FREEDOM OF INFORMATION SUMMARY

ORIGINAL ABBREVIATED NEW ANIMAL DRUG APPLICATION

ANADA 200-361

Acepromazine Maleate Injection
(acepromazine maleate)

Tranquilizer

For use as an aid in tranquilization and as a preanesthetic agent in dogs, cats, and horses.

Sponsored by:
Boehringer Ingelheim Vetmedica, Inc.
FREEDOM OF INFORMATION SUMMARY

1. GENERAL INFORMATION:
   a. File Number: ANADA 200-361
   b. Sponsor: Boehringer Ingelheim Vetmedica, Inc.
      2621 North Belt Highway
      St. Joseph, MO 64506-2002
      Drug Labeler Code: 000010
   c. Established Name: Acepromazine maleate
   d. Proprietary Name: Acepromazine Maleate Injection
   e. Dosage Form: Sterile solution
   f. How Supplied: 50 mL multidose vials
   g. How Dispensed: Rx
   h. Amount of Active Ingredients: 10 mg acepromazine maleate per mL of sterile finished product
   i. Route of Administration: Intravenous, intramuscular or subcutaneous injection
   j. Species/Class: Dogs, cats, and horses
   k. Recommended Dosage: The dosage should be individualized, depending upon the degree of tranquilization required. As a general rule, the dosage requirement in mg/lb of body weight decreases as the weight of the animal increases. The following schedule may be used as a guide to intravenous, intramuscular, or subcutaneous injection:

      Dogs – 0.25 mg-0.5 mg/lb of body weight
      Cats – 0.5-1 mg/lb of body weight
      Horses – 2-4 mg/100 lb of body weight

      Intravenous doses should be administered slowly, and a period of at least 15 minutes should be allowed for the drug to take full effect.
1. Pharmacological Category: Tranquilizer

m. Indications:

Dogs and Cats: Acepromazine Maleate Injection can be used as an aid in controlling intractable animals during examination, treatment, grooming, x-ray and minor surgical procedures; to alleviate itching as a result of skin irritation; as an antiemetic to control vomiting associated with motion sickness. Acepromazine Maleate Injection is particularly useful as a preanesthetic agent (1) to enhance and prolong the effects of barbiturates, thus reducing the requirements for general anesthesia; (2) as an adjunct to surgery under local anesthesia.

Horses: Acepromazine Maleate Injection can be used as an aid in controlling fractious animals during examination, treatment, loading and transportation. Particularly useful when used in conjunction with local anesthesia for firing, castration, neurectomy, removal of skin tumors, ocular surgery and applying casts.

n. Pioneer Product: PROMACE Injectable; acepromazine maleate; NADA 015-030; Fort Dodge Animal Health, Division of Wyeth

2. TARGET ANIMAL SAFETY AND DRUG EFFECTIVENESS:

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 (pioneer product). 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 shows the generic product is bioequivalent to the pioneer, 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 time for the generic product should also be conducted. For certain dosage forms, the agency will grant a waiver from the requirement of 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, Boehringer Ingelheim Vetmedica, Inc. was granted a waiver from the requirement of an in vivo bioequivalence study for the generic product Acepromazine Maleate Injection. The generic product is administered as an intravenous, intramuscular or subcutaneous injection, contains the same active ingredient in the same concentration and dosage form as the pioneer product, and contains no inactive ingredients that may significantly affect the absorption of the active ingredient. The pioneer product PROMACE Injectable (acepromazine maleate), the subject of Fort Dodge Animal Health, Division of Wyeth, NADA 015-030, was approved on April 8, 1964.

3. HUMAN SAFETY:

This drug is intended for use in dogs, cats and horses, which are non-food animals. Because this new animal drug is not intended for use in food producing animals, data on human safety pertaining to drug residues in food were not required for approval of this ANADA.

4. AGENCY CONCLUSIONS:

This ANADA submitted under section 512(b) of the Federal Food, Drug, and Cosmetic Act satisfies the requirements of section 512(n) of the Act and demonstrates that Acepromazine Maleate Injection, when used under its proposed conditions of use, is safe and effective for its labeled indications.

5. ATTACHMENTS:

Facsimile generic labeling and currently approved pioneer labeling are attached as follows:

Generic Labeling for ANADA 200-361:
Acepromazine Maleate Injection; vial labels and package insert

Pioneer Labeling for NADA 015-030:
PROMACE Injectable; vial labels and package insert
PromAce® Tablets
ACEPROMAZINE MALEATE TABLETS, USP

DESCRIPTION
PromAce® (acepromazine maleate, USP), a potent neuroleptic agent with a low order of toxicity, is of particular value in the tranquilization of dogs, cats and horses. Its rapid action and lack of hypnotic effect are added advantages. According to Baker, the scope of possible applications for this compound in veterinary practice is only limited by the imagination of the practitioner.

CHEMISTRY
Acepromazine [10-[(dimethylamino) propyl]phenothiazin-2-yi-methylketone] Maleate, USP has the following chemical structure:

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\includegraphics[width=0.5\textwidth]{chemical_structure.png}
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ACTIONS
PromAce® has a depressant effect on the central nervous system and, therefore, causes sedation, muscular relaxation and a reduction in spontaneous activity. It acts rapidly, exerting a prompt and pronounced calming effect.

INDICATIONS
Dogs and Cats: PromAce® Injectable and Tablets can be used as an aid in controlling intractable animals during examination, treatment, grooming, x-ray and minor surgical procedures; to alleviate itching as a result of skin irritation; as an antihistamine to control vomiting associated with motion sickness.

Horses: PromAce® Injectable can be used as an aid in controlling fractious animals during examination, treatment, loading and transportation. Particularly useful when used in conjunction with local anesthesia for firing, castration, neurectomy, removal of skin tumors, ocular surgery and applying casts.

CONTRAINDICATIONS
Phenothiazines may potentiate the toxicity of organophosphates and the activity of procaine hydrochloride. Therefore, do not use PromAce® (acepromazine maleate, USP) to control tremors associated with organic phosphate poisoning. Do not use in conjunction with organophosphorus vermifuges or ester-pasteuricides, including flea collars. Do not use with procaine hydrochloride.

WARNING
Not for use in animals intended for food.

PRECAUTIONS
Tranquilizers are potent central nervous system depressants and they can cause marked sedation with suppression of the sympathetic nervous system. Tranquilizers can produce prolonged depression or motor restlessness when given in excessive amounts or when given to sensitive animals.

Tranquilizers are additive in action to the actions of other depressants and will potentiate general anesthesia. Tranquilizers should be administered in smaller doses and with greater care during general anesthesia and also to animals exhibiting symptoms of stress, debilitation, cardiac disease, sympathetic blockade, hypovolemia or shock. PromAce®, like other phenothiazine derivatives, is detoxified in the liver; therefore, it should be used with caution in animals with a previous history of liver dysfunction or leukopenia.

Hypotension can occur after rapid intravenous injection causing cardiovascular collapse.

Epinephrine is contraindicated for treatment of acute hypotension produced by phenothiazine-derivative tranquilizers since further depression of blood pressure can occur. Other pressor amines, such as noradrenaline or phenylephrine, are the drugs of choice.

In horses, paralysis of the retractor penis muscle has been associated with the use of phenothiazine-derivative tranquilizers. Such cases have occurred following the use of PromAce®. This risk should be duly considered prior to the administration of PromAce® to male horses (castrated and uncastrated). When given, the dosage should be carefully limited to the minimum necessary for the desired effect. At the time of tranquilization, it is not possible to differentiate between reversible protrusion of the penis (a normal clinical sign of narcosis) and the irreversible paralysis of the retractor muscle. The cause of this side reaction has not been determined. It has been postulated that such paralysis may occur when a tranquilizer is used in conjunction with testosterone (or in stallions).

Accidental intracardiac injection in horses can produce clinical signs ranging from disorientation to convulsive seizures and death.

CAUTION
A few rare but serious occurrences of idiosyncratic reactions to Acepromazine may occur in dogs following oral or parenteral administration. These potentially serious adverse reactions
include behavioral disorders in dogs such as aggression, biting/chewing, and nervousness.

ADMINISTRATION AND DOSAGE

The dosage should be individualized, depending upon the degree of tranquilization required. As a general rule, the dosage requirement in mg/lb of body weight decreases as the weight of the animal increases.

**PROMACE Injectable**
(acetpromazine maleate injection, USP)

May be given intravenously, intramuscularly or subcutaneously.

The following schedule may be used as a guide to IV, IM or SC injections:

Dogs: 0.25-0.5 mg/lb of body weight
Cats: 0.5-1 mg/lb of body weight
Horses: 2-4 mg/100 lb of body weight

IV doses should be administered slowly, and a period of at least 15 minutes should be allowed for the drug to take full effect.

**PROMACE Tablets**
(acetpromazine maleate tablets, USP)

Dogs: 0.25-1 mg/lb of body weight
Cats: 0.5-1 mg/lb of body weight

Dosage may be repeated as required.

**HOW SUPPLIED**

Each mL contains 10 mg PROMACE (acetpromazine maleate, USP). Also contains sodium citrate 0.36%, citric acid 0.075%, benzyl alcohol 1% and Water for Injection, USP) in 50 mL vials.

Each light orange tablet contains 5 mg of PROMACE and is available in bottles of 100. Each orange tablet contains 10 mg of PROMACE and is available in bottles of 100 and 500.

NDC 0856-0040-01 - 5 mg - bottles of 100
NDC 0856-0070-01 - 10 mg - bottles of 100
NDC 0856-0070-02 - 10 mg - bottles of 500
NDC 0856-0070-03 - 25 mg - bottles of 100
NDC 0856-0070-04 - 25 mg - bottles of 500
NDC 0856-0070-05 - 50 mg - bottles of 100
Store at controlled room temperature 15° to 30°C (59° to 86°F)

**TOXICOLOGY**

Acute and chronic toxicity studies have shown a very low order of toxicity.

**Acute toxicity:** The LD50 dose of PROMACE in mice was determined by means of a probit transformation with the following results:

- Intravenous route: 61.37 mg/kg
- Subcutaneous route: 130.5 mg/kg
- Oral route: 256.8 mg/kg

**Chronic toxicity:** Tests in rats revealed no deleterious effects on renal or hepatic function or on hemopoeitic activity. In several groups of two male and two female beagle hounds treated for six months with daily oral doses of 20 to 40 mg/kg, no untoward effects were encountered. Hematologic studies and urinalysis gave values within normal limits. Another group of four dogs, given gradually increasing oral doses up to a level of 220 mg/kg daily and reaching a total daily dose of 22 g per dog, showed some signs of pulmonary edema and hyperemia of the internal organs, but no animal died.

When administered intramuscularly PROMACE (acetpromazine maleate, USP) causes a brief sensation of stinging comparable with that observed with other phenothiazine tranquilizers.

**CLINICAL DATA**

Controlled clinical studies in the United States and Canada have demonstrated the effectiveness and safety of PROMACE as a tranquilizer.

Good to excellent results were reported in dogs, cats and horses given PROMACE Injectable for restraint during examination, treatment and minor surgery and for preanesthetic sedation. In dogs, the drug reportedly helps control convulsions associated with distemper.

In both dogs and cats, good to excellent results were obtained when PROMACE Tablets were used to control nervousness, excess vocalization, nervous and excitable behavior, vomiting associated with motion sickness, coughing and itching caused by dermalitis.

In horses, Bauman found good results using the drug as an aid in the control of painful spasms due to colic.

Other practitioners found the drug useful as a preanesthetic sedative for nervous or aggressive horses, but it had to be administered while the animals were quiet and not in an excited state. In a trial on more than 200 horses with a wide variety of disorders, PROMACE Injectable proved to be both effective and safe.

**REFERENCES**

4. Veterinary Medical Records, Ayerst Laboratories.

Manufactured for
Fort Dodge Animal Health
Fort Dodge, Iowa 50501 USA
by Fort Dodge Animal Health
Fort Dodge, Iowa 50501 USA

Rouses Point, NY 12979
(Tabets)

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