIPIL® Concentrate 24
24 Cal/fl oz (see footnotes for preparation)

Nutrient	per 100 Cal	per Liter
Energy, Cal	100	813
Volume, mL	123	1000
Protein, g	2.7	22
% of total calories [†]	10.8	10.8
Fat, g	5.3	43
% of total calories ^{††}	47.2	47.2
Linoleic acid, mg	932	7611
Carbohydrate, g	10.5	85
% of total calories [§]	42	42
Water, g	108	883
Minerals		
Calcium, mg (mEq)	116 (5.9)	940 (47)
Phosphorus, mg (mEq)	64 (2.1)	520 (17)
Magnesium, mg	8	65
Iron, mg	1.8	14.6
Zinc, mg	1.23	10
Manganese, mcg	15	122
Copper, mcg	116	940
Molybdenum, mcg	—	—
Iodine, mcg	20	162
Selenium, mcg	2.8	23
Sodium, mg (mEq)	34 (1.5)	280 (12.2)
Potassium, mg (mEq)	105 (2.7)	850 (21.8)
Chloride, mg (mEq)	77 (2.2)	620 (17.5)
Vitamins		
Vitamin A, IU	440	3600
Vitamin D, IU	78	630
Vitamin E, IU	3.8	31
Vitamin K, mcg	8	65
Thiamine (B ₁), mcg	188	1530
Riboflavin (B ₂), mcg	194	1570
Vitamin B ₆ , mcg	96	780
Vitamin B ₁₂ , mcg	0.3	2.4
Niacin, mcg	1900	15400
Folic acid (Folacin), mcg	25	200
Pantothenic acid, mcg	820	6700
Biotin, mcg	5.7	46
Vitamin C (Ascorbic acid), mg	15.6	127
Choline, mg	24	195
Inositol, mg	28	230
L-Carnitine, mg	2	16.2
Taurine, mg	6	49
Nucleotide fortification, mg	4.2	34
Renal Solute Load, mOsm	23.9	193.9
Osmolality, mOsm/kg H₂O	255	255
Osmolarity, mOsm/L	226	226

[†] Protein Source: Whey protein concentrate 60%, nonfat milk 40%.

^{††} Fat Source: High oleic vegetable oil 34%, soy oil 29%, MCT oil 20%, coconut oil 14.5%, and single-cell oil blend rich in DHA and ARA.

[§] Carbohydrate Source: Maltodextrin 60%, lactose 40%.

Preparation: Enfamil EnfaCare Lipil 3 fl oz Nursette + 12 mL Enfamil Lipil liquid concentrate (provides volume based dilution 90% Enfamil EnfaCare Lipil + 10% Enfamil Lipil liquid concentrate).

Enfamil® EnfaCare® LIPIL® + Enfamil® LIPIL® Concentrate 27

Enfamil® EnfaCare® LIPIL® + Enfamil® LIPIL® Concentrate 27
27 Cal/fl oz (see footnotes for preparation)

Nutrient	per 100 Cal	per Liter
Energy, Cal	100	878
Volume, mL	114	1000
Protein, g	2.6	24
% of total calories [†]	10.4	10.4
Fat, g	5.3	48
% of total calories ^{††}	47.2	47.2
Linoleic acid, mg	920	8071
Carbohydrate, g	10.6	97
% of total calories [§]	42.4	42.4
Water, g	100	875
Minerals		
Calcium, mg (mEq)	107 (5.4)	963 (48)
Phosphorus, mg (mEq)	59 (1.9)	531 (17.1)
Magnesium, mg	8	73
Iron, mg	1.8	16.4
Zinc, mg	1.18	10.8
Manganese, mcg	15	137
Copper, mcg	107	963
Molybdenum, mcg	—	—
Iodine, mcg	17.7	152
Selenium, mcg	2.8	26
Sodium, mg (mEq)	33 (1.4)	297 (12.9)
Potassium, mg (mEq)	106 (2.7)	931 (23.8)
Chloride, mg (mEq)	74 (2.1)	666 (18.8)
Vitamins		
Vitamin A, IU	410	3700
Vitamin D, IU	74	680
Vitamin E, IU	3.4	31
Vitamin K, mcg	8	73
Thiamine (B ₁), mcg	164	1500
Riboflavin (B ₂), mcg	182	1660
Vitamin B ₆ , mcg	88	800
Vitamin B ₁₂ , mcg	0.3	2.7
Niacin, mcg	1700	15500
Folic acid (Folacin), mcg	23	210
Pantothenic acid, mcg	750	6800
Biotin, mcg	5.1	47
Vitamin C (Ascorbic acid), mg	14.8	135
Choline, mg	24	220
Inositol, mg	23	210
L-Carnitine, mg	2	18.3
Taurine, mg	6	55
Nucleotide fortification, mg	4.2	38
Renal Solute Load, mOsm	22.7	199.2
Osmolality, mOsm/kg H₂O	260	260
Osmolarity, mOsm/L	228	228

[†] Protein Source: Whey protein concentrate 60%, nonfat milk 40%.

^{††} Fat Source: High oleic vegetable oil 34%, soy oil 29%, MCT oil 20%, coconut oil 14.5%, and single-cell oil blend rich in DHA and ARA.

[§] Carbohydrate Source: Maltodextrin 60%, lactose 40%.

Preparation: Enfamil EnfaCare Lipil 3 fl oz Nursette + 35 mL Enfamil Lipil liquid concentrate (provides volume based dilution 70% Enfamil EnfaCare Lipil + 30% Enfamil Lipil liquid concentrate).



Enfamil® Premature LIPIL® 24 + Enfamil® LIPIL® Concentrate 30

Enfamil® Premature LIPIL® 24 + Enfamil® LIPIL® Concentrate 30

30 Cal/fl oz (see footnotes for preparation)

Nutrient	per 100 Cal	per Liter
Energy, Cal	100	1030
Volume, mL	97	1000
Protein, g	2.6	26
% of total calories [†]	10.4	10.4
Fat, g	5.2	53
% of total calories ⁺⁺	46.8	47
Linoleic acid, mg	836	8614
Carbohydrate, g	11	112
% of total calories [§]	42.8	43
Water, g	122	1250
Minerals		
Calcium, mg (mEq)	130 (6.4)	1320 (66)
Phosphorus, mg (mEq)	67 (2.2)	680 (22.3)
Magnesium, mg	8.6	87
Iron, mg	1.8	18.3
Zinc, mg	1.3	13.2
Manganese, mcg	9.8	99
Copper, mcg	102	1030
Molybdenum, mcg	0.24	2.4
Iodine, mcg	19	193
Selenium, mcg	2.8	28
Sodium, mg (mEq)	46 (2)	470 (20.4)
Potassium, mg (mEq)	102 (2.6)	1030 (26.4)
Chloride, mg (mEq)	79 (2.2)	814 (22.9)
Vitamins		
Vitamin A, IU	870	8800
Vitamin D, IU	168	1700
Vitamin E, IU	4.6	47
Vitamin K, mcg	8	81
Thiamine (B ₁), mcg	152	1540
Riboflavin (B ₂), mcg	240	2400
Vitamin B ₆ , mcg	114	1160
Vitamin B ₁₂ , mcg	0.27	2.7
Niacin, mcg	2800	28000
Folic acid (Folacin), mcg	30	300
Pantothenic acid, mcg	920	9300
Biotin, mcg	3.6	37
Vitamin C (Ascorbic acid), mg	16.8	170
Choline, mg	22	220
Inositol, mg	29	290
L-Carnitine, mg	2.2	22
Taurine, mg	6	61
Nucleotide fortification, mg	4.2	43
Renal Solute Load, mOsm	23	235.8
Osmolality, mOsm/kg H₂O	300	300
Osmolarity, mOsm/L	255	255

[†] Protein Source: Whey protein concentrate 60%, nonfat milk 40%

⁺⁺ Fat Source: High oleic vegetable oil 34%, soy oil 29%, MCT oil 20%, coconut oil 14.5%, and single-cell oil blend rich in DHA and ARA.

[§] Carbohydrate Source: Maltodextrin 60%, lactose 40%.

Preparation: Enfamil Premature Lipil 24 with iron 3 fl oz Nursette + 60 mL Enfamil Lipil liquid concentrate (provides volume based dilution 60% Enfamil Premature Lipil + 40% Enfamil Lipil liquid concentrate).

Enfamil® Premature LIPIL® 20 with Iron *
Enfamil® Premature LIPIL® 20 low Iron **
 20 Cal/fl oz (ready to use)

Nutrient	per 100 Cal	per Liter
Energy, Cal	100	676
Volume, mL	148	1000
Protein, g	3	20.3
% of total calories [†]	12	12
Fat, g	5.1	34.5
% of total calories ^{††}	44	44
Linoleic acid, mg	810	5476
Carbohydrate, g	11	74.4
% of total calories [§]	44	44
Water, g	133	899
Minerals		
Calcium, mg (mEq)	165 (8.2)	1115 (55.8)
Phosphorus, mg (mEq)	83	561
Magnesium, mg	9	61
Iron, mg	1.8* (0.5)**	12.2* (3.4)**
Zinc, mg	1.5	10.1
Manganese, mcg	6.3	43
Copper, mcg	120	811
Molybdenum, mcg	0.4	2.7
Iodine, mcg	25	169
Selenium, mcg	2.8	18.9
Sodium, mg (mEq)	58 (2.5)	392 (16.9)
Potassium, mg (mEq)	98 (2.5)	662 (17)
Chloride, mg (mEq)	90 (2.5)	608 (17.1)
Vitamins		
Vitamin A, IU	1250	8450
Vitamin D, IU	240	1622
Vitamin E, IU	6.3	43
Vitamin K, mcg	8	54
Thiamine (B ₁), mcg	200	1352
Riboflavin (B ₂), mcg	300	2028
Vitamin B ₆ , mcg	150	1014
Vitamin B ₁₂ , mcg	0.25	1.69
Niacin, mcg	4000	27040
Folic acid (Folacin), mcg	40	270
Pantothenic acid, mcg	1200	8112
Biotin, mcg	4	27
Vitamin C (Ascorbic acid), mg	20	135
Choline, mg	20	135
Inositol, mg	44	297
L-Carnitine, mg	2.4	16.2
Taurine, mg	6	40.6
Nucleotide fortification, mg	—	—
Renal Solute Load, mOsm	27	182.5
Osmolality, mOsm/kg H₂O	240	240
Osmolarity, mOsm/L	220	220

* The addition of iron to this formula conforms to the recommendation of the Committee on Nutrition of the American Academy of Pediatrics.

** Supplemental vitamin E and iron (when using Low Iron) should also be considered.

† Protein Source: Whey protein concentrate and nonfat milk.

†† Fat Source: Medium-chain triglycerides, soy oil, high oleic vegetable oil, and single-cell oil blend rich in DHA and ARA.

§ Carbohydrate Source: Corn syrup solids and lactose.

Enfamil® Premature LIPIL® 24 with Iron*

Enfamil® Premature LIPIL® 24 low Iron**

24 Cal/fl oz (ready to use)

Nutrient	per 100 Cal	per Liter
Energy, Cal	100	813
Volume, mL	123	1000
Protein, g	3	24.4
% of total calories [†]	12	12
Fat, g	5.1	41.5
% of total calories ^{††}	44	44
Linoleic acid, mg	810	6585
Carbohydrate, g	11	89.4
% of total calories [§]	44	44
Water, g	108	878
Minerals		
Calcium, mg (mEq)	165 (8.2)	1341 (67)
Phosphorus, mg (mEq)	83	674
Magnesium, mg	9	73
Iron, mg	1.8* (0.5)**	14.6* (4.1)**
Zinc, mg	1.5	12.2
Manganese, mcg	6.3	51
Copper, mcg	120	976
Molybdenum, mcg	0.4	3.2
Iodine, mcg	25	203
Selenium, mcg	2.8	22.8
Sodium, mg (mEq)	58 (2.5)	471 (20.5)
Potassium, mg (mEq)	98 (2.5)	797 (20.4)
Chloride, mg (mEq)	90 (2.5)	732 (20.6)
Vitamins		
Vitamin A, IU	1250	10163
Vitamin D, IU	240	1951
Vitamin E, IU	6.3	51
Vitamin K, mcg	8	65
Thiamine (B ₁), mcg	200	1626
Riboflavin (B ₂), mcg	300	2439
Vitamin B ₆ , mcg	150	1220
Vitamin B ₁₂ , mcg	0.25	2.03
Niacin, mcg	4000	32520
Folic acid (Folacin), mcg	1200	9756
Pantothenic acid, mcg	4	32
Biotin, mcg	20	163
Vitamin C (Ascorbic acid), mg	20	163
Choline, mg	20	358
Inositol, mg	44	19.5
L-Carnitine, mg	2.4	49
Taurine, mg	6	—
Nucleotide fortification, mg	—	—
Renal Solute Load, mOsm	27	219.5
Osmolality, mOsm/kg H₂O	300	300
Osmolarity, mOsm/L	260	260

* The addition of iron to this formula conforms to the recommendation of the Committee on Nutrition of the American Academy of Pediatrics.

** Supplemental vitamin E and iron (when using Low Iron) should also be considered.

† Protein Source: Whey protein concentrate and nonfat milk.

†† Fat Source: Medium-chain triglycerides, soy oil, high oleic vegetable oil, and single-cell oil blend rich in DHA and ARA.

§ Carbohydrate Source: Corn syrup solids and lactose

Enfamil LIPIL® with Iron powder
Enfamil LIPIL® with Iron (40 Cal/fl oz) concentrate
Enfamil LIPIL® with Iron ready to use
 20 Cal/fl oz (see dilution tables for mixing instructions)

Nutrient	per 100 Cal	per Liter
Energy, Cal	100	676
Volume, mL	148	1000
Protein, g	2.1	14.2
% of total calories †	8.5	8.5
Fat, g	5.3	35.8
% of total calories ‡	48	48
Linoleic acid, mg	860	5814
Carbohydrate, g	10.9	73.7
% of total calories §	43.5	43.5
Water, g	134	906
Minerals		
Calcium, mg (mEq)	78 (3.9)	527 (26.3)
Phosphorus, mg (mEq)	43	290
Magnesium, mg	8	54
Iron, mg	1.8*	12*
Zinc, mg	1	6.8
Manganese, mcg	15	101
Copper, mcg	75	507
Molybdenum, mcg	—	—
Iodine, mcg	10	68
Selenium, mcg	2.8	18.9
Sodium, mg (mEq)	27 (1.2)	183 (8)
Potassium, mg (mEq)	108 (2.8)	730 (18.7)
Chloride, mg (mEq)	63 (1.8)	426 (12)
Vitamins		
Vitamin A, IU	300	2028
Vitamin D, IU	60	406
Vitamin E, IU	2	13.5
Vitamin K, mcg	8	54
Thiamine (B ₁), mcg	80	541
Riboflavin (B ₂), mcg	140	947
Vitamin B ₆ , mcg	60	406
Vitamin B ₁₂ , mcg	0.3	2
Niacin, mcg	1000	6760
Folic acid (Folacin), mcg	16	108
Pantothenic acid, mcg	500	3380
Biotin, mcg	3	20
Vitamin C (Ascorbic acid), mg	12	81
Choline, mg	24	162
Inositol, mg	6	41
L-Carnitine, mg	2	13.5
Taurine, mg	6	41
Nucleotide fortification, mg	—	—
Renal Solute Load, mOsm	18.9	128
Osmolality, mOsm/kg H₂O	300	300
Osmolarity, mOsm/L	270	270

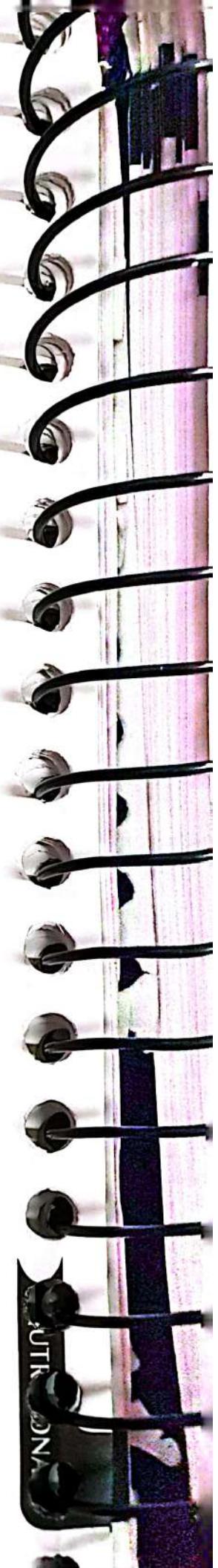
* The addition of iron to this formula conforms to the recommendation of the Committee on Nutrition of the American Academy of Pediatrics.

† Protein Source: Reduced minerals whey and nonfat milk.

‡ Fat Source: Palm olein, soy, coconut and high-oleic sunflower oils, and single-cell oil blend rich in DHA and ARA.

§ Carbohydrate Source: Lactose

WARNING: Powdered infant formulas are not sterile and should not be fed to premature infants or infants who might have immune problems.



Enfamil A.R.[®] LIPIL[®] ready to use

20 Cal/fl oz

Nutrient	per 100 Cal	per Liter
Energy, Cal	100	676
Volume, mL	148	1000
Protein, g	2.5	16.9
% of total calories [†]	10	10
Fat, g	5.1	34.5
% of total calories ^{††}	46	46
Linoleic acid, mg	860	5814
Carbohydrate, g	11	74.4
% of total calories [§]	44	44
Water, g	134	906
Minerals		
Calcium, mg (mEq)	78 (3.9)	527 (26.3)
Phosphorus, mg (mEq)	53	358
Magnesium, mg	8	54
Iron, mg	1.8*	12.2*
Zinc, mg	1	6.8
Manganese, mcg	15	101
Copper, mcg	75	507
Molybdenum, mcg	—	—
Iodine, mcg	10	68
Selenium, mcg	2.8	18.9
Sodium, mg (mEq)	40 (1.7)	270 (11.7)
Potassium, mg (mEq)	108 (2.8)	730 (18.7)
Chloride, mg (mEq)	75 (2.1)	507 (14.3)
Vitamins		
Vitamin A, IU	300	2028
Vitamin D, IU	60	406
Vitamin E, IU	2	13.5
Vitamin K, mcg	8	54
Thiamine (B ₁), mcg	80	541
Riboflavin (B ₂), mcg	140	946
Vitamin B ₆ , mcg	60	406
Vitamin B ₁₂ , mcg	0.3	2.03
Niacin, mcg	1000	6760
Folic acid (Folacin), mcg	16	108
Pantothenic acid, mcg	500	3380
Biotin, mcg	3	20
Vitamin C (Ascorbic acid), mg	12	81
Choline, mg	24	162
Inositol, mg	6	41
L-Carnitine, mg	2	13.5
Taurine, mg	6	40.6
Nucleotide fortification, mg	—	—
Renal Solute Load, mOsm	22	149
Osmolality, mOsm/kg H₂O	240	240
Osmolarity, mOsm/L	220	220

* The addition of iron to this formula conforms to the recommendation of the Committee on Nutrition of the American Academy of Pediatrics.

† Protein Source: Nonfat milk

†† Fat Source: Palm olein, soy, coconut and high-oleic sunflower oils, and single-cell oil blend rich in DHA and ARA.

§ Carbohydrate Source: Lactose, rice starch, maltodextrin.

Enfamil® LactoFree® LIPIL® powder
Enfamil® LactoFree® LIPIL® (40 Cal/fl oz) concentrate
Enfamil® LactoFree® LIPIL® ready to use
 20 Cal/fl oz (see dilution tables for mixing instructions)

Nutrient	per 100 Cal	per Liter
Energy, Cal	100	676
Volume, mL	148	1000
Protein, g	2.1	14.2
% of total calories [†]	8.5	8.5
Fat, g	5.3	35.8
% of total calories ⁺⁺	48	48
Linoleic acid, mg	860	5814
Carbohydrate, g	10.9	73.7
% of total calories [§]	43.5	43.5
Water, g	134	906
Minerals		
Calcium, mg (mEq)	82 (4.1)	554 (27.7)
Phosphorus, mg (mEq)	46	311
Magnesium, mg	8	54
Iron, mg	1.8*	12.2*
Zinc, mg	1	6.8
Manganese, mcg	15	101
Copper, mcg	75	507
Molybdenum, mcg	—	—
Iodine, mcg	15	101
Selenium, mcg	2.8	18.9
Sodium, mg (mEq)	30 (1.3)	203 (8.8)
Potassium, mg (mEq)	110 (2.8)	744 (19.1)
Chloride, mg (mEq)	67 (1.9)	453 (12.8)
Vitamins		
Vitamin A, IU	300	2028
Vitamin D, IU	60	406
Vitamin E, IU	2	13.5
Vitamin K, mcg	8	54
Thiamine (B ₁), mcg	80	541
Riboflavin (B ₂), mcg	140	946
Vitamin B ₆ , mcg	60	406
Vitamin B ₁₂ , mcg	0.3	2
Niacin, mcg	1000	6760
Folic acid (Folacin), mcg	16	108
Pantothenic acid, mcg	500	3380
Biotin, mcg	3	20
Vitamin C (Ascorbic acid), mg	12	81
Choline, mg	24	162
Inositol, mg	6	41
L-Carnitine, mg	2	13.5
Taurine, mg	6	40.6
Nucleotide fortification, mg	—	—
Renal Solute Load, mOsm	19.2	130
Osmolality, mOsm/kg H₂O	200	200
Osmolarity, mOsm/L	182	182

* The addition of iron to this formula conforms to the recommendation of the Committee on Nutrition of the American Academy of Pediatrics.

† Protein Source: Milk protein isolate.

++ Fat Source: Palm olein, soy, coconut, high-oleic sunflower oils, and single-cell oil blend rich in DHA and ARA.

§ Carbohydrate Source: Corn syrup solids.

WARNING: Powdered infant formulas are not sterile and should not be fed to premature infants or infants who might have immune problems.

Enfamil® ProSobee® LIPIL® powder
 Enfamil® ProSobee® LIPIL® (40 Cal/fl oz) concentrate
 Enfamil® ProSobee® LIPIL® ready to use
 20 Cal/fl oz (see dilution tables for mixing instructions)

Nutrient	per 100 Cal	per Liter
Energy, Cal	100	676
Volume, mL	148	1000
Protein, g	2.5	16.9
% of total calories [†]	10	10
Fat, g	5.3	35.8
% of total calories ^{††}	48	48
Linoleic acid, mg	860	5814
Carbohydrate, g	10.6	71.7
% of total calories [§]	42	42
Water, g	133	899
Minerals		
Calcium, mg (mEq)	105 (5.2)	710 (35.5)
Phosphorus, mg (mEq)	69	466
Magnesium, mg	11	74
Iron, mg	1.8	12.2
Zinc, mg	1.2	8.1
Manganese, mcg	25	169
Copper, mcg	75	507
Molybdenum, mcg	—	—
Iodine, mcg	15	101
Selenium, mcg	2.8	18.9
Sodium, mg (mEq)	36 (1.6)	243 (10.6)
Potassium, mg (mEq)	120 (3.1)	811 (20.8)
Chloride, mg (mEq)	80 (2.3)	541 (15.2)
Vitamins		
Vitamin A, IU	300	2028
Vitamin D, IU	60	406
Vitamin E, IU	2	13.5
Vitamin K, mcg	8	54
Thiamine (B ₁), mcg	80	541
Riboflavin (B ₂), mcg	90	608
Vitamin B ₆ , mcg	60	406
Vitamin B ₁₂ , mcg	0.3	2
Niacin, mcg	1000	6760
Folic acid (Folacin), mcg	16	108
Pantothenic acid, mcg	500	3380
Biotin, mcg	3	20
Vitamin C (Ascorbic acid), mg	12	81
Choline, mg	24	162
Inositol, mg	6	41
L-Carnitine, mg	2	13.5
Taurine, mg	6	41
Nucleotide fortification, mg	—	—
Renal Solute Load, mOsm	23	156
Osmolality, mOsm/kg H₂O	170	170
Osmolarity, mOsm/L	153	153

[†] Protein Source: Soy protein isolate

^{††} Fat Source: Palm olein, soy, coconut, and high-oleic sunflower oils, and single-cell oil blend rich in DHA and ARA.

[§] Carbohydrate Source: Corn syrup solids.

Potential Allergens: Contains soy protein.

WARNING: Powdered infant formulas are not sterile and should not be fed to premature infants or infants who might have immune problems.

Pregestimil® LIPIL® ready to use
20 Cal/fl oz

Nutrient	per 100 Cal	per Liter
Energy, Cal	100	676
Volume, mL	148	1000
Protein, g	2.8	18.9
% of total calories [†]	11	11
Fat, g	5.6	37.9
% of total calories ^{††}	48	48
Linoleic acid, mg	940	6354
Carbohydrate, g	10.2	69
% of total calories [§]	41	41
Water, g	133	899
Minerals		
Calcium, mg (mEq)	94 (4.7)	635 (31.8)
Phosphorus, mg (mEq)	52	352
Magnesium, mg	11	74
Iron, mg	1.8*	12.2*
Zinc, mg	1	6.8
Manganese, mcg	25	169
Copper, mcg	75	507
Molybdenum, mcg	—	—
Iodine, mcg	15	101
Selenium, mcg	2.8	18.9
Sodium, mg (mEq)	47 (2)	318 (13.8)
Potassium, mg (mEq)	110 (2.8)	744 (19)
Chloride, mg (mEq)	86 (2.4)	581 (16.4)
Vitamins		
Vitamin A, IU	380	2569
Vitamin D, IU	50	338
Vitamin E, IU	4	27
Vitamin K, mcg	12	81
Thiamine (B ₁), mcg	80	541
Riboflavin (B ₂), mcg	90	608
Vitamin B ₆ , mcg	60	406
Vitamin B ₁₂ , mcg	0.3	2.03
Niacin, mcg	1000	6760
Folic acid (Folacin), mcg	16	108
Pantothenic acid, mcg	500	3380
Biotin, mcg	3	20
Vitamin C (Ascorbic acid), mg	12	81
Choline, mg	24	162
Inositol, mg	17	115
L-Carnitine, mg	2	13.5
Taurine, mg	6	40.6
Nucleotide fortification, mg	—	—
Renal Solute Load, mOsm	25	169
Osmolality, mOsm/kg H₂O	290	290
Osmolarity, mOsm/L	260	260

* The addition of iron to this formula conforms to the recommendation of the Committee on Nutrition of the American Academy of Pediatrics.

† Protein Source: Casein hydrolysate.

†† Fat Source: Medium-chain triglycerides, soy oil, high-oleic vegetable oil, and single-cell oil blend rich in DHA and ARA.

§ Carbohydrate Source: Corn syrup solids and modified corn starch.

Pregestimil® LIPIL® ready to use

24 Cal/fl oz

Nutrient	per 100 Cal	per Liter
Energy, Cal	100	813
Volume, mL	123	1000
Protein, g	2.8	22.8
% of total calories [†]	11	11
Fat, g	5.6	45.5
% of total calories ^{††}	48	48
Linoleic acid, mg	940	7642
Carbohydrate, g	10.2	82.9
% of total calories [§]	41	41
Water, g	108	878
Minerals		
Calcium, mg (mEq)	94 (4.7)	764 (46.7)
Phosphorus, mg (mEq)	52	423
Magnesium, mg	11	89
Iron, mg	1.8*	14.6*
Zinc, mg	1	8.1
Manganese, mcg	25	203
Copper, mcg	75	610
Molybdenum, mcg	—	—
Iodine, mcg	15	122
Selenium, mcg	2.8	22.8
Sodium, mg (mEq)	47 (2)	382 (16.6)
Potassium, mg (mEq)	110 (2.8)	894 (23)
Chloride, mg (mEq)	86 (2.4)	699 (19.7)
Vitamins		
Vitamin A, IU	380	3089
Vitamin D, IU	50	407
Vitamin E, IU	4	32.5
Vitamin K, mcg	12	98
Thiamine (B ₁), mcg	80	650
Riboflavin (B ₂), mcg	90	732
Vitamin B ₆ , mcg	60	488
Vitamin B ₁₂ , mcg	0.3	2.4
Niacin, mcg	1000	8130
Folic acid (Folacin), mcg	16	130
Pantothenic acid, mcg	500	4065
Biotin, mcg	3	24
Vitamin C (Ascorbic acid), mg	12	98
Choline, mg	24	195
Inositol, mg	17	138
L-Carnitine, mg	2	16.3
Taurine, mg	6	49
Nucleotide fortification, mg	—	—
Renal Solute Load, mOsm	25	203
Osmolality, mOsm/kg H₂O	340	340
Osmolarity, mOsm/L	300	300

* The addition of iron to this formula conforms to the recommendation of the Committee on Nutrition of the American Academy of Pediatrics.

† Protein Source: Casein hydrolysate.

†† Fat Source: Medium-chain triglycerides, soy oil, high-oleic vegetable oil, and single-cell oil blend rich in DHA and ARA.

§ Carbohydrate Source: Corn syrup solids and modified corn starch.

Pregestimil® LIPIL® powder

20 Cal/fl oz (when mixed to standard dilution)

Nutrient	per 100 Cal	per Liter
Energy, Cal	100	676
Volume, mL	148	1000
Protein, g	2.8	18.9
% of total calories †	11	11
Fat, g	5.6	37.9
% of total calories ‡	50	50
Linoleic acid, mg	940	6354
Carbohydrate, g	10.2	69
% of total calories §	41	41
Water, g	134	906
Minerals		
Calcium, mg (mEq)	94 (4.7)	635 (31.8)
Phosphorus, mg (mEq)	52	352
Magnesium, mg	11	74
Iron, mg	1.8*	12.2*
Zinc, mg	1	6.8
Manganese, mcg	25	169
Copper, mcg	75	507
Molybdenum, mcg	—	—
Iodine, mcg	15	101
Selenium, mcg	2.8	18.9
Sodium, mg (mEq)	47 (2)	318 (13.8)
Potassium, mg (mEq)	110 (2.8)	744 (19)
Chloride, mg (mEq)	86 (2.4)	581 (16.4)
Vitamins		
Vitamin A, IU	380	2569
Vitamin D, IU	50	338
Vitamin E, IU	4	27
Vitamin K, mcg	12	81
Thiamine (B ₁), mcg	80	541
Riboflavin (B ₂), mcg	90	608
Vitamin B ₆ , mcg	60	406
Vitamin B ₁₂ , mcg	0.3	2.03
Niacin, mcg	1000	6760
Folic acid (Folacin), mcg	16	108
Pantothenic acid, mcg	500	3380
Biotin, mcg	3	20
Vitamin C (Ascorbic acid), mg	12	81
Choline, mg	24	162
Inositol, mg	17	115
L-Carnitine, mg	2	13.5
Taurine, mg	6	40.6
Nucleotide fortification, mg	—	—
Renal Solute Load, mOsm	25	169
Osmolality, mOsm/kg H ₂ O	320	320
Osmolarity, mOsm/L	290	290

* The addition of iron to this formula conforms to the recommendation of the Committee on Nutrition of the American Academy of Pediatrics.

† Protein Source: Casein hydrolysate.

‡ Fat Source: Medium-chain triglycerides, soy oil, corn oil, and high-oleic vegetable oils, and single-cell oil blend rich in DHA and ARA.

§ Carbohydrate Source: Corn syrup solids, modified corn starch and dextrose.

WARNING: Powdered infant formulas are not sterile and should not be fed to premature infants or infants who might have immune problems.

Enfamil® Gentlelease® LIPIL® powder

20 Cal/fl oz (when mixed to standard dilution)

Nutrient	per 100 Cal	per Liter
Energy, Cal	100	676
Volume, mL	148	1000
Protein, g	2.3	15.6
% of total calories [†]	9	9
Fat, g	5.3	35.8
% of total calories ^{††}	48	48
Linoleic acid, mg	860	5814
Carbohydrate, g	10.8	73
% of total calories [§]	43	43
Water, g	134	906
Minerals		
Calcium, mg (mEq)	82 (4.1)	554 (27.7)
Phosphorus, mg (mEq)	46	311
Magnesium, mg	8	54
Iron, mg	1.8*	12.2*
Zinc, mg	1	6.8
Manganese, mcg	15	101
Copper, mcg	75	507
Molybdenum, mcg	-	-
Iodine, mcg	10	68
Selenium, mcg	2.8	18.9
Sodium, mg (mEq)	32 (1.4)	216 (9.4)
Potassium, mg (mEq)	108 (2.8)	730 (18.7)
Chloride, mg (mEq)	63 (1.8)	426 (12)
Vitamins		
Vitamin A, IU	300	2028
Vitamin D, IU	60	406
Vitamin E, IU	2	13.5
Vitamin K, mcg	8	54
Thiamine (B ₁), mcg	80	541
Riboflavin (B ₂), mcg	140	946
Vitamin B ₆ , mcg	60	406
Vitamin B ₁₂ , mcg	0.3	2.0
Niacin, mcg	1000	6760
Folic acid (Folacin), mcg	16	108
Pantothenic acid, mcg	500	3380
Biotin, mcg	3	20
Vitamin C (Ascorbic acid), mg	12	81
Choline, mg	24	162
Inositol, mg	6	41
L-Carnitine, mg	2	13.5
Taurine, mg	6	41
Nucleotide fortification, mg	-	-
Renal Solute Load, mOsm	20	135
Osmolality, mOsm/kg H₂O	220	220
Osmolarity, mOsm/L	200	200

* The addition of iron to this formula conforms to the recommendation of the Committee on Nutrition of the American Academy of Pediatrics.

† Protein Source: Protein Source: partially hydrolyzed nonfat milk and whey protein concentrate (60% whey and 40% casein).

†† Fat Source: palm olein, soy, coconut, high oleic sunflower oils, single-cell oils rich in DHA and ARA.

§ Carbohydrate Source: corn syrup solids and lactose.

WARNING: Powdered infant formulas are not sterile and should not be fed to premature infants or infants who might have immune problems.

Enfaport® LIPIL® with 84% of fat as MCT oil for infants with chylothorax or LCHAD* (30 Cal/fl oz ready to use)

Nutrient	per 100 Cal	per Liter
Energy, Cal	100	1010
Volume, mL	99	1000
Protein, g	3.5	35
% of total calories †	14	141
Fat, g	5.4	54.5
% of total calories ‡	45	454
Linoleic acid, mg	350	3535
Alpha-Linolenic acid, mg	50	505
Carbohydrate, g	10.2	103
% of total calories §	41	414
Water, g	83	838
Minerals		
Calcium, mg	94	949
Phosphorus, mg	52	525
Magnesium, mg	11	111
Iron, mg	1.8	18
Zinc, mg	1	10
Manganese, mcg	25	252
Copper, mcg	75	757
Iodine, mcg	15	151
Selenium, mcg	2.8	28
Sodium, mg (mEq)	30 (1.3)	303 (13.1)
Potassium, mg (mEq)	115 (2.9)	1161 (29.3)
Chloride, mg (mEq)	87 (2.5)	879 (25.3)
Vitamins		
Vitamin A, IU	350	3535
Vitamin D, IU	50	505
Vitamin E, IU	4	40
Vitamin K, mcg	12	121
Thiamin B ₁ , mcg	80	808
Riboflavin B ₂ , mcg	90	909
Vitamin B ₆ , mcg	68	687
Vitamin B ₁₂ , mcg	0.3	3
Niacin, mcg	1000	10101
Folic acid, mcg	16	162
Pantothenic acid, mcg	500	5050
Biotin, mcg	3	30
Vitamin C, mg	12	121
Choline, mg	24	242
Inositol, mg	17	172
Renal Solute Load, mOsm	29	293
Osmolality, mOsm/kg H ₂ O	280	280
Osmolarity, mOsm/L	240	240

* Long chain 3-hydroxyacyl-CoA dehydrogenase is a rare inherited disorder of fatty oxidation.

† Protein Source: Calcium caseinate and sodium caseinate.

‡ Fat Source: MCT oil, soy oil, and 3% single-cell oil blend rich in DHA and ARA.

§ Carbohydrate source: Corn syrup solids.

Nutramigen® LIPIL® 20**Nutramigen® LIPIL® powder****Nutramigen® LIPIL® (40 Cal/fl oz) concentrate****Nutramigen® LIPIL® ready to use**

20 Cal/fl oz (see dilution tables for mixing instructions)

Nutrient	per 100 Cal	per Liter
Energy, Cal	100	676
Volume, mL	148	1000
Protein, g	2.8	18.9
% of total calories [†]	11	11
Fat, g	5.3	35.8
% of total calories ^{††}	48	48
Linoleic acid, mg	860	5813
Carbohydrate, g	10.3	69.6
% of total calories [§]	41	41
Water, g	133	899
Minerals		
Calcium, mg (mEq)	94 (4.7)	635 (31.8)
Phosphorus, mg (mEq)	52	352
Magnesium, mg	11	74
Iron, mg	1.8*	12.2*
Zinc, mg	1	6.8
Manganese, mcg	25	169
Copper, mcg	75	507
Molybdenum, mcg	—	—
Iodine, mcg	15	101
Selenium, mcg	2.8	18.9
Sodium, mg (mEq)	47 (2)	318 (13.8)
Potassium, mg (mEq)	110 (2.8)	744 (19.1)
Chloride, mg (mEq)	86 (2.4)	581 (16.4)
Vitamins		
Vitamin A, IU	300	2028
Vitamin D, IU	50	338
Vitamin E, IU	2	13.5
Vitamin K, mcg	8	54
Thiamine (B ₁), mcg	80	541
Riboflavin (B ₂), mcg	90	608
Vitamin B ₆ , mcg	60	406
Vitamin B ₁₂ , mcg	0.3	2
Niacin, mcg	1000	6760
Folic acid (Folacin), mcg	16	108
Pantothenic acid, mcg	500	3380
Biotin, mcg	3	20
Vitamin C (Ascorbic acid), mg	12	81
Choline, mg	24	162
Inositol, mg	17	115
L-Carnitine, mg	2	13.5
Taurine, mg	6	41
Nucleotide fortification, mg	—	—
Renal Solute Load, mOsm	25	169
Osmolality, mOsm/kg H₂O	300	300
Osmolarity, mOsm/L	270	270

* The addition of iron to this formula conforms to the recommendation of the Committee on Nutrition of the American Academy of Pediatrics.

† Protein Source: Casein hydrolysate.

†† Fat Source: Palm olein, soy, coconut, high-oleic sunflower oils, and single-cell oil blend rich in DHA and ARA.

§ Carbohydrate Source: Corn syrup solids, modified corn starch.

CAUTION: This product is not recommended for routine use in very low-birth-weight infants. Some of these infants may be at increased risk of developing gastrointestinal complications.

WARNING: Powdered infant formulas are not sterile and should not be fed to premature infants or infants who might have immune problems.

Nutramigen® AA™ LIPIL®

Nutramigen® AA™ LIPIL® Hypoallergenic Amino Acid-Based Formula
20 Cal/fl oz (when mixed to standard dilution)

Nutrient	per 100 Cal	per Liter
Energy, Cal	100	676
Volume, mL	148	1000
Protein, g	2.8	18.9
% of total calories [†]	11	11
Fat, g	5.3	35.8
% of total calories ^{††}	48	48
Linoleic acid, mg	860	5811
Linolenic acid, mg	80	540
Carbohydrate, g	10.3	69.6
% of total calories [§]	41	41
Water, g	133	899
Minerals		
Calcium, mg	94	635
Phosphorus, mg	52	351
Magnesium, mg	11	74
Iron, mg	1.8	12.2
Zinc, mg	1	6.8
Manganese, mcg	60	405
Copper, mcg	75	507
Iodine, mcg	15	101
Selenium, mcg	2.8	18.9
Sodium, mg (mEq)	47 (2)	318 (13.8)
Potassium, mg (mEq)	110 (2.8)	743 (19)
Chloride, mg (mEq)	86 (2.4)	581 (16.4)
Vitamins		
Vitamin A, IU	300	2027
Vitamin D, IU	50	338
Vitamin E, IU	2	13.5
Vitamin K, mcg	8	54
Thiamin B ₁ , mcg	80	541
Riboflavin B ₂ , mcg	90	608
Vitamin B ₆ , mcg	60	405
Vitamin B ₁₂ , mcg	0.3	2
Niacin, mcg	1000	6756
Folic Acid, mcg	16	108
Pantothenic Acid, mcg	500	3378
Biotin, mcg	3	20
Vitamin C, mg	12	81
Choline, mg	24	162
Inositol, mg	17	115
Carnitine, mg	2	13.5
Taurine, mg	6	40.5
Renal Solute Load, mOsm	25	169
Osmolality, mOsm/kg H₂O	350	350
Osmolarity, mOsm/L	320	320

[†] Protein Source: 100% free amino acids.

^{††} Fat Source: Palm olein, soy, coconut, high-oleic sunflower oils, and 2.5% single-cell oil blend rich in DHA and ARA.

[§] Carbohydrate source: Corn syrup solids and modified tapioca starch.

CAUTION: This product is not recommended for routine use in very low-birth weight infants.

Some of these infants may be at increased risk of developing gastrointestinal complications.

Good Start® DHA & ARA powder

Good Start® DHA & ARA (40 Cal/fl oz) concentrate

Good Start® DHA & ARA ready-to-feed

20 Cal/fl oz (see dilution tables for mixing instructions)

Nutrient	per 100 Cal	per Liter
Energy, Cal	100	670
Volume, mL	148	1000
Protein, g	2.2	14.7
% of total calories [†]	9	9
Fat, g	5.1	34.2
% of total calories ^{††}	46	46
Linoleic acid, mg	900	6030
Carbohydrate, g	11.2	75.7
% of total calories [§]	45	45
Water, g	134	900
Minerals		
Calcium, mg (mEq)	67 (3.3)	449 (22.6)
Phosphorus, mg (mEq)	38 (1.3)	255 (8.4)
Magnesium, mg	7	46.6
Iron, mg	1.5	10.1
Zinc, mg	0.8	5.4
Manganese, mcg	15	101
Copper, mcg	80	536
Molybdenum, mcg	—	—
Iodine, mcg	12	80.4
Selenium, mcg	3	20.1
Sodium, mg (mEq)	27 (1.2)	181 (7.8)
Potassium, mg (mEq)	108 (2.8)	724 (18.5)
Chloride, mg (mEq)	65 (1.8)	436 (12.3)
Vitamins		
Vitamin A, IU	300	2010
Vitamin D, IU	60	402
Vitamin E, IU	2	13.4
Vitamin K, mcg	8	54
Thiamine (B ₁), mcg	100	670
Riboflavin (B ₂), mcg	140	938
Vitamin B ₆ , mcg	75	503
Vitamin B ₁₂ , mcg	0.33	2.2
Niacin, mcg	1050	7035
Folic acid (Folacin), mcg	15	101
Pantothenic acid, mcg	450	3015
Biotin, mcg	4.4	29.5
Vitamin C (Ascorbic acid), mg	9	60.3
Choline, mg	24	161
Inositol, mg	6	40.2
L-Carnitine, mg	—	—
Taurine, mg	—	—
Nucleotide fortification, mg	5	34
Renal Solute Load, mOsm	19	131
Osmolality, mOsm/kg H₂O	250	250
Osmolarity, mOsm/L	224	224

[†] Protein Source: Enzymatically Hydrolyzed Reduced Minerals Whey Protein Concentrate (From Cow's Milk)

^{††} Fat Source: Vegetable Oils (Palm Olein, Soy, Coconut, and High-Oleic Safflower or High-Oleic Sunflower), and C. cohnii¹ and M. alpina² oils.
DHA and ARA are 0.32 and 0.64% of total fat.

¹ A source of docosahexaenoic acid (DHA).

² A source of arachidonic acid (ARA).

[§] Carbohydrate Source: Lactose, Corn Maltodextrin

Potential Allergens: Contains milk protein.

WARNING: Powdered infant formulas are not sterile and should not be fed to premature infants or infants who might have immune problems.

Neocate® 20

Neocate® With Iron Infant Formula*
20 Cal/fl oz (see footnotes for preparation)

Nutrient	per 100 Cal	per Liter
Energy, Cal	100	676
Volume, mL	148	1000
Protein, g	3.1	20.9
% of total calories †	12	12
Fat, g	4.5	30.4
% of total calories ‡‡	41	41
Linoleic acid, mg	677	4577
Carbohydrate, g	11.7	79.1
% of total calories §	47	41
Water, g	131	886
Minerals		
Calcium, mg (mEq)	124 (6.2)	838 (41.9)
Phosphorus, mg (mEq)	93	629
Magnesium, mg	12.4	83.8
Iron, mg	1.85*	12.5*
Zinc, mg	1.66	11.2
Manganese, mcg	90	608
Copper, mcg	124	838
Molybdenum, mcg	4.75	32.1
Iodine, mcg	15.4	104
Selenium, mcg	3.73	25.2
Sodium, mg (mEq)	37.3 (1.6)	252 (11)
Potassium, mg (mEq)	155.1 (4)	1048 (26.9)
Chloride, mg (mEq)	77.2 (2.2)	522 (14.8)
Vitamins		
Vitamin A, IU	391	2643
Vitamin D, IU	59.9	405
Vitamin E, IU	1.14	7.7
Vitamin K, mcg	8.79	59.4
Thiamine (B ₁), mcg	92.6	626
Riboflavin (B ₂), mcg	137.8	932
Vitamin B ₆ , mcg	123.5	835
Vitamin B ₁₂ , mcg	0.26	1.76
Niacin, mcg	1544	10437
Folic acid (Folacin), mcg	10.2	69
Pantothenic acid, mcg	620	4191
Biotin, mcg	3.1	21
Vitamin C (Ascorbic acid), mg	9.26	62.6
Choline, mg	13.1	89
Inositol, mg	23.3	158
L-Carnitine, mg	—	—
Taurine, mg	—	—
Nucleotide fortification, mg	—	—
Renal Solute Load, mOsm	28.5	192.6
Osmolality, mOsm/kg H₂O	375	375
Osmolarity, mOsm/L	332	332

* The addition of iron to this formula conforms to the recommendation of the Committee on Nutrition of the American Academy of Pediatrics.

† Protein Source: L-amino acids.

‡‡ Fat Source: High Oleic Safflower Oil (11%), Refined Vegetable Oil (Coconut 6%, Soy 3%).

§ Carbohydrate Source: Corn syrup solids.

Preparation (20 Cal/fl oz):

Use one unpacked level scoop (4.75 g), enclosed, of powder for each fluid ounce of final volume of prepared formula. Add fluid to powder and adjust to 1 oz level.

WARNING: Powdered infant formulas are not sterile and should not be fed to premature infants or infants who might have immune problems.

NEOFAX® 2009

Medium Chain Triglyceride Oil

Medium chain triglycerides (MCT) are lipid fractions of coconut oil consisting of triglycerides with chain lengths of 6 to 10 carbons. Used to supplement orally, or added to tube feeding formulas. Mixes easily with enteral formulas.

MCT Oil

Nutrient	per mL	per 15 mL (1 tbsp)	per 89 mL (3 fl oz)
Calories	7.7	115	685.3
Protein, g	0	0	0
Fat, g	0.94	14	44.5
Carbohydrate, g	0	0	0
Water, g	0	0	0
Linoleic Acid, g	0.367	5.5	32.63

Fatty Acid Distribution

Shorter than carbon 8	<6%
Caprylic C8:0	67%
Capric C10:0	23%
Longer than C10:0	<4%

Osmolality (mOsm/kg water): Not Available

Supplied: 1 quart glass bottles.

Ingredients: Medium chain triglycerides.

For oral use only. Do not give parenterally (IV). Use within 60 to 90 days after a bottle is opened. Do not store in plastic container. MCT may break or soften plastic containers.

Microlipid® is a 50% safflower oil fat emulsion with 4.5 Cal/mL. Used to supplement orally, or added to tube feeding formulas. Mixes easily with enteral formulas.

Nutrient	per mL	per 15 mL (1 tbsp)	per 89 mL (3 fl oz)
Calories	4.5	67.5	400
Protein, g	0	0	0
Fat, g	0.5	7.54	44
Carbohydrate, g	0	0.04	0
Water, g	0.45	6.7	40
Linoleic Acid, g	0.4	5.9	35

Fatty Acid Distribution

Polyunsaturated	78%
Monounsaturated	12%
Saturated	10%
PUFA:SFA	8:1

Osmolality (mOsm/kg water): Not available

Supplied: 48 three ounce bottles per case.

Ingredients: Safflower oil, water, polyglycerol esters of fatty acids, soy lecithin, xanthan gum, ascorbic acid.

For oral use only. Do not give parenterally (IV). Shake well before opening. Opened product should be recapped, refrigerated, and discarded after 5 days. Store unopened bottles at room temperature. Protect from freezing.

Dose & Administration

Begin at 0.5 g/kg per day IV increasing by 0.5 g/kg per day to a maximum of 3 g/kg per day. Infusion rate should not exceed 0.15 g/kg per hour. 24 hour infusion times are preferred. Essential fatty acid deficiency may be prevented with 0.5 to 1 g/kg per day.

Fat Emulsion

	Intralipid® 20%	Liposyn II® 20%	Liposyn III® 20%
Oils (%)			
Safflower	0	10	0
Soybean	20	10	20
Fatty Acid Content (%)			
Linoleic	50	65.8	54.5
Oleic	26	17.7	22.4
Palmitic	10	8.8	10.5
Linolenic	9	4.2	8.3
Stearic	3.5	3.4	4.2
Egg yolk phospholipid (%)	1.2	1.2	1.2
Glycerine (%)	2.25	2.5	2.5
Calories (per mL)	2	2	2
Osmolarity (mOsm/L)	260	258	292

Uses

Parenteral nutrition source of calories and essential fatty acids.

Monitoring

Monitor serum triglycerides (<200 mg/dL), liver function test, platelet count, albumin, glucose, and bilirubin.

Adverse Effects/Precautions**Black Box Warning**

According to the manufacturer's black box warning, deaths due to intravascular fat accumulation in the lungs of preterm infants after infusion of IV fat emulsion have been reported. Strict adherence to the recommended total daily dose and hourly infusion rates is recommended. Infusion rates should not exceed 1 g/kg in four hours.

Hypertriglyceridemia and hyperglycemia. The minimum dose should be used in infants with severe hyperbilirubinemia, sepsis, or severe pulmonary dysfunction. Extravasation may cause tissue inflammation and necrosis.

Pharmacology

Intravenous fat emulsions are high caloric (2 Cal/mL) isotonic emulsions of either soybean or safflower oil. Fat particle size is between 0.4 and 0.5 microns in diameter, similar to endogenous chylomicrons. Clearance is via endogenous lipoprotein lipase activity, which is limited in very premature (<28 weeks gestation) and infected infants. Twenty percent emulsions are preferred due to lower total phospholipid and liposome content per gram of triglyceride. Ten percent emulsions have been associated with hypercholesterolemia and hyperphospholipidemia. Destabilization of lipid emulsions (flocculation and separation) may occur when they are co-infused with Dex/AA solutions containing calcium and high concentrations (>1 units/mL) of heparin. This risk may be decreased by 1) minimizing the contact time; 2) using low (\leq 1 units/mL) concentrations of heparin; and 3) adding a multivitamin preparation to the Dex/AA solution.

Fat Emulsion

Special Considerations/Preparation

Liposyn® and Intralipid® are available in 10% and 20% concentrations in 50, 100, 250, and 500 mL bottles. Store at room temperature

Do not freeze.

Use within 24 hours when dispensed in syringes.

There are no specific data regarding the compatibility of dobutamine or dopamine and fat emulsions. Dobutamine and dopamine are most stable in solutions with a pH at or below 5. In alkaline solutions, the catechol moieties are oxidized, cyclized, and polymerized to colored materials. All fat emulsions have pH ranges from 6 to 9. Caution is urged when co-infusing dobutamine or dopamine and fat emulsion together; dobutamine or dopamine may degrade over time in this alkaline pH resulting in lower than expected clinical effects.

Solution Compatibility: D₅W, D₁₀W, and NS.

Terminal Injection Site Compatibility: Dex/AA. Aminophylline, ampicillin, aztreonam, bumetanide, caffeine citrate, calcium chloride, calcium gluconate, cefazolin, cefotaxime, cefoxitin, ceftazidime, ceftriaxone, chloramphenicol, cimetidine, clindamycin, dexamethasone, digoxin, enalaprilat, erythromycin lactobionate, famotidine, fentanyl, fluconazole, furosemide, gentamicin, heparin (≤ 1 unit/mL), hydrocortisone, imipenem/cilastatin, insulin, isoproterenol, lidocaine, meropenem, metoclopramide, metronidazole, morphine, nafcillin, netilmicin, norepinephrine, oxacillin, penicillin G, piperacillin, piperacillin/tazobactam, potassium chloride, pyridoxine, ranitidine, sodium bicarbonate, sodium nitroprusside, ticarcillin, ticarcillin/clavulanate, tobramycin, trimethoprim/sulfamethoxazole, vancomycin, and zidovudine.

Incompatibility: Acyclovir, amikacin, amphotericin B, lorazepam, magnesium chloride, midazolam, octreotide acetate, pentobarbital, phenobarbital, and phenytoin.

Selected References

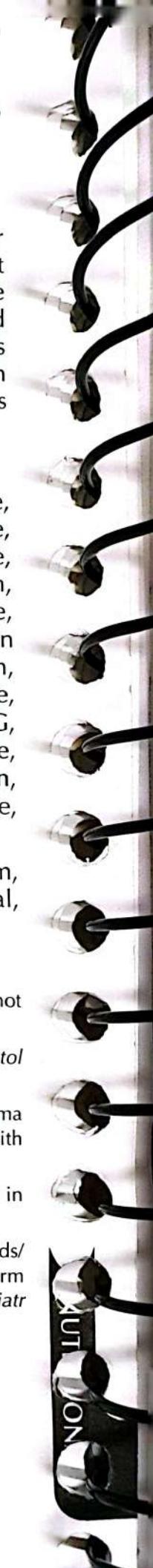
- ◆ Silvers KM, Darlow BA, Winterbourn CC: Pharmacologic levels of heparin do not destabilize neonatal parenteral nutrition. *J Parenter Enter Nutr* 1998;22:311-314.
- ◆ Lipsky CL, Spear ML: Recent advances in parenteral nutrition. *Clin Perinatol* 1995;22:141-155.
- ◆ Haumont D, Deckelbaum RJ, Richelle M, Dahlan W, et al: Plasma lipid and plasma lipoprotein concentration in low birth weight infants given parenteral nutrition with twenty or ten percent lipid emulsion. *J Pediatr* 1989;115:787-93.
- ◆ Brans YW, Andrews DS, Carrillo DW, Dutton EP, et al: Tolerance of fat emulsions in very-low-birth-weight neonates. *Am J Dis Child* 1988;142:145-152.
- ◆ Kao LC, Cheng MH, Warburton D: Triglycerides, free fatty acids, free fatty acids/albumin molar ratio, and cholesterol levels in serum of neonates receiving long-term lipid infusions: Controlled trial of continuous and intermittent regimens. *J Pediatr* 1984;104:429-435.
- ◆ Product Information, Hospira, 2005

Adverse Effects/Precautions updated 3/2009

Special Considerations updated 3/2008

Compatibility updated 3/2008

Added 3/1999



**RECOMMENDED
CONCENTRATIONS
FOR
ADMINISTRATION**

Generic Name	Route	Units	Available	Concentration		
				Default	High	Low
Acyclovir	IV	mg/mL	50*	7	7	5
Amikacin	IV	mg/mL	50*	10	10	5
Amikacin	IM	mg/mL	50	50	50	10
Amphotericin B	IV	mg/mL	5*	0.1	0.1	0.05
Amphotericin B Lipid Complex	IV	mg/mL	5*	2	2	0.5
Amphotericin B Liposome	IV	mg/mL	4*	2	2	1
Ampicillin	IV	mg/mL	125 or 250*	50	100	20
Ampicillin	IM	mg/mL	250	250	250	125
Azithromycin	IV	mg/mL	100*	2	2	2
Aztreonam	IV	mg/mL	100	50	66	20
Aztreonam	IM	mg/mL	125 or 250	167	333	83
Caspofungin	IV	mg/mL	5.2*	0.2	0.5	0.1
Cefepime	IV	mg/mL	100	100	160	100
Cefepime	IM	mg/mL	280	280	280	160
Cefazolin	IV	mg/mL	225*	100	125	20
Cefazolin	IM	mg/mL	225	330	330	100
Cefotaxime	IV	mg/mL	50 or 100	50	100	25
Cefotaxime	IM	mg/mL	230 or 300	300	330	100
Cefoxitin	IV	mg/mL	100*	40	100	20
Ceftazidime	IV	mg/mL	50	100	200	50
Ceftazidime	IM	mg/mL	200	200	100	50
Ceftriaxone	IV	mg/mL	40 or 100*	40	40	20
Ceftriaxone	IM	mg/mL	250	250	250	100
Chloramphenicol	IV	mg/mL	100 *	10	100	5
Clindamycin	IV	mg/mL	150*	10	18	6
Erythromycin Lactobionate	IV	mg/mL	50*	5	5	1
Fluconazole	IV	mg/mL	2	2	2	2
Ganciclovir	IV	mg/mL	50*	5	10	5
Gentamicin	IV	mg/mL	10	10	10	2
Gentamicin	IM	mg/mL	40	10	40	10
Imipenem - Cilastatin	IV	mg/mL	2.5 or 5	5	5	2.5
Linezolid	IV	mg/mL	2	2	2	2
Meropenem	IV	mg/mL	50	50	50	25
Metronidazole	IV	mg/mL	5	5	5	5
Micafungin	IV	mg/mL	50 or 100*	1	1.5	0.5
Nafcillin	IV	mg/mL	250*	40	40	20
Netilmicin	IM	mg/mL	100*	5	100	2.5
Oxacillin	IV	mg/mL	50	25	100	25

* See Neofax Special Consideration/Preparation section for dilution details

NEOFAX® 2000

Antimicrobials

375

Generic Name	Route	Units	Concentration			
			Available	Default	High	Low
Penicillin G	IV	U/mL	500,000	100,000	500,000	50,000
Piperacillin	IV	mg/mL	200	100	200	50
Piperacillin	IM	mg/mL	400	300	400	100
Piperacillin - Tazobactam	IV	mg/mL	200	100	200	50
Rifampin	IV	mg/mL	60*	3	6	3
Ticarcillin - Clavulanate	IV	mg/mL	200	50	100	10
Tobramycin	IV	mg/mL	10	10	10	2
Tobramycin	IM	mg/mL	40	40	40	10
Vancomycin	IV	mg/mL	50*	5	5	2.5
Zidovudine (ZDV, AZT)	IV	mg/mL	10*	4	4	2

Biologics**Concentration**

Generic Name	Route	Units	Available	Default	High	Low
Epoetin alfa	IV	U/mL	2,000	2,000	4,000	2,000
Epoetin alfa	SC	U/mL	2,000	2,000	4,000	2,000

Cardiovascular**Concentration**

Generic Name	Route	Units	Available	Default	High	Low
Adenosine	IV	mcg/mL	3000*	300	3,000	200
Alteplase	IV	mg/mL	1	1	1	1
Amiodarone	IV	mg/mL	50*	2	6	2
Atropine	IV	mg/mL	0.4*	0.05	0.1	0.05
Digoxin	IV	mcg/mL	100*	10	100	10
Enalaprilat	IV	mcg/mL	1250*	25	50	25
Enoxaparin	IV	mg/mL	100	100	100	100
Esmolol	IV	mcg/mL	10,000	10,000	10,000	1,000
Hydralazine	IV	mg/mL	20*	1	1	1
Indomethacin	IV	mg/mL	0.5 to 1	0.5	1	0.5
Milrinone	IV	mcg/mL	1000*	200	200	50
Procainamide	IV	mg/mL	100	2	4	2
Propranolol	IV	mg/mL	1*	1	1	0.1
Prostaglandin E1	IV	mcg/mL	500*	10	20	10
Sodium nitroprusside	IV	mg/mL	25	0.1	0.2	.01

* See Neofax Special Consideration/Preparation section for dilution details

NEOFAX® 2009

Generic Name	Route	Units	Concentration			
			Available	Default	High	Low
Fentanyl	IV	mcg/mL	50	10	20	5
Fosphenytoin	IV	mg PE/mL	50	25	25	1.5
Fosphenytoin	IM	mg PE/mL	50	50	50	50
Lorazepam	IV	mg/mL	2 or 4*	0.4	2	0.2
Midazolam	IV	mg/mL	1 or 5*	0.5	1	0.5
Mivacurium	IV	mg/mL	2	0.2	2	0.2
Morphine	IV	mg/mL	0.5 to 50*	0.4	5	0.1
Pancuronium	IV	mg/mL	1 or 2	1	2	0.5
Pentobarbital	IV	mg/mL	50*	5	50	5
Rocuronium	IV	mg/mL	10	1	5	1
Vecuronium	IV	mg/mL	1*	0.4	1	0.1

Diuretics

Generic Name	Route	Units	Concentration			
			Available	Default	High	Low
Bumetanide	IV	mg/mL	0.25*	0.125	0.25	0.05
Bumetanide	IM	mg/mL	0.25*	0.125	0.25	0.05
Furosemide	IV	mg/mL	10*	2	10	2
Furosemide	IM	mg/mL	10*	10	10	5

GI

Generic Name	Route	Units	Concentration			
			Available	Default	High	Low
Cimetidine	IV	mg/mL	150*	15	15	6
Famotidine	IV	mg/mL	10*	1	10	1
Metoclopramide	IV	mg/mL	5*	0.1	1	0.1
Ranitidine	IV	mg/mL	1 and 25*	2	4	0.5

Respiratory

377

Concentration						
Generic Name	Route	Units	Available	Default	High	Low
Aminophylline	IV	mg/mL	25*	5	25	5
Dexamethasone	IV	mg/mL	4 or 10	0.2	1	0.1

Miscellaneous

Concentration						
Generic Name	Route	Units	Available	Default	High	Low
Hydrocortisone succinate	IV	mg/mL	100	10	10	1
Insulin	IV	U/mL	100*	1	5	0.2
Levothyroxine (T4)	IV	mcg/mL	40 or 100	20	40	20
Octreotide Acetate	IV	mcg/mL	50	25	100	10

NEWBORN METRIC CONVERSION TABLES

Newborn Metric Conversion Tables

Temperature in Fahrenheit (F) to Celsius (C)

°F	°C	°F	°C	°F	°C	°F	°C
93.2 . . . 34.0	34.0	96.2 . . . 35.7	35.7	99.2 . . . 37.3	37.3	102.2 . . . 39.0	39.0
93.4 . . . 34.1	34.1	96.4 . . . 35.8	35.8	99.4 . . . 37.4	37.4	102.4 . . . 39.1	39.1
93.6 . . . 34.2	34.2	96.6 . . . 35.9	35.9	99.6 . . . 37.6	37.6	102.6 . . . 39.2	39.2
93.8 . . . 34.3	34.3	96.8 . . . 36.0	36.0	99.8 . . . 37.7	37.7	102.8 . . . 39.3	39.3
94.0 . . . 34.4	34.4	97.0 . . . 36.1	36.1	100.0 . . . 37.8	37.8	103.0 . . . 39.4	39.4
94.2 . . . 34.6	34.6	97.2 . . . 36.2	36.2	100.2 . . . 37.9	37.9	103.2 . . . 39.6	39.6
94.4 . . . 34.7	34.7	97.4 . . . 36.3	36.3	100.4 . . . 38.0	38.0	103.4 . . . 39.7	39.7
94.6 . . . 34.8	34.8	97.6 . . . 36.4	36.4	100.6 . . . 38.1	38.1	103.6 . . . 39.8	39.8
94.8 . . . 34.9	34.9	97.8 . . . 36.6	36.6	100.8 . . . 38.2	38.2	103.8 . . . 39.9	39.9
95.0 . . . 35.0	35.0	98.0 . . . 36.7	36.7	101.0 . . . 38.3	38.3	104.0 . . . 40.0	40.0
95.2 . . . 35.1	35.1	98.2 . . . 36.8	36.8	101.2 . . . 38.4	38.4	104.2 . . . 40.1	40.1
95.4 . . . 35.2	35.2	98.4 . . . 36.9	36.9	101.4 . . . 38.6	38.6	104.4 . . . 40.2	40.2
95.6 . . . 35.3	35.3	98.6 . . . 37.0	37.0	101.6 . . . 38.7	38.7	104.6 . . . 40.3	40.3
95.8 . . . 35.4	35.4	98.8 . . . 37.1	37.1	101.8 . . . 38.8	38.8	104.8 . . . 40.4	40.4
96.0 . . . 35.6	35.6	99.0 . . . 37.2	37.2	102.0 . . . 38.9	38.9	105.0 . . . 40.6	40.6

Note: °C = ($^{\circ}\text{F} - 32$) $\times \frac{5}{9}$. Celsius temperature equivalents rounded to one decimal place by adding 0.1 when second decimal place is 5 or greater. The metric system replaces the term Centigrade with Celsius (name of the inventor of the scale).

Body Mass to Body Surface Area Approximation

$$\text{BSA (m}^2\text{)} = (0.05 \times \text{kg}) + 0.05$$

Weight (kg)	Approximate Surface Area (m ²)	Weight (kg)	Approximate Surface Area (m ²)
0.4	0.07	2.8	0.19
0.6	0.08	3	0.2
0.8	0.09	3.2	0.21
1	0.1	3.4	0.22
1.2	0.11	3.6	0.23
1.4	0.12	3.8	0.24
1.6	0.13	4	0.25
1.8	0.14	4.2	0.26
2	0.15	4.4	0.27
2.2	0.16	4.6	0.28
2.4	0.17	4.8	0.29
2.6	0.18	5	0.3

Newborn Metric Conversion Tables

Length in inches (in.) to centimeters (cm)

1-in. increments. Example: To obtain centimeters equivalent to 22 in., read "20" on top scale, "2" on side scale; equivalent is 55.9 cm.

Inches	0	10	20	30	40
0	0	25.4	50.8	76.2	101.6
1	2.5	27.9	53.3	78.7	104.1
2	5.1	30.5	55.9	81.3	106.7
3	7.6	33.0	58.4	83.8	109.2
4	10.2	35.6	61.0	86.4	111.8
5	12.7	38.1	63.5	88.9	114.3
6	15.2	40.6	66.0	91.4	116.8
7	17.8	43.2	68.6	94.0	119.4
8	20.3	45.7	71.1	96.5	121.9
9	22.9	48.3	73.7	99.1	124.5

1/4-in. increments. Example: To obtain centimeters equivalent to 14^{3/4} in., read "14" on top scale, "3/4" on side scale; equivalent is 37.5 cm.

Inches	10	11	12	13	14	15
0	25.4	27.9	30.5	33.0	35.6	38.1
1/4	26.0	28.6	31.1	33.7	36.2	38.7
1/2	26.7	29.2	31.8	34.3	36.8	39.4
3/4	27.3	29.8	32.4	34.9	37.5	40.0
Inches	16	17	18	19	20	21
0	40.6	43.2	45.7	48.3	50.8	53.3
1/4	41.3	43.8	46.4	48.9	51.4	54.0
1/2	41.9	44.5	47.0	49.5	52.1	54.6
3/4	42.5	45.1	47.6	50.2	52.7	55.2

Note: 1 in. = 2.54 cm. Centimeter equivalents are rounded one decimal place by adding 0.1 when second decimal place is 5 or greater; for example, 33.48 becomes 33.5.

Fluid Volume in ounces (oz) to milliliters (mL)

$$1 \text{ fl oz} = 29.57 \text{ mL}$$

| (oz) . . . (mL) |
|-----------------|-----------------|-----------------|-----------------|
| 0.5 . . . 14.8 | 3 . . . 88.7 | 9 . . . 266.2 | 18 . . . 532.3 |
| 0.75 . . . 22.2 | 3.5 . . . 103.5 | 10 . . . 295.7 | 20 . . . 591.5 |
| 1 . . . 29.6 | 4 . . . 118.3 | 11 . . . 325.3 | 22 . . . 650.6 |
| 1.25 . . . 37.0 | 4.5 . . . 133.1 | 12 . . . 354.9 | 24 . . . 709.8 |
| 1.5 . . . 44.4 | 5 . . . 147.9 | 13 . . . 384.5 | 26 . . . 768.9 |
| 1.75 . . . 51.8 | 6 . . . 177.4 | 14 . . . 414.0 | 28 . . . 828.1 |
| 2 . . . 59.1 | 7 . . . 207.0 | 15 . . . 443.6 | 30 . . . 887.2 |
| 2.5 . . . 73.9 | 8 . . . 236.6 | 16 . . . 473.2 | 32 . . . 946.4 |

Index

- TRIS buffer 317
 THAM acetate 292
- Tri-Vi-Sol® Multivitamin Drops 317
 Vi-Sol® Multivitamin Products .. 317
- Tromethamine
 THAM acetate 292
- Tropicamide (Ophthalmic) 293
- Tylenol®
 Acetaminophen 188
- U**
- Ursodeoxycholic acid
 Ursodiol 250
- Ursodiol 250
- V**
- Vancocin®
 Vancomycin 86
- Vancomycin 86
- Vasotec®
 Enalaprilat 146
- Vecuronium 224
- Ventolin®
 Albuterol 252
- Versed®
 Midazolam 204
- Viagra®
 Sildenafil 182
- Vi-Daylin® Multivitamin
 Products 316
- Viramune®
 Nevirapine 66
- Vi-Sol® Multivitamin Drops 317
- Vi-Sol® Multivitamin Products .. 317
- Vitamin A 309
- Vitamin B6
 Pyridoxine 308
- Vitamin D 310
- Vitamin E 312
- Vitamin K₁ 314
- X**
- Xylocaine®
 Lidocaine - Antiarrhythmic 168
- Z**
- Zantac®
 Ranitidine 248
- Zegerid®
 Omeprazole 246
- Zemuron
 Rocuronium 220
- Zidovudine (ZDV, AZT) 88
- Zithromax®
 Azithromycin 14
- Zolicef®
 Cefazolin 20
- Zosyn®
 Piperacillin-Tazobactam 74
- Zovirax®
 Acyclovir 2
- Zyvox®
 Linezolid 52

Index

Symbols

- 5-FC
Flucytosine 40
- A**
- Abelcet®
Amphotericin B Lipid Complex .. 10
- Acetaminophen 188
- ActHIB®
Haemophilus b (Hib) Conjugate Vaccine 102
- Actigal®
Ursodiol 250
- Activase®
Alteplase 126
- Acyclovir 2
- Adenocard®
Adenosine 122
- Adenosine 122
- Adrenalin®
Epinephrine (Adrenaline) 150
- Albuterol 252
- Aldactone®
Spironolactone 235
- Alprostadil
Alprostadil (Prostaglandin E₁) ... 124
- Alprostadil (Prostaglandin E₁) ... 124
- Alteplase 126
- AmBisome®
Amphotericin B Liposome 11
- Amikacin 4
- Amikin®
Amikacin 4
- Aminophylline 254
- Amiodarone 128
- Amphadase®
Hyaluronidase 278
- Amphotericin B 8
- Amphotericin B Lipid Complex .. 10
- Amphotericin B Liposome 11
- Ampicillin 12
- Ancef®
Cefazolin 20
- Ancobon®
Flucytosine 40
- Apresoline®
Hydralazine 160
- AquaADEKs™ Pediatric Liquid .. 296
- AquaMEPHYTON®
Vitamin K₁ 314
- Aquasol A® Parenteral
Vitamin A 309

- Aquasol E®
Vitamin E 312
- Aquavite E®
Vitamin E 312
- Ativan®
Lorazepam 200
- Atropine 132
- Atrovent®
Ipratropium 262
- Atrovent® HFA
Ipratropium 262
- Axid®
Nizatidine 245
- Azactam®
Aztreonam 16
- Azithromycin 14
- Aztreonam 16
- B**
- Bactocill®
Oxacillin 68
- Bactroban®
Mupirocin 60
- BayHepB®
Hepatitis B Immune Globulin (Human) 104
- Benzylpenicillin
Penicillin G 70
- Beractant
Survanta® 271
- Betapace®
Sotalol 186
- Brevibloc®
Esmolol 154
- Bumetanide 228
- Bumex®
Bumetanide 228
- C**
- Cafcit®
Caffeine Citrate 256
- Caffeine Citrate 256
- Calcium - Oral 297
- Calcium carbonate
Calcium - Oral 297
- Calcium chloride 10% 298
- Calcium glubionate
Calcium - Oral 297
- Calcium gluconate
Calcium - Oral 297
- Calcium gluconate 10% 300
- Calfactant
Infasurf® 270

Cancidas®	
Caspofungin	18	
Capoten®	
Captopril	134	
Captopril	134	
Cardene® I.V.	
Nicardipine	174	
Carimune® NF (IVIG)	
Intravenous Immune Globulin (Human)	110	
Caspofungin	18	
Cathflo® Activase®	
Alteplase	126	
Cefazolin	20	
Cefepime	22	
Cefotaxime	24	
Cefoxitin	26	
Ceftazidime	28	
Ceftriaxone <i>Befort</i>	30	
Cerebyx®	
Fosphenytoin	194	
Chloral hydrate	189	
Chloramphenicol	32	
Chloromycetin®	
Chloramphenicol	32	
Chlorothiazide	230	
cholecalciferol (D3)	
Vitamin D	310	
Cimetidine	238	
Claforan®	
Cefotaxime	24	
Cleocin®	
Clindamycin	34	
Clindamycin	34	
COMVAX®	
Hib Conjugate/Hepatitis B Combination Vaccine	108	
Cordarone®	
Amiodarone	128	
Curosurf®	268	
CycloGel®	
Cyclopentolate (Ophthalmic) ...	274	
Cyclopentolate (Ophthalmic) ...	274	
Cytovene®	
Ganciclovir	42	
D	
DAPTACEL®	
DTaP Vaccine	96	
Decadron®	
Dexamethasone	258	
Dexamethasone	258	
Diazoxide	275	
Diffucan®	
Fluconazole	38	
Digoxin	136	
Dilantin®	
Phenytoin	218	
Dilution Table	320	
Dilution Table - EleCare®	
Powder	343	
Diuril®	
Chlorothiazide	230	
Dobutamine	138	
Dobutrex®	
Dobutamine	138	
Dolophine®	
Methadone	202	
Dopamine	142	
Dornase alfa	261	
DT Vaccine	94	
DTaP Vaccine	96	
DTaP-HepB-IPV Combination Vaccine	98	
E	
E.E.S.®	
Erythromycin	36	
EleCare®	342	
EMLA®	276	
Enalapril maleate	145	
Enalaprilat	146	
Enfamil A.R.® LIPIL® 20	356	
Enfamil® EnfaCare® LIPIL® + Enfamil® LIPIL® Concentrate 24	350	
Enfamil® EnfaCare® LIPIL® + Enfamil® LIPIL® Concentrate 27	351	
Enfamil® EnfaCare® LIPIL® 22 ..	349	
Enfamil® Gentlelease® LIPIL® ..	362	
Enfamil® Human Milk Fortifier ..	325	
Enfamil® LactoFree® LIPIL® 20 ..	357	
Enfamil LIPIL® with Iron 20 ..	355	
Enfamil® Premature LIPIL® 20 ..	353	
Enfamil® Premature LIPIL® 24 ..	354	
Enfamil® Premature LIPIL® 24 + Enfamil® LIPIL® Concentrate 30	352	
Enfamil® ProSobee® LIPIL® 20 ..	358	
Enfaport® LIPIL®	363	
Engerix-B®	
Hepatitis B Vaccine (Recombinant)	106	

Enoxaparin	148	Gentamicin	44
Epinephrine (Adrenaline)	150	Glucagon	277
Epivir®		Glucagon®	
Lamivudine (3TC)	50	Glucagon	277
Epoetin alfa	100	Good Start® DHA & ARA	366
Epogen®		H	
Epoetin alfa	100	Haemophilus b (Hib) Conjugate Vaccine	102
Ergocalciferol (D2)		H-BIG®	
Vitamin D	310	Hepatitis B Immune Globulin (Human)	104
EryPed®		Heparin	158
Erythromycin	36	Hepatitis B Immune Globulin (Human)	104
Erythromycin	36	Hepatitis B Vaccine (Recombinant)	106
Esmolol	154	Hib Conjugate/Hepatitis B Combination Vaccine	108
F		HibTITER®	
Famotidine	240	Haemophilus b (Hib) Conjugate Vaccine	102
Fat Emulsion	370	Human Milk (Mature)	321
Fentanyl	190	Hyaluronidase	278
Fer-In-Sol®		Hydase™	
Ferrous sulfate.....	302	Hyaluronidase	278
Ferrous sulfate	302	Hydralazine	160
Flagyl®		Hydrochlorothiazide	234
Metronidazole	56	Hydrocortisone	280
Flebogamma® (IVIG)		HyperHEP® B S/D	
Intravenous Immune Globulin (Human)	110	Hepatitis B Immune Globulin (Human)	104
Flecainide	156	I	
Fluconazole	38	Ibuprofen Lysine	102
Flucytosine	40	Imipenem/Cilastatin	4
Flumazenil	192	Inderal®	
Fortaz®		Propranolol	180
Ceftazidime	28	Indocin®	
Fosphenytoin	194	Indomethacin	164
Fungizone®		Indomethacin	164
Amphotericin B	8	INFANRIX®	
Furosemide	232	DTaP Vaccine	96
G		Infasurf®	270
Gammagard® (IVIG)		INFeD®	
Intravenous Immune Globulin (Human)	110	Iron Dextran	306
Gammar®-P (IVIG)		INFUVITE® Pediatric	304
Intravenous Immune Globulin (Human)	110	iNO	
Gamunex® (IVIG)		Nitric Oxide.....	264
Intravenous Immune Globulin (Human)	110	INOmax	
Ganciclovir	42	Nitric Oxide.....	264
Garamycin®		Insulin	282
Gentamicin	44		

Intralipid®		Merrem®	
Fat Emulsion	370	Meropenem	54
Intravenous Immune Globulin (Human)	110	Methadone	202
IPOL®		Metoclopramide	244
Poliovirus Vaccine Enhanced-Inactivated	115	Metronidazole	56
Ipratropium	262	Micafungin	58
Iron		Microlipid®	369
Ferrous sulfate.....	302	Midazolam	<u>204</u>
Iron Dextran	306	Milrinone	172
Isoproterenol	166	Morphine	208
Isuprel®		Mupirocin	60
Isoproterenol	166	Mycamine®	
Iveegam® (IVIG)		Micafungin	58
Intravenous Immune Globulin (Human)	110	Mycostatin®	
K		Nystatin	67
Kefzol®		Mydral®	
Cefazolin	20	Tropicamide (Ophthalmic)	293
Keppra®		Mydriacyl®	
Levetiracetam	196	Tropicamide (Ophthalmic)	293
L		N	
Lamivudine (3TC)	50	Nabi-HB®	
Lanoxin®		Hepatitis B Immune Globulin (Human)	104
Digoxin	136	Nafcillin	62
Lansoprazole	242	Naloxone	210
Lasix®		Narcan®	
Furosemide	232	Naloxone	210
Levetiracetam	196	Nembutal®	
Levothroid®		Pentobarbital	214
Levothyroxine (T ₄)	284	Neocate® 20	367
Levothyroxine (T₄)	284	Neoprofen®	
Lidocaine - Antiarrhythmic	168	Ibuprofen Lysine	162
Lidocaine - Anticonvulsant	198	Neostigmine	211
Lignocaine		Neo-Synephrine®	
Lidocaine - Anticonvulsant	198	Phenylephrine (Ophthalmic)	288
Linezolid	52	Netilmicin	64
Liposyn®		Nevirapine	66
Fat Emulsion	370	Nexterone®	
Lorazepam	200	Amiodarone	128
Lovenox®		Nicardipine	174
Enoxaparin	148	Nilstat®	
	341	Nystatin	67
M		Nipride®	
Maxipime®		Sodium Nitroprusside	184
Cefepime	22	Nitric Oxide	264
MCT Oil	368	Nitropress®	
Mefoxin®		Sodium Nitroprusside	184
Cefoxitin	26	Nizatidine	245
Meropenem	54	Norcuron®	
		Vecuronium	224
		Nutramigen® AA™ LIPIL®	365

- Nutramigen® LIPIL® 20 364
Nystatin 67
- O**
- Octagam® (IVIG)
Intravenous Immune Globulin
(Human) 110
- Octreotide 286
- Omeprazole 246
- Oxacillin 68
- P**
- Palivizumab 112
- Panadol®
Acetaminophen 188
- Pancuronium 212
- Panglobulin® NF
Intravenous Immune Globulin
(Human) 110
- Papaverine 176
- Pavulon®
Pancuronium 212
- PEDIARIX®
DTaP-HepB-IPV Combination
Vaccine 98
- PediaSure® 347
- PediaSure® Enteral 348
- PedvaxHIB®
Haemophilus b (Hib)
Conjugate Vaccine 102
- Penicillin G 70
- Pentobarbital 214
- Pepcid®
Famotidine 240
- Pfizerpen®
Penicillin G 70
- Phenobarbital 216
- Phentolamine 177
- Phenylephrine (Ophthalmic) 288
- Phenytoin 218
- phytonadione
Vitamin K₁ 314
- Piperacillin 72
- Piperacillin-Tazobactam 74
- Pipracil®
Piperacillin 72
- Pneumococcal 7-Valent Conjugate
Vaccine 114
- Poliovirus Vaccine
Enhanced-Inactivated 115
- Polygam® (IVIG)
Intravenous Immune Globulin
(Human) 110
- Poly-Vi-Sol® Multivitamin Drops
Vi-Sol® Multivitamin Drops 317
- Poractant alfa
Curosurf® 158
- Potassium chloride
- Prefrin Liquifilm®
Phenylephrine (Ophthalmic) 288
- Pregestimil® LIPIL® 20 359
- Pregestimil® LIPIL® 24 360
- Pregestimil® LIPIL® Powder 20 361
- Preterm Human Milk + Enfamil®
Human Milk Fortifier 323
- Preterm Human Milk + Prolact+
H²MF™ Human Milk Fortifier .. 324
- Preterm Human Milk + Similac®
Human Milk Fortifier 322
- Preterm Human Milk + Similac®
Special Care® 30 (1:1 ratio) 328
- Prevacid®
Lansoprazole 242
- Prevnar®
Pneumococcal 7-Valent
Conjugate Vaccine 114
- Prilosec®
Omeprazole 246
- Primacor®
Milrinone 172
- Primaxin®
Imipenem/Cilastatin 48
- Procainamide 178
- Procrit®
Epoetin alfa 100
- Proglycem®
Diazoxide 275
- Prolact+ H²MF™ Human Milk
Fortifier 327
- Pronestyl®
Procainamide 178
- Propranolol 180
- Prostaphlin®
Oxacillin 68
- Prostigmin®
Neostigmine 211
- Prostin VR Pediatric®
Alprostadil (Prostaglandin E₁) ... 124
- Protamine 181
- Proventil®
Albuterol 252
- Pseudomonic acid A
Mupirocin 60
- Pulmozyme®
Dornase alfa 261
- Pyridoxine 308

Contents

Abbreviations	vii	
Antimicrobials	1	
Acyclovir	2	Hepatitis B Vaccine (Recombinant)
Amikacin	4	106
Amphotericin B	8	Hib Conjugate/Hepatitis B Combination Vaccine
Amphotericin B Lipid Complex	10	108
Amphotericin B Liposome	11	Intravenous Immune Globulin (Human)
Ampicillin	12	110
Azithromycin	14	Palivizumab
Aztreonam	16	112
Caspofungin	18	Pneumococcal 7-Valent Conjugate Vaccine
Cefazolin	20	114
Cefepime	22	Poliovirus Vaccine Enhanced-Inactivated
Cefotaxime	24	115
Cefoxitin	26	Rotavirus Vaccine (Rotarix®)
Ceftazidime	28	116
Ceftriaxone	30	Rotavirus Vaccine (RotaTeq®)
Chloramphenicol	32	118
Clindamycin	34	
Erythromycin	36	
Fluconazole	38	Cardiovascular Drugs 121
Flucytosine	40	Adenosine
Ganciclovir	42	122
Gentamicin	44	Alprostadil (Prostaglandin E ₁)
Imipenem/Cilastatin	48	124
Lamivudine (3TC)	50	Alteplase
Linezolid	52	126
Meropenem	54	Amiodarone
Metronidazole	56	128
Micafungin	58	Atropine
Mupirocin	60	132
Nafcillin	62	Captopril
Netilmicin	64	134
Nevirapine	66	Digoxin
Nystatin	67	136
Oxacillin	68	Dobutamine
Penicillin G	70	138
Piperacillin	72	Dopamine
Piperacillin-Tazobactam	74	142
Quinupristin/Dalfopristin	76	Enalapril maleate
Rifampin	78	145
Ticarcillin/Clavulanate	80	Enalaprilat
Tobramycin	82	146
Vancomycin	86	Enoxaparin
Zidovudine (ZDV, AZT)	88	148
Biologics	91	Epinephrine (Adrenaline)
DT Vaccine	94	150
DTaP Vaccine	96	Esmolol
DTaP-HepB-IPV Combination Vaccine	98	154
Epoetin alfa	100	Flecainide
Haemophilus b (Hib) Conjugate Vaccine	102	156
Hepatitis B Immune Globulin (Human)	104	Heparin
		158
		Hydralazine
		160
		Ibuprofen Lysine
		162
		Indomethacin
		164
		Isoproterenol
		166
		Lidocaine - Antiarrhythmic ..
		168
		Milrinone
		172
		Nicardipine
		174
		Papaverine
		176
		Phentolamine
		177
		Procainamide
		178
		Propranolol
		180
		Protamine
		181
		Sildenafil
		182
		Sodium Nitroprusside
		184
		Sotalol
		186
CNS Drugs	187	
Acetaminophen	188	
Chloral hydrate	189	
Fentanyl	190	
Flumazenil	192	
Fosphenytoin	194	
Levetiracetam	196	
Lidocaine - Anticonvulsant ...	198	