Ponazuril belongs to the triazine family and is a primary metabolite of toltrazuril. It has anticoxi-
cidal 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
certain species of avian coccidian parasites.¹⁻² Disruption of the nu-
clear 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, elec-
tron 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 pas-
sive diffusion.⁴

A pharmacokinetic study⁴ 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 effi-
cacy trial,³ 101 horses were randomly selected to receive either 5 or 10
mg/kg of ponazuril for 28 consecutive days. Treatment success was de-
termined by either clinical improvement of at least one grade (on a 0 to
5 neurologic grading scale) or con-
version to negative status on Western
blot for *S. neurona* antibodies by 3
months after treatment.³

For treatment to be considered suc-
cessful, the horse had to maintain im-
proved status for 90 days after stop-
ping treatment.⁵ Twenty-eight of 47
horses treated with 5 mg/kg of pon-
azuril 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.³ This may in-
dicate that some horses require treat-
ment for longer than 28 days.

**CAUTIONS**

Most horses tolerate ponazuril very
well.⁶ Adverse effects are rare and usu-
ally minimal.⁶ In a field study,⁵⁶ ad-
verse 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

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Client Counseling Information

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

In a study in which toltrazuril was administered at 10 times the recommended dose for 10 days, 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.

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

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. 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.

STORAGE AND HANDLING

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

REFERENCES