IMPORTANT SAFETY INFORMATION

Use of Protazil® (1.56% diclazuril) is contraindicated in horses with known hypersensitivity to diclazuril. Safe use in horses used for breeding purposes, during pregnancy, or in lactating mares has not been evaluated. The safety of Protazil® (1.56% diclazuril) with concomitant therapies in horses has not been evaluated. For use in horses only. Do not use in horses intended for human consumption. Not for human use. Keep out of reach of children. For complete information, refer to the product label.

Protazil® Pharmacokinetics

- Labeled dose of 1 mg/kg attained plasma and CSF drug concentrations known to inhibit Sarcocystis neurona
- Active ingredient, diclazuril, quickly reaches therapeutic levels
- Plasma drug concentrations well above minimum inhibitory concentration (MIC=1ng/mL) within 12 hours of administering a single dose
- Long elimination half-life

Diclazuril Pharmacokinetics

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>$T_{\text{max}}$</td>
<td>226 hours (~9.4 days)</td>
</tr>
<tr>
<td>$C_{\text{max}}$</td>
<td>910 ng/ml</td>
</tr>
<tr>
<td>$t_{1/2}$</td>
<td>54.3 hours (~2.3 days)</td>
</tr>
<tr>
<td>CSF concentration at steady state</td>
<td>26 ng/ml</td>
</tr>
</tbody>
</table>

**RAPID ABSORPTION OF DICLAZURIL WITHOUT A LOADING DOSE**

"EPM is a serious disease threat in Ohio. The Protazil treatment regimen achieves therapeutic blood levels quickly and without a loading dose. I've used Protazil to treat my own horses and client horses too. Protazil is easy to use, horses find the pellets palatable plus it's priced competitively. Protazil has an excellent safety profile, is FDA-approved and backed by Merck Animal Health. Horse owners appreciate that assurance.”

Daniel Yates, D.V.M. — Wilmington, Ohio

"We have been using Protazil in our practice with excellent results. Client compliance in treatment has increased due to the ease of administration and palatability of Protazil over oral pastes. We've observed some horses will preferentially eat the Protazil over concentrate feeds. With increased client compliance we can achieve better treatment results with our patients and better outcomes for our clients."

Greggory S. Bell, D.V.M. — Pagosa Springs, Colorado

1 Hunyadi L, Papich MG, Pusterla N. Pharmacokinetics of a low-dose and FDA-labeled dose of diclazuril administered orally as a pelleted top dressing in adult horses. J of Vet Pharmacology and Therapeutics (accepted) 2014, doi: 10.111/jvp.12176. The correlation between pharmacokinetic data and clinical effectiveness is unknown

2 HR Freedom of Information Summary Data on file at Merck Animal Health
PROTAZIL® (1.56% diclazuril) Antiprotozoal Pellets were administered to 24 horses (12 males and 12 females, ranging from 2 to 8 years of age). Three groups of 4 horses/sex/group received 0, 1, or 5 mg diclazuril/kg body weight/day for 42 days as a top-dress on the grain ration of the horse. The variables measured during the study included: clinical and physical observations, body weights, food and water consumption, hematology, serum chemistry, urinalysis, fecal analysis, organ weights, and histopathologic examinations. The safety of diclazuril top-dress administered to horses at 1 mg/kg once daily cannot be determined based solely on this study because of the lack of an adequate control group (control horses tested positive for the target drug in plasma and CSF). However, no test article-related findings associated with the drug were limited to elevations in BUN, creatinine, and SDH and less than anticipated weight gain. Definitive test article-related effects were decreased grain/top-dress consumption in horses in the 50 mg/kg group.

In a second target animal safety study, PROTAZIL® (1.56% diclazuril) Antiprotozoal Pellets were administered to 24 horses (12 males and 12 females, ranging from 2 to 8 years of age). Three groups of 4 horses/sex/group received 0, 1, or 5 mg diclazuril/kg body weight/day for 42 days as a top-dress on the grain ration of the horse. The variables measured during the study included: physical examinations, body weights, food and water consumption, hematology, and serum chemistry. There were no test article-related findings seen during the study.

STORAGE INFORMATION
Store between 15°C to 30°C (59°F to 86°F).

HOW SUPPLIED
PROTAZIL® (1.56 % diclazuril) Antiprotozoal Pellets are supplied in 2.4 lb (1.1 kg) and 10-lb (4.5 kg) buckets.

REFERENCES

Internet Inc dba Merck Animal Health, 556 Morris Avenue, Summit, NJ 07901
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NAC No.: 1047490.2

<table>
<thead>
<tr>
<th>Weight Range of Horse (lb)</th>
<th>mLs of Pellets</th>
<th>Weight Range of Horse (lb)</th>
<th>mLs of Pellets</th>
</tr>
</thead>
<tbody>
<tr>
<td>275 - 524</td>
<td>20</td>
<td>1275 - 1524</td>
<td>60</td>
</tr>
<tr>
<td>525 - 774</td>
<td>30</td>
<td>1525 - 1774</td>
<td>70</td>
</tr>
<tr>
<td>775 - 1024</td>
<td>40</td>
<td>1775 - 2074</td>
<td>80</td>
</tr>
<tr>
<td>1025 - 1274</td>
<td>50</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

One 2.4-lb bucket of PROTAZIL® will treat one 1274-lb horse for 28 days. One 10-lb bucket of PROTAZIL® will treat five 1100-lb horses for 29 days.

CONTRAINDICATIONS
Use of PROTAZIL® (1.56 % diclazuril) Antiprotozoal Pellets is contraindicated in horses with known hypersensitivity to diclazuril.

WARNINGS

PRECAUTIONS
The safe use of PROTAZIL® (1.56 % diclazuril) Antiprotozoal Pellets in horses used for breeding purposes, during pregnancy, or in lactating mares has not been evaluated. The safety of PROTAZIL® (1.56% diclazuril) Antiprotozoal Pellets with concomitant therapies in horses has not been evaluated.