Antiprotozoal Oral Paste

For Oral Use Only

DESCRIPTION: MARQUIS® (15% w/w ponazuril) Antiprotozoal Oral Paste is supplied in a ready-to-use syringe containing 127 grams of paste. Each gram of paste contains 150 mg of ponazuril (15% w/w). MARQUIS is designed to be delivered as an orally administered paste.

Each syringe barrel of MARQUIS contains enough paste to treat one (1) 1,200 lb (544 kg) horse for seven (7) days, at a dose of 5 mg/kg (2.27 mg/lb) body weight or to treat one 1,200 lb (544 kg) horse with a single loading dose of 15 mg/kg (8.81 mg/lb) body weight and for four days subsequently at a rate of 5 mg/kg (2.27 mg/lb) body weight. The plunger contains a dose of 5 mg/kg (2.27 mg/lb) body weight and marked for horse of 5 mg/kg body weight from 600 to 1,200 lbs (272 to 544 kg). The syringe barrel is packaged with a reusable plunger. The syringes are packaged in units of four with reusable plungers and in single syringe units with one reusable plunger.

Ponazuril is an anticoagulant (antiprotozoal) compound with activity against several genera of the phylum Apicomplexa.

CHEMICAL NOMENCLATURE AND STRUCTURE: Ponazuril 1,3,5-Trizine-2,4,6(1H, 3H, 5H)-trione, 1-methyl-3-(3-methyl- 4-A-[trifluoromethyl]oxy)phenyl)(hexyl)-IC5

CLINICAL PHARMACOLOGY: The activity of ponazuril has been demonstrated in several Apicomplexans™. Lindsay, Dubey and Kennedy® showed that the administration of MARQUIS necessary to kill Sarcocystis neurona in vitro was 0.1 to 1.0 μg/mL. Furr and Kennedy® evaluated the pharmacokinetics of ponazuril in serum and CSF in normal horses treated daily at 5 mg/kg for 28 days. At peak serum concentrations Cmax was 6.83 μg/mL and the maximum serum concentration (Cmax) was 5.59 (± 0.22) μg/mL. The terminal elimination half-life for serum (calculated using Day 28 to 42 data) was 450 (± 65) days. In Cmax, T1/2 was 14.98 (± 7.89) days and Cmin was 0.21 (± 0.07) μg/mL. A pharmacokinetic study was conducted to collect serum and cerebrospinal fluid (CSF) samples of ponazuril after a single dose of 5 mg/kg body weight. The estimated parameter values were used to model time concentration profiles for ponazuril in serum and CSF. The model results were used to estimate the size of the loading dose needed to support the achievement of steady state serum and CSF levels after the first dose. The appropriate loading dose, calculated on the basis of the accumulation ratio i.e. the fold increase in serum drug concentrations once steady state conditions have been achieved, was 15 mg/kg (8.81 mg/lb) body weight. This dose represents the range of estimated accumulation ratios of 2.3 to 3.3. Thus, a three-fold loading dose (3.75 mg/lb) was selected, leading to achievement of steady state blood levels in horses after one to two days of ponazuril administration.

INDICATIONS: MARQUIS is indicated for the treatment of equine protozoal myeloencephalitis (EPM) caused by Sarcocystis neurona.

EFFECTIVENESS SUMMARY: A field study was conducted at six sites with seven investigators across the United States. The study was conducted using historical controls. In this study, each animal’s response to treatment was compared to its pre-treatment values. The following standardized neurologic scale was used to grade the horses:

0 – Normal, no deficit detected
1 – Deficit just detected at normal gait
2 – Deficit easily detected and is exaggerated by backing, turning, swaying, loin pressure or neck extension
3 – Deficit very prominent on walking, turning, loin pressure or neck extension
4 – Gait is unsteady and can not be assessed
5 – Recumbent, unable to rise

Improvement was defined as a decrease of at least one grade.

Naturally occurring clinical cases of EPM, characterized by signalment and laboratory diagnostics, were randomly allotted to one of two treatment doses (5 or 10 mg/kg/day for a period of 28 days), then evaluated for clinical changes through 118 days. Acceptance into the study was based on the results from a standardized neurologic examination including radiography, cervical E. neurona IgM titer determination by Western Blot (WB), and a positive cerebrospinal fluid (CSF) titer for S. neurona IgG level by WB.

Response to treatment was determined by the investigator to be acceptable when a clinical improvement of at least one grade occurred by no later than 3 months after treatment, regardless of whether the CSF by WB was positive or negative.

Changes in clinical condition were evaluated first by the subjective scoring of the investigator, then by masked assessment of the study veterinarian. At 5 mg/kg for 28 days, 28 of 47 horses (60%) improved at least one grade by Day 118. Seventy-five percent (75%) of those improved, that had also been videotaped, were corroborated successes using videotape assessment. At 10 mg/kg, 32 of 55 animals (58%) improved at least one grade by Day 118. Seventy-five percent (75%) of those improved, that had also been videotaped, were corroborated successes by videotape assessment. At 10 mg/kg for 28 days, 28 of 47 horses (60%) improved at least one grade by Day 118 and 56% of those improved, that had also been videotaped, were corroborated successes by videotape assessment. With respect to the clinical investigators’ scores there was no statistical difference between 5 mg/kg and 10 mg/kg.

NOTE: The paste syringe is a multi-dose package. Ensure that the correct dose is administered with each use of the disposable syringe. The paste syringe can be used for up to three times within 6 days to complete treatment sequence steps 3 through 6 times, then continue with steps 7 and 8. Step 1: Remove end cap and gently apply pressure to the plunger until paste is seen at the tip of the syringe barrel. Return end cap to tip of paste syringe. Step 2: Determine weight of horse and ensure the horse’s mouth contains no feed. Step 3: To measure dose, dosing ring collar and barrel collar should be flush. Hold plunger and rotate dosing ring with the other hand to the weight of the drug. Step 4: Remove end cap from tip of syringe barrel. Step 5: The selected dose of paste should be deposited onto the back of the horse’s tongue. Introduce tip of paste syringe into the side of the horse’s mouth at the space between the front (incisor) and back (molar) teeth. Depose paste on the horse’s tongue by depressing the plunger of the syringe as far as the dose ring permits. Remove tip of syringe from horse’s mouth. Step 6: To aid swallowing of paste, immediately raise horse’s head for a few seconds after dosing. Step 7: Clean the tip of the syringe with a clean disposable towel and return end cap to tip of syringe barrel. Step 8: For the next daily dose, repeat steps 1-7. NOTE: At the end of the prescribed treatment period, partially used syringes should be discarded.

HOW SUPPLIED: Code: 84728731 Carton contains one (1) x 127 gram syringe applicator and one (1) reusable plunger syringe. Code: 84728766 Carton contains four (4) x 127 gram syringe applicators and four (4) reusable plunger syringes.


NADA #141-188, Approved by FDA ©2015 Merial, Inc. All rights reserved.

MARQUIS is a registered trademark, and *The Horse Head Logo is a trademark of Merial.

For additional information about adverse drug experience reporting for animal drugs, contact FDA at 1-888-FDA-VETS or online at http://www.fda.gov/AnimalVeterinary/SafetyHealth/ProductSafetyInformation.