**EQUIDONE® Gel** (domperidone)

**DESCRIPTION**

EQUIDONE Gel is a 2-dopamine receptor antagonist. Chemically, domperidone is 6-chloro-3-[1-[3-(2-oxo-3H-benzimidazol-1-yl)propyl]piperidin-4-yl]-1H-benzimidazol-2-one. The structural formula is:

Molecular Formula: C_{21}H_{21}ClN_{2}O_{2}

Molecular Weight: 425.91

**INDICATIONS**

For prevention of feces toxicosis in periparturient mares.

**DOSAGE AND ADMINISTRATION**

Orally administer 0.5 mg/lb (1.1 mg/kg) daily once starting 10 to 15 days prior to Expected Foaling Date (EFD). Treatment may be continued for up to 5 days after foaling. Mares may be re-treated with EQUIDONE Gel after milk has foaled.

**DIRECTIONS FOR ADMINISTRATION**

1. Determine the appropriate dose for the body weight of the mare based on the dosing table below. One cc will treat 220 lb (100 kg) of body weight.

<table>
<thead>
<tr>
<th>Weight (lb)</th>
<th>Weight (kg)</th>
<th>cc</th>
<th>Dose</th>
<th>Domperidone (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>500-660</td>
<td>226-300</td>
<td>3</td>
<td>3</td>
<td>0.5</td>
</tr>
<tr>
<td>661-880</td>
<td>301-400</td>
<td>4</td>
<td>4</td>
<td>0.5</td>
</tr>
<tr>
<td>881-1110</td>
<td>401-500</td>
<td>5</td>
<td>5</td>
<td>0.5</td>
</tr>
<tr>
<td>1110-1320</td>
<td>501-600</td>
<td>6</td>
<td>6</td>
<td>0.5</td>
</tr>
</tbody>
</table>

2. Turn the dial ring until the edge of the ring nearest the tip of the syringe lines up with the desired cc to be delivered.
3. Remove the cap ring.
4. Make sure the horse’s mouth is free of food or other obstructions.
5. Insert the nozzle of the syringe opposite the horse’s mouth and deposit the gel on the back of the tongue by depressing the plunger.
6. Recap the syringe.

**CRITICAL INFORMATION**

This is a 25 cc multi-dose syringe. Please note that for subsequent doses, it will be necessary to adjust for previous doses. For example, if the intended dose for a horse is 0.5 mg/lb (1.1 mg/kg), the dose for the first 5 cc dose will be 0.5 mg/lb (1.1 mg/kg) for the second dose 0.25 mg/lb (0.55 mg/kg) for the fourth dose, and 0.125 mg/lb (0.27 mg/kg) for the fifth dose.

**CONTRAINDICATIONS**

Horses with hypersecretion to domperidone should not receive EQUIDONE Gel.

**WARNINGS**

Failure of passive transfer of immunoglobulins (IgG) may occur when using EQUIDONE Gel. This may result in loss of absorption of colostrum or milk. All foals born to mares treated with EQUIDONE Gel should be tested for serum IgG concentrations. Do not use in horses intended for human consumption.

**HUMAN CONSIDERATIONS**

Not for use in humans. For oral use in animals only. Keep this and all drugs out of the reach of children. Pregnant and lactating women should take care when handling EQUIDONE Gel as systemic exposure to domperidone may affect reproductive/hormonal functions. Domperidone is not approved for any indication in humans in the US. The safety of domperidone in lactating women and their nursing children has not been evaluated. Consult a physician in case of accidental human exposure.

**PRECAUTIONS**

EQUIDONE Gel may lead to premature birth, low birth weight foals or fetal morbidity if administered >15 days prior to the expected foaling date. Accurate breeding dates and an expected foaling date are needed for the safe use of EQUIDONE Gel.

The safety of EQUIDONE Gel was evaluated in breeding programs and lactating mares other than in the last 45 days of pregnancy and the first 15 days of lactation (see Animal Safety). The safety in stallions has not been evaluated. The long term effects on foals born to mares, longevity of EQUIDONE Gel-evaluated and non-EQUIDONE Gel-evaluated. Do not use in horses with suspected or confirmed gastrointestinal hemorrhage, as domperidone is a prokinetic drug it stimulates gut motility.

Use of EQUIDONE Gel may cause a false positive on the milk calcium test used to predict foaling.

Domperidone is a known P-glycoprotein substrate and its main metabolic pathway in the dog includes metabolism by cytochrome P450 3A4. In the dog, exposure to domperidone is increased when co-administered with drugs that inhibit CYP3A4 such as atenolol and verapamil.

This could result in significantly greater domperidone drug exposure (multi-fold increase) when used with these drugs.

**ADVERSE REACTIONS**

The most common adverse reactions associated with treatment with EQUIDONE Gel are gastrointestinal events of milk drift prior to foaling and failure of passive transfer.

In a laboratory effectiveness study with 32 periparturient mares (7 treated with EQUIDONE Gel and 25 treated with vehicle control) 3/7 (43%) of mares treated with EQUIDONE Gel experienced premature lactation, the 16 (10%) of mares treated with EQUIDONE Gel and 9 (45%) of controls evaluated for passive transfer lacked detectable levels of colostrum. Three treatment groups were evaluated: 1X, 1.75 mg/lb (3.6 mg/kg); 3X, 3.5 mg/lb (7.1 mg/kg). Failure of passive transfer in foals of mares treated with EQUIDONE Gel was not solely due to physical loss of colostrum or milk. Foals of mares treated with EQUIDONE Gel had higher concentration of 400-800 mg/dL.

Failure of passive transfer occurred in all groups; however, there was a greater incidence of IgG concentrations <400 mg/dL. In foals of mares treated with EQUIDONE Gel the incidence of failure of passive transfer also occurred in foals. All mares that dripped milk for 3 or more days prior to parturition had false positive IgG concentrations <800 mg/dL, and one treated mare that did not drip milk had a foal with an IgG concentration of 450-900 mg/dL.

**CLINICAL PHARMACOLOGY**

Domperidone is a 2-dopamine receptor antagonist that blocks the agonistic action of feces toxicosis at the cellular level. Unlike other 2-dopamine antagonists, domperidone does not readily cross the blood-brain barrier. Distribution studies with radiolabeled drug in animals have shown wide tissue distribution, but low brain concentrations. Small amounts of the drug cross placenta in rats. Small amounts of the drug cross placenta in rats. In humans, domperidone is 91-95% bound to plasma proteins. Domperidone in humans undergoes rapid and extensive hepatic metabolism by hydroxylation and N-dealkylation, and the metabolites are excreted in the feces. Domperidone is inactive when administered orally, and most of the orally administered dose is excreted in the feces. The average terminal plasma half-life of domperidone administered orally to horses is approximately 6 hours with very low systemic bioavailability.

**EFFECTIVENESS**

A randomized, masked, controlled, laboratory effectiveness study evaluated the effectiveness of 1 mg/kg EQUIDONE Gel administered once daily beginning 10 to 15 days prior to expected foaling date (EFD) and continued treatment for 5 days after foaling and continuing and day up to 5 days after foaling for the prevention of feces toxicosis. In this study, 13 (100%) of the 13 foals examined in horses that were treated with EQUIDONE Gel had a detectable radio-labeled drug in the foal’s milk whereas only 7 (58%) of the 12 foals examined in the vehicle control group had detectable radio-labeled drug in the foal’s milk. Failure of passive transfer occurred in 10/13 (77%) foals of mares treated with EQUIDONE Gel and 8/9 (89%) foals of control mares. Failure of passive transfer in foals of mares treated with EQUIDONE Gel and 8/9 (89%) foals of control mares. Failure of passive transfer occurred in all groups; however, there was a greater incidence of IgG concentrations <400 mg/dL. In foals of mares treated with EQUIDONE Gel the incidence of failure of passive transfer also occurred in foals. All mares that dripped milk for 3 or more days prior to parturition had false positive IgG concentrations <800 mg/dL, and one treated mare that did not drip milk had a foal with an IgG concentration of 450-900 mg/dL.

**DESCRIPTION**

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