Date of Approval: July 2, 2018

FREEDOM OF INFORMATION SUMMARY

ORIGINAL ABBREVIATED NEW ANIMAL DRUG APPLICATION

ANADA 200-624

REVERTIDINE™

(atipamezole hydrochloride)

Sterile Injectable Solution

Dogs

For the reversal of the sedative and analgesic effects of dexmedetomidine hydrochloride and medetomidine hydrochloride in dogs.

Sponsored by:

Modern Veterinary Therapeutics, LLC

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I. GENERAL INFORMATION:

A. File Number

ANADA 200-624

B. Sponsor

Modern Veterinary Therapeutics, LLC
14343 SW 119th Ave
Miami, Florida 33186

Drug Labeler Code: 015914

C. Proprietary Name

REVERTIDINE™

D. Product Established Name

atipamezole hydrochloride

E. Pharmacological Category

Alpha$_2$-adrenoreceptor antagonist

F. Dosage Form

Sterile injectable solution

G. Amount of Active Ingredient

5 mg/mL

H. How Supplied

10 mL vial

I. Dispensing Status

Rx

J. Dosage Regimen

REVERTIDINE™ is administered intramuscularly (IM) for reversal of sedation and analgesia regardless of the route used for dexmedetomidine or medetomidine. The atipamezole dose for the reversal of IV dexmedetomidine or medetomidine is 3750 mcg/m^2. The atipamezole dose for the reversal of IM dexmedetomidine or medetomidine is 5000 mcg/m^2.

The dosage of REVERTIDINE™ is calculated based on body surface area. Use the following tables to determine the correct injection volume or the correct REVERTIDINE™ dosage on the basis of kilograms of body weight.

Note that the mcg/kg dosage decreases as body weight increases.

Table 1: Atipamezole dosing for reversal of IV dexmedetomidine- or medetomidine-induced sedation/analgesia:

Dose table for REVERTIDINE™ (3750 mcg/m^2) when dexmedetomidine or medetomidine is given IV

For # lb	For # kg	Dose = mcg/kg	Volume = mL REVERTIDINE™
4-7	2-3	300	0.1
7-9	3-4	250	0.15
9-11	4-5	230	0.2
11-22	5-10	200	0.3
22-33	10-15	170	0.4
33-44	15-20	150	0.5
44-55	20-25	140	0.6
55-66	25-30	130	0.7
66-81	30-37	120	0.8
81-99	37-45	110	0.9
99-110	45-50	105	1.0
110-132	50-60	100	1.1
132-143	60-65	95	1.2
143-165	65-75	93	1.3
165-176	75-80	91	1.4
>176	>80	90	1.5

Table 2: Atipamezole dosing for reversal of IM dexmedetomidine- or medetomidine- induced sedation/analgesia:

Dose table for REVERTIDINE™ (5000 mcg/m^2) when dexmedetomidine or medetomidine is given IM

For # lb	For # kg	Dose = mcg/kg	Volume = mL REVERTIDINE™
4-7	2-3	400	0.15
7-9	3-4	350	0.2
9-11	4-5	300	0.3
11-22	5-10	250	0.4
22-29	10-13	230	0.5
29-33	13-15	210	0.6
33-44	15-20	200	0.7
44-55	20-25	180	0.8
55-66	25-30	170	0.9
66-73	30-33	160	1.0
73-81	33-37	150	1.1

For # lb	For # kg	Dose = mcg/kg	Volume = mL REVERTIDINE™
81-99	37-45	145	1.2
99-110	45-50	140	1.3
110-121	50-55	135	1.4
121-132	55-60	130	1.5
132-143	60-65	128	1.6
143-154	65-70	125	1.7
154-176	70-80	123	1.8
>176	>80	120	1.9

K. Route of Administration

Intramuscular injection

L. Species/Class

Dogs

M. Indication

REVERTIDINE™ is indicated for the reversal of the sedative and analgesic effects of dexmedetomidine hydrochloride and medetomidine hydrochloride in dogs.

N. Reference Listed New Animal Drug

ANTISEDAN®; (atipamezole hydrochloride); NADA 141-033; Orion Corp.

II. BIOEQUIVALENCE:

Under the provisions of the Federal Food, Drug, and Cosmetic Act, as amended by the Generic Animal Drug and Patent Term Restoration Act (GADPTRA) of 1988, an abbreviated new animal drug application (ANADA) may be submitted for a generic version of an approved new animal drug (reference listed new animal drug (RLNAD)). New target animal safety and effectiveness data and human food safety data (other than tissue residue data) are not required for approval of an ANADA.

Ordinarily, the ANADA sponsor is required to show that the generic product is bioequivalent to the RLNAD, which has been shown to be safe and effective. If bioequivalence is demonstrated through a clinical endpoint study, then a tissue residue study to establish the withdrawal period for the generic product should also be conducted. For certain dosage forms, the agency will grant a waiver from the requirement of performing an *in vivo* bioequivalence study (55 FR 24645, June 18, 1990; Fifth GADPTRA Policy Letter; Bioequivalence Guideline, October 9, 2002).

Based on the formulation characteristics of the generic product, Modern Veterinary Therapeutics, LLC, was granted a waiver from the requirement to perform an *in vivo* bioequivalence study for the generic product REVERTIDINE™ *(*atipamezole hydrochloride*)* Sterile Injectable Solution. The generic drug product is a sterile injectable solution, contains the same active ingredient in the same concentration and dosage form as the RLNAD, and contains no inactive ingredients that may significantly

affect the bioavailability of the active ingredient. The RLNAD is ANTISEDAN® *(*atipamezole hydrochloride*)* Sterile Injectable Solution, sponsored by Orion Corp., under NADA 141-033, and was approved for use in dogs on August 6, 1996.

III. EFFECTIVENESS:

CVM did not require effectiveness studies for this approval.

IV. TARGET ANIMAL SAFETY:

CVM did not require target animal safety studies for this approval.

V. HUMAN FOOD SAFETY:

Data on human food safety, pertaining to drug residues in food, were not required for approval of this application. This drug is approved for use in dogs, which are not food producing animals.

VI. USER SAFETY:

CVM did not require user safety studies for this approval.
The product labeling contains the following information regarding safety to humans handling, administering, or exposed to REVERTIDINE™:

- "Not for human use", "For intramuscular use in dogs only", "Keep out of reach of children.",

- "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 (for example, increased heart rate, tremor, muscle cramps), seek medical attention. In case of accidental oral exposure or injection, seek medical attention. Caution should be used while handling and using filled syringes. Users with cardiovascular disease (for example, hypertension or ischemic heart disease) should take special precautions to avoid any exposure to this product."

- "Note to Physician: This product contains an alpha$_2$-adrenergic antagonist."

VII. AGENCY CONCLUSIONS:

This information submitted in support of this ANADA satisfies the requirements of section 512(n) of the Federal Food, Drug, and Cosmetic Act and demonstrates that REVERTIDINE™, when used according to the label, is safe and effective.