ACYCLOVIR

(ay-sye-kloe-vir) Zovirax®

ANTIVIRAL (HERPES)

Prescriber Highlights

- Used primarily in birds for Pacheco's disease; may be useful in cats for Herpes infection
- If given rapidly IV, may be nephrotoxic
- Oral use may cause GI distress
- Reduce dosage with renal insufficiency
- May be fetotoxic at high dosages

Uses/Indications

Acyclovir may be useful in treating herpes infections in a variety of avian species and in cats with corneal or conjunctival herpes infections. Its use in veterinary medicine is not well established, however, and it should be used with caution. Acyclovir has relatively mild activity against *Feline Herpesvirus-1* when compared to some of the newer antiviral agents (*e.g.*, ganciclovir, cidofovir, or penciclovir).

Acyclovir is being investigated as a treatment for equine herpes virus type-1 myeloencephalopathy in horses, but clinical efficacy has not yet been proven and the drug's poor oral bioavailability is problematic. There continues to be interest in finding a dosing regimen that can achieve therapeutic levels and be economically viable, particularly since the drug's use during a recent outbreak appeared to have some efficacy in reducing morbidity and mortality (not statistically proven). Also, intravenous acyclovir may be economically feasible to treat some neonatal foals.

Pharmacology/Actions

Acyclovir has antiviral activity against a variety of viruses including herpes simplex (types I and II), cytomegalovirus, *Epstein-Barr*, and *varicella-Zoster*. It is preferentially taken up by these viruses, and converted into the active triphosphate form where it inhibits viral DNA replication.

Pharmacokinetics

In dogs, acyclovir bioavailability varies with the dose. At doses of 20 mg/kg and below, bioavailability is about 80%, but declines to about 50% at 50 mg/kg. Bioavailability in horses after oral administration is very low (<4%) and oral doses of up to 20 mg/kg may not yield sufficient levels to treat equine herpes virus. Elimination half-lives in dogs, cats and horses are approximately 3 hours, 2.6 hours, and 10 hours, respectively.

In humans, acyclovir is poorly absorbed after oral administration (approx. 20%) and absorption is not significantly affected by the presence of food. It is widely distributed throughout body tissues and fluids including the brain, semen, and CSF. It has low protein binding and crosses the placenta. Acyclovir is primarily hepatically metabolized and has a half-life of about 3 hours in humans. Renal disease does not significantly alter half-life unless anuria is present.

Contraindications/Precautions/Warnings

Acyclovir is potentially contraindicated (assess risk vs. benefit) during dehydrated states, pre-existing renal function impairment, hypersensitivity to it or other related antivirals, neurologic deficits, or previous neurologic reactions to other cytotoxic drugs.

Adverse Effects

With parenteral therapy potential adverse effects include thrombophlebitis, acute renal failure, and ecephalopathologic changes (rare). GI disturbances may occur with either oral or parenteral therapy.

Preliminary effects noted in cats, include leukopenia and anemias, which are apparently reversible with discontinuation of therapy.

Reproductive/Nursing Safety

Acyclovir crosses the placenta, but rodent studies have not demonstrated any teratogenic effects thus far. Acyclovir crosses into maternal milk but associated adverse effects have not been noted. In humans, the FDA categorizes this drug as category ***C*** for use during pregnancy (*Animal studies have shown an adverse effect on the fetus, but there are no adequate studies in humans; or there are no animal reproduction studies and no adequate studies in humans.*)

Acyclovir concentrations in milk of women following oral administration have ranged from 0.6 to 4.1 times those found in plasma. These concentrations would potentially expose the breastfeeding infant to a dose of acyclovir up to 0.3 mg/kg/day. Data for animals was not located. Use caution when administering to a nursing patient.

Overdosage/Acute Toxicity

Oral overdose is unlikely to cause significant toxicity. In a review of 105 dogs ingesting acyclovir (Richardson 2000), 10 animals were considered cases of acyclovir toxicosis. Adverse effects included vomiting, anorexia, diarrhea and lethargy. One dog developed polyuria/polydipsia and another dog developed a mildly elevated BUN and serum creatinine 24 hours after ingesting 2068 mg/kg of acyclovir. Per the APCC database, acute renal injury was reported in one dog at a dose of 250 mg/kg. Treatment consists of standard decontamination procedures and supportive therapy. Contact an animal poison control center for further information, if necessary.

There were 92 exposures to acyclovir reported to the ASPCA Animal Poison Control Center (APCC; www.apcc.aspca.org) during 2005–2006. In these cases 90 were dogs with 7 showing clinical signs; the remaining 2 cases were cats that showed no clinical signs. Common findings recorded in decreasing frequency included vomiting, diarrhea, lethargy, anorexia, and crystalluria.

Drug Interactions

The following drug interactions have either been reported or are theoretical in humans or animals receiving acyclovir and may be of significance in veterinary patients:

- **NEPHROTOXIC MEDICATIONS:** Concomitant administration of IV acyclovir with nephrotoxic medications may increase the potential for nephrotoxicity occurring. Amphotericin B may potentiate the antiviral effects of acyclovir but it also increases chances for development of nephrotoxicity.
- **ZIDOVUDINE:** Concomitant use with zidovudine may cause additional CNS depression.

Doses

- **BIRDS:**

  For treatment of Pacheco's Disease:

  a) 80 mg/kg PO q8h or 40 mg/kg q8h IM (do not use parenterally for more than 72 hours as it can cause tissue necrosis at site of injection) (Oglesbee and Bishop 1994)

  b) 80 mg/kg in oral suspension once daily PO; mix suspension with peanut butter or add to drinking water 50 mg in 4 oz of water for 7–14 days (Jenkins 1993)

  c) When birds are being individually treated: 80 mg/kg PO or IM twice daily (Speer 1999)

d) For prophylaxis: Exposed birds are given 25 mg/kg IM once (give IM with caution as it is very irritating), and then acyclovir is added to drinking water at 1 mg/mL and to the food at 400 mg/quart of seed for a minimum of 7 days. Quaker parrots have been treated with a gavage of acyclovir at 80 mg/kg q8h for 7 days. (Johnson-Delaney 2005b)

■ **CATS:**

For Herpesvirus-1 infections:

a) 10–25 mg/kg PO twice daily. Never begin therapy until diagnostic evaluation is completed. May be toxic in cats; monitor CBC every 2–3 weeks. (Lappin 2003b)

■ **HORSES:**

a) Although efficacy is undetermined, anecdotal use of acyclovir orally at 10 mg/kg PO 5 times daily or 20 mg/kg PO q8h may have had some efficacy in preventing or treating horses during EHV-1 outbreaks. Additional studies may further clarify the usefulness of such dosing regimens—Plumb 2007; based upon (Wilkins 2004a) & (Henninger, Reed et al. 2007)

Monitoring

■ Renal function tests (BUN, Serum Cr) with prolonged or IV therapy

■ Cats: CBC

Chemistry/Synonyms

An antiviral agent, acyclovir (also known as ACV or acycloguanosine), occurs as a white, crystalline powder. 1.3 mg are soluble in one mL of water. Acyclovir sodium has a solubility of greater than 100 mg/mL in water. However, at a pH of 7.4 at 37°C it is practically all unionized and has a solubility of only 2.5 mg/mL in water. There is 4.2 mEq of sodium in each gram of acyclovir sodium.

Acyclovir may be known as: aciclovirum, acycloguanosine, acyclovir, BW-248U, *Zovirax®*, *Acic®*, *Aciclobene®*, *Aciclotyrol®*, *Acivir®*, *Acyrax®*, *Cicloviral®*, *Geavir®*, *Geavir®*, *Herpotern®*, *Isavir®*, *Nycovir®*, *Supraviran®*, *Viclovir®*, *Virherpes®*, *Viroxy®*, *Xorox®*, or *Zovirax®*.

Storage/Stability/Compatibility

Acyclovir capsules and tablets should be stored in tight, light resistant containers at room temperature. Acyclovir suspension and sodium sterile powder should be stored at room temperature.

When reconstituting acyclovir sodium do not use bacteriostatic water with parabens as precipitation may occur. The manufacturer does not recommend using bacteriostatic water for injection with benzyl alcohol because of the potential toxicity in neonates. After reconstitution with 50–100 mL of a standard electrolyte or dextrose solution, the resulting solution is stable at 25°C for 24 hours. Acyclovir is reportedly **incompatible** with biologic or colloidial products (*e.g.*, blood products or protein containing solutions). It is also **incompatible** with dopamine HCl, dobutamine, fludarabine phosphate, foscarnet sodium, meperidine and morphine sulfate. Many other drugs have been shown to be **compatible** in specific situations. Compatibility is dependent upon factors such as pH, concentration, temperature and diluent used; consult specialized references or a hospital pharmacist for more specific information.

Dosage Forms/Regulatory Status

VETERINARY-LABELED PRODUCTS: None

HUMAN-LABELED PRODUCTS:

Acyclovir Tablets: 400 mg & 800 mg; *Zovirax®* (GlaxoWellcome); generic; (Rx)

Acyclovir Capsules: 200 mg; *Zovirax®* (GlaxoWellcome); generic; (Rx)

Acyclovir Suspension: 200 mg/5 mL in 473 mL; *Zovirax®* (GlaxoWellcome); generic; (Rx)

Acyclovir Sodium Injection (for IV infusion only): 50 mg/mL (as sodium): generic; (Rx)

Acyclovir Powder for Injection: 500 mg/vial (as sodium) in 10 mL vials; 1000 mg/vial (as sodium) in 20 mL vials; 500 mg/vial Lyophilized in 10 mL vials; *Zovirax®* (GlaxoWellcome); generic; (Rx)

Acyclovir Ointment: 5% (50 mg/g) in 15 g; *Zovirax®* (Biovail); (Rx)

Acyclovir Cream: 5% (50 mg/g) in 2g tubes; *Zovirax®* (Biovail); (Rx)

AGLEPRISTONE

(a-gle-*pris*-tone) Alizin®, Alizine®

INJECTABLE PROGESTERONE BLOCKER

Prescriber Highlights

- **Injectable progesterone blocker indicated for pregnancy termination in bitches; may also be of benefit in inducing parturition or in treating pyometra complex in dogs & progesterone-dependent mammary hyperplasia in cats**
- **Not currently available in USA; marketed for use in dogs in Europe, South America, etc.**
- **Localized injection site reactions are most commonly noted adverse effect; other adverse effects reported in >5% of patients include: anorexia (25%), excitation (23%), depression (21%), & diarrhea (13%)**

Uses/Indications

Aglepristone is labeled (in the U.K. and elsewhere) for pregnancy termination in bitches up to 45 days after mating.

In dogs, aglepristone may prove useful in inducing parturition or treating pyometra complex (often in combination with a prostaglandin F analog such as cloprostenol).

In cats, it may be of benefit for pregnancy termination (one study documented 87% efficacy when administered at the recommended dog dose at day 25) or in treating mammary hyperplasias or pyometras.

Pharmacology/Actions

Aglepristone is a synthetic steroid that binds to the progesterone (P4) receptors thereby preventing biological effects from progesterone. It has an affinity for uterine progesterone receptors approximately three times that of progesterone. As progesterone is necessary for maintaining pregnancy, pregnancy can be terminated or parturition induced. Abortion occurs within 7 days of administration.

Benign feline mammary hyperplasias (fibroadenomatous hyperplasia; FAHs) are usually under the influence of progesterone and aglepristone can be used to medically treat this condition.

When used for treating pyometra in dogs, aglepristone can cause opening of the cervix and resumption of miometral contractility.

Within 24 hours of administration, aglepristone does not appreciably affect circulating plasma levels of progesterone, cortisol, prostaglandins or oxytocin. Plasma levels of prolactin are increased within 12 hours when used in dogs during mid-pregnancy which is probably the cause of mammary gland congestion often seen in these dogs.