DEXMEDETOMIDINE

(deks-mee-deh-*toe*-mih-deen) Dexdomitor®

ALPHA-2 ADRENERGIC AGONIST

Prescriber Highlights

- Alpha-2 agonist similar to medetomidine used as a pre-anesthetic & for sedation, analgesia in dogs & cats
- Contraindications: cardiac disease, liver or kidney diseases, shock, severe debilitation, or animals stressed due to heat, cold or fatigue; caution in very old or young animals, animals with seizure disorders, respiratory, renal or kidney disorders
- Adverse Effects: Bradycardia, occasional AV blocks, decreased respiration, hypothermia, urination, vomiting, hyperglycemia, & pain on injection (IM). Rarely: prolonged sedation, paradoxical excitation, hypersensitivity, apnea & death from circulatory failure
- Dosed in dogs based upon body surface area, not weight
- Effects may be reversed with atipamezole

Note: *This compound has been approved for use in dogs in the USA, but at the time of writing (Autumn 2007) it had not yet been marketed in the USA and the package insert was not available for review. The following should be considered a preliminary monograph.*

Uses/Indications

In the USA, dexmedetomidine for dogs is approved for use as a sedative and analgesic to facilitate clinical examinations, clinical procedures, minor surgical procedures, and minor dental procedures, and as a preanesthetic to general anesthesia.

In Europe, dexmedetomidine is additionally indicated for use in cats similarly to dogs above, but when used as premed it is indicated for use prior to ketamine general anesthesia.

Pharmacology/Actions

Dexmedetomidine is the dextrorotatory enantiomer of the alpha-2 adrenergic agonist, medetomidine. The other enantiomer, levomedetomidine is thought to be pharmacologically inactive so dexmedetomidine is about two times more potent than medetomidine.

Dexmedetomidine is much more specific than xylazine for alpha$_2$ receptors versus alpha$_1$ receptors. The pharmacologic effects of dexmedetomidine include: depression of CNS (sedation, anxiolysis), analgesia, GI (decreased secretions, varying affects on intestinal muscle tone) and endocrine functions, peripheral and cardiac vasoconstriction, bradycardia, respiratory depression, diuresis, hypothermia, analgesia (somatic and visceral), muscle relaxation (but not enough for intubation), and blanched or cyanotic mucous membranes. Effects on blood pressure are variable, but dexmedetomidine can cause hypertension longer than does xylazine.

Pharmacokinetics

In dogs after IM administration, dexmedetomidine is absorbed (bioavailability 60%) and reaches peak plasma levels in about 35 minutes. Volume of distribution is 0.9 L/kg and elimination half-life is approximately 40–50 minutes. The drug is primarily metabolized in the liver via glucuronidation and N-methylation. No metabolites are active and they are eliminated primarily in the urine and to lesser extent in the feces.

In cats after IM administration, dexmedetomidine is absorbed and reaches peak plasma levels of about 17 ng/mL occur in about 15 minutes. Volume of distribution is 2.2 L/kg and elimination half-life is approximately 1 hour. Metabolites are eliminated primarily in the urine and to lesser extent in the feces.

In humans after IV administration, dexmedetomidine is rapidly distributed, undergoes almost complete biotransformation via both glucuronidation and CY-450 enzymes systems and has a terminal elimination half-life of about 2 hours. Metabolites are eliminated in the urine and feces.

Contraindications/Precautions/Warnings

The European labeling states not to use in puppies less than 6 months old or in kittens less than 5 months old; in animals with cardiovascular disorders; in animals with severe systemic disease or that are moribund; or in animals known to be hypersensitive to the active substance or any of the excipients.

Use with caution in animals with, or prone to developing, seizures. Dexmedetomidine lowered the seizure threshold in cats undergoing anesthesia with enflurane.

Adverse Effects

The adverse effects reported with medetomidine or dexmedetomidine are essentially extensions of their pharmacologic effects including bradycardia, muscle tremors, transient hypertension, occasional AV blocks, decreased respiration, hypothermia, urination, vomiting, hyperglycemia, and pain on injection (IM). Rare effects that have been reported, include: prolonged sedation, paradoxical excitation, hypersensitivity, pulmonary edema, apnea, and death from circulatory failure.

Reproductive/Nursing Safety

The drug is not recommended for use in pregnant dogs or those used for breeding purposes because safety data for use during pregnancy is insufficient; therefore use only when the benefits clearly outweigh the drug's risks. However, no teratogenic effects were observed when rats were given up to 200 mcg/kg SC from days 5–16 of gestation or when rabbits were given up 96 mcg/kg IV from days 6–18 of gestation. 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.*)

Dexmedetomidine is distributed into the milk of lactating rats; safe use during nursing has not been established.

Overdosage/Acute Toxicity

Single doses of up to 5X (IV) and 10X (IM) were tolerated in dogs, but adverse effects can occur (see above). Because of the potential of additional adverse effects occurring (heart block, PVC's, or tachycardia), treatment of medetomidine-induced bradycardia with anticholinergic agents (atropine or glycopyrrolate) is usually not recommended. Atipamezole is probably a safer choice to treat any medetomidine-induced effect.

Drug Interactions

Note: Before attempting combination therapy with dexmedetomidine, it is strongly advised to access references from veterinary anesthesiologists familiar with the use of this product.

- **ANESTHETICS, OPIATES, SEDATIVE/HYPNOTICS:** Effects may be additive; dosage reduction of one or both agents may be required

The following drug interactions have either been reported or are theoretical in humans or animals receiving medetomidine (a related compound) and may be of significance in veterinary patients:

- **ATROPINE, GLYCOPYRROLATE:** The use of atropine or glycopyrrolate to prevent or treat medetomidine-caused bradycardia is controversial as tachycardia and hypertension may result. This is more

important when using higher doses of medetomidine and concomitant use is discouraged.

- **YOHIMBINE:** May reverse the effects of medetomidine; but atipamezole is preferred for clinical use to reverse the drug's effects

Laboratory Considerations

- Medetomidine (and presumably dexmedetomidine) can inhibit ADP-induced **platelet aggregation** in cats.

Doses

- **DOGS:**
  a) For sedation and analgesia: 375 mcg/m2 body surface area (BSA) IV; 500 mcg/m2 BSA IM. The mcg/kg dosage decreases as body weight increases.

  As a preanesthetic: Depending on duration and severity of the procedure and anesthetic regimen: 125–375 mcg/m2 IM. (FOI Summary; *Dexdomitor*®—Orion)
- **CATS:**
  a) For sedation and analgesia, or as a preanesthetic: 40 mcg/kg IM. Expected sedative and analgesic effects are reached within 15 minutes and maintained for up to 60 minutes. (*Dexdomitor*®—Pfizer U.K.)

Monitoring

- Level of sedation and analgesia; heart rate; body temperature
- Heart rhythm, blood pressure, respiration rate, and pulse oximetry should be considered, particularly in higher risk patients

Client Information

- This drug should be administered and monitored by veterinary professionals only
- Clients should be made aware of the potential adverse effects associated with its use, particularly in dogs at risk (older, preexisting conditions)

Chemistry/Synonyms

Dexmedetomidine is the dextrorotatory enantiomer of medetomidine.

Dexmedetomidine HCl may also be known as (S)-medetomidine, (+)-medetomidine, MPV 1440, MPV 295, or MPV 785. Trade names include: *Precedex*® or *Dexdomitor*®.

Storage/Stability/Compatibility

Store the injection at room temperature (15–30°C); do not freeze.

Dexmedetomidine is **not compatible** with butorphanol when mixed in the same syringe.

Dosage Forms/Regulatory Status

VETERINARY-LABELED PRODUCTS:

Dexmedetomidine HCl 0.5 mg/mL (500 mcg/mL) in 10 mL multidose vials; *Dexdomitor*® (Orion); (Rx). **Note:** At time of writing, approved but not marketed in the USA.

HUMAN-LABELED PRODUCTS:

Dexmedetomidine HCl 100 mcg/mL, preservative free in 2 mL vials; *Precedex*® (Abbott); (Rx)

DEXPANTHENOL
D-PANTHENOL

(dex-*pan*-the-nole) Ilopan®

Prescriber Highlights

- Precursor to Coenzyme A that ostensibly aids in production of acetylcholine
- Potentially may be useful in the prevention of post-surgical ileus, but efficacy is in doubt
- Contraindications: Ileus secondary to mechanical obstruction or in cases of colic caused by the treatment of cholinergic anthelmintics

Uses/Indications

Dexpanthenol has been suggested for use in intestinal atony or distension, postoperative retention of flatus and feces, prophylaxis and treatment of paralytic ileus after abdominal surgery or traumatic injuries, equine colic (not due to mechanical obstruction) and any other condition when there is an impairment of smooth muscle function. Controlled studies are lacking with regard to proving the efficacy of the drug for any of these indications.

Pharmacology/Actions

A precursor to pantothenic acid, dexpanthenol acts as a precursor to coenzyme A that is necessary for acetylation reactions to occur during gluconeogenesis and in the production of acetylcholine. It has been postulated that post-surgical ileus can be prevented by giving high doses of dexpanthenol, thereby assuring adequate levels of acetylcholine. However, one study in normal horses (Adams, Lamar, and Masty 1984) failed to demonstrate any effect of dexpanthenol on peristalsis.

Pharmacokinetics

Dexpanthenol is rapidly converted to pantothenic acid *in vivo*, which is widely distributed throughout the body, primarily as coenzyme A.

Contraindications/Precautions/Warnings

Dexpanthenol is contraindicated in ileus secondary to mechanical obstruction, or in cases of colic caused by the treatment of cholinergic anthelmintics. It is also contraindicated in humans with hemophilia as it may exacerbate bleeding.

Adverse Effects

Adverse reactions are reportedly rare. Hypersensitivity reactions have been reported in humans, but may have been due to the preservative agents found in the injectable product. Potentially, GI cramping and diarrhea are possible.

Reproductive/Nursing Safety

Safety in use during pregnancy has not been established. 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.*)

Overdosage/Acute Toxicity

The drug is considered non-toxic even when administered in high doses.