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PHARM PROFILE

PONAZURIL

- **Kills several types of protozoal parasites, including the causative agent of equine protozoal myeloencephalitis**

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Ponazuril belongs to the triazine family and is a primary metabolite of toltrazuril. It has anticoccidial activity against several parasites, including *Sarcocystis neurona*, which is the causative agent of equine protozoal myeloencephalitis (EPM). Ponazuril is the first approved medication for treating EPM.[1]

PHARMACOLOGY

Although ponazuril's mechanism of action is unknown, it is believed to work similarly to toltrazuril, its parent compound. Toltrazuril has been shown to have activity on the mitochondria and respiratory chain of certain species of avian coccidian parasites.[1–2] Disruption of the nuclear division of schizonts has also been noted. In addition, ponazuril may have activity against the plastid body, an organelle located in many apicomplexan parasites that functions in amino acid synthesis, electron transport, and energy metabolism.[1–2] This plastid body is not found in vertebrate cells, making it an excellent drug target.[2] Ponazuril is a weak acid with high lipid solubility that enables it to cross the blood–brain barrier. After the agent crosses the blood–brain barrier, it reaches the central nervous system (CNS) and kills the *S. neurona* parasite.[3] The compound is believed to enter the cerebrospinal fluid (CSF) by passive diffusion.[4]

A pharmacokinetic study[4] of 10 healthy horses showed that ponazuril is readily absorbed and penetrates the CSF in therapeutic concentrations.[4] Serum concentrations of ponazuril are approximately 25 times higher than CSF concentrations. Oral absorption was rapid and a steady state was achieved after approximately 7 days, at a serum concentration of 4.33 ± 1.10 mg/L. The half-life of ponazuril in the serum was approximately 4.3 ± 0.6 days. There was no drug accumulation in either compartment (serum or CSF). Once treatment was discontinued, the drug was rapidly cleared from both the serum and CSF.[4]

INDICATIONS

Ponazuril is the first agent approved to treat EPM. In a recent efficacy trial,[5] 101 horses were randomly selected to receive either 5 or 10 mg/kg of ponazuril for 28 consecutive days. Treatment success was determined by either clinical improvement of at least one grade (on a 0 to 5 neurologic grading scale) or conversion to negative status on Western blot for *S. neurona* antibodies by 3 months after treatment.[5]

For treatment to be considered successful, the horse had to maintain improved status for 90 days after stopping treatment.[5] Twenty-eight of 47 horses treated with 5 mg/kg of ponazuril and 35 of 54 horses treated with 10 mg/kg for 28 days showed improvement of at least one grade by day 28. Outcome was unfavorable in 38 horses, although several of these had shown improvement during the treatment period but regressed during the 3-month follow-up.[5] This may indicate that some horses require treatment for longer than 28 days.

CAUTIONS

Most horses tolerate ponazuril very well.[6] Adverse effects are rare and usually minimal.[6] In a field study,[3,6] adverse effects included blisters on the nose and mouth, skin rash or hives, loose stools, mild colic, and a seizure. The horse that experienced the seizure, however, was known to have a history of seizures. In a study in

Client Counseling Information[8]

- Ponazuril effectively rids horses of *Sarcocystis neurona* but may have no effect on the irreversible, preexisting CNS damage caused by the parasite before treatment.
- Marquis™ is a tasteless product with a gel-like consistency that rapidly "coats" the tongue and buccal surfaces, allowing horses to readily accept the paste.
- One missed treatment is not likely to alter the outcome, but every effort must be made to use the product for 28 consecutive days.
- Ponazuril is for use in horses only and should not be used in horses intended for food.
- Keep out of the reach of children and other pets.

which horses were given two and six times the recommended dose,[6] adverse effects noted included loose feces and sporadic inappetence. However, these effects were also noted in the control horses.[6] Three of four mares that received six times the recommended dose experienced moderate edema in the lamina propria of the uterine epithelium.[6]

In a study in which toltrazuril was administered at 10 times the recommended dose for 10 days,[7] all horses tolerated treatment. Intermittent anorexia was seen in all animals, and a slight decrease in body weight was seen in five of seven horses. Mild colic was noted in one horse.[3,7]

The safe use of ponazuril in horses used for breeding purposes, during pregnancy, or in lactating mares has not been established.[1,3,6]

ACUTE TOXICITY

Data on acute toxicity in horses are currently unavailable.

DRUG INTERACTIONS

There are no data regarding drug interactions with ponazuril. The safety of ponazuril with concomitant therapies has not been evaluated.

DOSAGE AND ADMINISTRATION

The approved dosage of ponazuril for treating horses with EPM is 5 mg/kg body weight once daily for 28 days.[8] If the horse does not improve in 2 weeks on the 5-mg/kg dose, 10 mg/kg/day can be prescribed for an additional 28 days. Some veterinarians begin therapy with 10 mg/kg in horses with acute signs of EPM.[9]

PREPARATIONS

Ponazuril (Marquis™, Bayer Animal Health) is available in a 15% w/w ratio antiprotozoal oral paste supplied in ready-to-use syringes, each containing 127 g of paste. Each gram of paste contains 150 mg of ponazuril (15% w/w). One carton contains four 127-g syringe applicators and one reusable syringe plunger. The plunger contains a dosage ring calibrated for a dose rate of 5 mg/kg body weight. One carton contains enough medication to treat a 1200-lb horse for 28 days.[8]

STORAGE AND HANDLING

Ponazuril should be stored at a controlled room temperature of 15°C to 30°C (59°F to 86°F).[8] Studies indicate that there are no adverse effects on the stability of the product if freezing occurs.[1,3] Ponazuril has an 18-month shelf life.[1,3]

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