

Antisedan®

(atipamezole hydrochloride)

Sterile Injectable Solution—5.0 mg/mL

Medetomidine Reversing Agent

For intramuscular use in dogs only

NADA #141-033, Approved by FDA

CAUTION: Federal law restricts this drug to use by or on the order of a licensed veterinarian.

DESCRIPTION: Antisedan (atipamezole hydrochloride) is a synthetic α_2 -adrenergic antagonist which reverses the effects of Domitor® (medetomidine hydrochloride) in dogs. The chemical name is 4-(2-ethyl-2,3-dihydro-1H-inden-2-yl)-1H-imidazole hydrochloride. The molecular formula is $C_{14}H_{16}N_2 \cdot HCl$.

Each mL of Antisedan contains 5.0 mg atipamezole hydrochloride, 1.0 mg methylparaben (NF), 8.5 mg sodium chloride (USP), and water for injection (USP).

CLINICAL PHARMACOLOGY: Activation of peripheral and central α_2 -adrenergic receptors is known to induce a pattern of pharmacological responses including sedation, reduction of anxiety, analgesia, bradycardia, and transient hypertension with a subsequently reduced blood pressure. Atipamezole is a potent α_2 -antagonist which selectively and competitively inhibits α_2 -adrenergic receptors. The result of atipamezole administration in the dog is the rapid recovery from the sedation and other clinical effects produced by the α_2 -adrenergic agonist, medetomidine. Atipamezole is not expected to reverse the effects of other classes of sedatives, anesthetics, or analgesics.

Rapid absorption occurs following intramuscular injection, with a maximum serum concentration reached in approximately 10 minutes. Onset of arousal is usually apparent within 5 to 10 minutes of injection, depending on the depth and duration of medetomidine-induced sedation. Elimination half-life from serum is less than 3 hours. Atipamezole undergoes extensive hepatic biotransformation, with excretion of metabolites primarily in urine.

A transient, approximately 10% decrease in systolic blood pressure occurs immediately after administration of atipamezole to medetomidine-sedated dogs, followed by an increase in pressure within 10 minutes to the pre-atipamezole level. This is the opposite of the response to α_2 -agonist therapy, and is probably due to peripheral vasodilation.

Atipamezole will produce a rapid improvement in medetomidine-induced bradycardia. An increase in heart rate is usually apparent within approximately 3 minutes of injection, but approximately 40% of dogs are not expected to immediately return to presedative rate. Some dogs may experience brief heart rate elevations above baseline. Respiratory rate also increases following atipamezole injection.

INDICATIONS: Antisedan is indicated for the reversal of the clinical effects of the sedative and analgesic agent, Domitor (medetomidine hydrochloride), in dogs.

WARNING: Keep out of reach of children. Not for human use.

Atipamezole hydrochloride can be absorbed and may cause irritation following direct exposure to skin, eyes, or mouth. In case of accidental eye exposure, flush with water for 15 minutes. In case of accidental skin exposure, wash with soap and water. Remove contaminated clothing. If irritation or other adverse reaction occurs (e.g., increased heart rate, tremor, muscle cramps),

seek medical attention. In case of accidental oral exposure or injection, seek medical attention. Precaution should be used while handling and using filled syringes.

Users with cardiovascular disease (e.g., hypertension or ischemic heart disease) should take special precautions to avoid any exposure to this product.

The material safety data sheet (MSDS) contains more detailed occupational safety information.

To report adverse reactions in users or to obtain a copy of the MSDS for this product call 1-800-366-5288.

NOTE TO PHYSICIAN: This product contains an alpha-2-adrenergic antagonist.

PRECAUTIONS: Antisedan can produce an abrupt reversal of sedation and, presumably, analgesia. The potential for apprehensive or aggressive behavior should be considered in the handling of dogs emerging from sedation, especially those individuals predisposed to nervousness or fright. Persons handling dogs that have recently received Antisedan should use caution and also avoid situations where a dog could fall.

Information on use of atipamezole with concurrent drugs is inadequate; therefore, caution should be exercised when administering multiple drugs. Animals should be monitored closely, particularly for persistent hypothermia, bradycardia, and depressed respiration, until the animal has recovered completely. Caution should be used in administration of anesthetic agents to elderly or debilitated animals.

While atipamezole does reverse the clinical signs associated with medetomidine sedation, complete physiologic return to pretreatment status may not be immediate and should be monitored.

Antisedan has not been evaluated in breeding animals; therefore, the drug is not recommended for use in pregnant or lactating animals, or in animals intended for breeding.

SIDE EFFECTS: Occasional vomiting may occur. Rarely, a brief state of excitement or apprehensiveness may be seen in treated dogs. Other potential side effects of α_2 -antagonists include hypersalivation, diarrhea, and tremors.

ANIMAL SAFETY: Atipamezole was tolerated in healthy dogs receiving doses 10-fold the recommended dose and in dogs receiving repeated doses at 1-, 3-, and 5-fold doses, in the absence of medetomidine. Signs of overdose were dose-related and consistent with those expected in nonsedated dogs having received a stimulant. Signs seen at elevated doses included excitement, panting, trembling, vomiting, soft or liquid feces or vasodilation (injection) of the sclera. Some localized skeletal muscle injury was seen at the injection site; but no associated clinical signs or complications were observed. Dogs receiving the proper dose in the absence of medetomidine, or 3-fold overdose after medetomidine sedation, exhibited no significant clinical signs.

DOSAGE AND ADMINISTRATION: Antisedan is administered intramuscularly regardless of the route used for Domitor. The concentration of Antisedan has been formulated such that the volume of injection is the same (mL for mL) as the recommended dose volume of Domitor, and may be given at any time following Domitor administration. Although injection volumes are the same, the concentration of Antisedan (5.0 mg/mL) is 5 times that of Domitor (1.0 mg/mL). Dogs that are sedated but ambulatory may be treated with Antisedan, if warranted.

The dosage of Antisedan is calculated based upon body surface area. Use the table below to determine the proper injection volume based on body weight:

Antisedan Injection Volume (mL) IM	Body Wt (lb) If Domitor Given IM*	Body Wt (lb) If Domitor Given IV*
0.1		3–4
0.15	4–5	5–7
0.2	6–7	8–11
0.25	8–9	12–15
0.3	10–14	16–21
0.4	15–20	22–31
0.5	21–27	32–43
0.6	28–35	44–55
0.7	36–44	56–68
0.8	45–53	69–82
0.9	54–63	83–97
1.0	64–78	98–121
1.2	79–101	122–156
1.4	102–126	157–194
1.6	127–165	195+
2.0	166+	

*The IM dose of Domitor is 1.0 mg/m² of body surface area and the IV dose is 0.75 mg/m².

STORAGE: Store protected from light at controlled room temperature 15°–30°C (59°–86°F).

HOW SUPPLIED: Antisedan is supplied in 10-mL, multidose vials containing 5.0 mg of atipamezole hydrochloride per mL.

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Orion Pharma
Orion Corporation
Espoo, Finland

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Pfizer Animal Health
Exton, PA 19341, USA
Div. of Pfizer Inc
NY, NY 10017

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