Zimeta® (dipyrone injection)

500 mg/mL injection

For intraocular use in horses

Non-steroidal anti-inflammatory drug (NSAID)

CAUTION: Federal law (U.S.A.) restricts this drug to use by or on the order of a licensed veterinarian.

Description: Dipyrone belongs to the pyrazole class of non-steroidal anti-inflammatory (NSAID) drugs. Chemically, dipyrone is metamizole sodium. Each mL of this clear sterile solution for intraocular injection contains 500 mg dipyrone and 10 mL 95% propylene alcohol in water.

The structural formula of dipyrone is:

Molecular Formula: C23H24N4NaO5S

H2O Molecular Weight: 351.4

Indications: Zimeta® (dipyrone injection) is indicated for the control of pyrexia in horses.

Dosage and Administration: Always provide the Client Information Sheet with the prescription. Administer Zimeta by intraocular injection, once or twice daily, at 12 hour intervals, for up to 3 days, at a dosage of 10 mg/kg (13.6 mg/lb). The total number of doses and duration of treatment with Zimeta is dependent on the response observed (fever reduction). Zimeta may be re-administered based on recurrence of fever for up to 3 days. Zimeta is provided in a multi-dose vial and contains a preservative.

Contraindications: Horses with hypersensitivity to dipyrone should not receive Zimeta. Due to the prolongation of prothrombin time (PT) and/or activated partial thromboplastin time (APTT), Zimeta should be used with caution in horses at risk for hemorrhage. Horses with hypersensitivity to dipyrone should not receive Zimeta. Due to the prolongation of prothrombin time (PT) and/or activated partial thromboplastin time (APTT), Zimeta should be used with caution in horses at risk for hemorrhage.

Hypersensitivity to dipyrone should not be given Zimeta if he/she:

• Has previously had an allergic reaction to another NSAID or a corticosteroid.

Your horse should not be given Zimeta if he/she:

• Has previously had an allergic reaction to other NSAIDs
• Has an allergic reaction to dipyrone, the active ingredient in Zimeta

Your horse may receive Zimeta if he/she:

• Has an allergy reaction to dipyrone, the active ingredient in Zimeta
• Has previously had an allergic reaction to other NSAIDs
• Is presently taking other NSAIDs or corticosteroids including but not limited to aspirin, phenylbutazone, flunixin, metacam, diclofenac, ketoprofen, flurbiprofen, or ibuprofen
• Has not been determined in horses less than three years of age or in breeding horses, pregnant or lactating mares

Zimeta is available as a 500 mg/mL solution in a 100 mL, 20° and 25°C (68° and 77°F); with excursions permitted between 15° and 30°C (59° and 86°F). Zimeta is a sterile solution. Zimeta is non-steroidal anti-inflammatory drug for intravenous use in horses only.

Zimeta® (dipyrone injection) is administered once or twice daily for up to 3 days for the control of pyrexia in horses. The overall duration of treatment with Zimeta (dipyrone injection) will be dependent on the response observed (fever reduction), but should not exceed 3 days. Zimeta should not be administered more frequently than every 12 hours.

This summary contains important information about Zimeta. You should read this information before using Zimeta. It is provided as a summary and does not take the place of instructions from your veterinarian. Talk to your veterinarian if you do not understand any of this information or you want to know more about Zimeta.

WHAT IS ZIMETA?

Zimeta is a non-steroidal, non-steroidal anti-inflammatory drug (NSAID) of the pyrazole class used to control fever in horses by veterinary prescription only. Fever is an elevation in body temperature due to a variety of infectious and inflammatory conditions in the horse.

HOW TO GIVE ZIMETA TO YOUR HORSE

Zimeta should be given according to your veterinarian’s instructions. Do not change the way you give Zimeta without your veterinarian’s consent.

WHAT KIND OF RESULTS CAN I EXPECT WHEN MY HORSE IS BEING TREATED WITH ZIMETA FOR A FEVER?

Zimeta can control fever that is a result of infection or inflammation; however, it is not a cure for the underlying disease. Consult your veterinarian to identify the underlying cause of your horse’s elevated body temperature. Response to Zimeta varies from horse to horse.

WHICH HORSES SHOULD NOT RECEIVE ZIMETA?

Your horse should not be given Zimeta if he/she:

• Has an allergy reaction to dipyrone, the active ingredient in Zimeta
• Has previously had an allergic reaction to other NSAIDs
• Is presently taking other NSAIDs or corticosteroids including but not limited to aspirin, phenylbutazone, flunixin, metacam, diclofenac, ketoprofen, flurbiprofen, or ibuprofen
• Has not been determined in horses less than three years of age or in breeding horses, pregnant or lactating mares

ZIMETA SHOULD BE GIVEN INTRAOCULARLY TO HORSES ONLY

Zimeta is not for use in horses intended for human food consumption. Do not use in any food producing animals, including lactating dairy animals.

Horse owners: Care should be taken to ensure that dipyrone is not accidentally injected into humans as studies have indicated that dipyrone can cause agranulocytosis in humans.

For use in horses only. Do not use in horses intended for human consumption. Do not use in any food producing animals, including lactating dairy animals.

Veterinarians: Keep Zimeta, Zimeta should be given according to your veterinarian’s instructions. Do not change the way you give Zimeta without your veterinarian’s consent.

WHAT TO TELL YOUR VETERINARIAN BEFORE GIVING ZIMETA

Tell your veterinarian:

• The signs of infection or inflammation you have observed in your horse, such as nasal discharge or coughing
• If any tests, such as bloodwork, will be done before Zimetia is prescribed
• How often your horse may need to be examined by your veterinarian
• The risks and benefits of using Zimeta
• Other medical problems or allergies that your horse has now, or has had in the past
• All medications that you are giving or plan to give to your horse, including those you can get without a prescription and any dietary supplements
• Any recent surgeries

Table 1: Adverse Reactions Reported During the Field Study with Zimeta

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>Zimeta-Induced (mean ± SD)</th>
<th>Control Product (mean ± SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diarrhea</td>
<td>1 (1%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Prolonged PT</td>
<td>1 (1%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Prolonged APTT</td>
<td>1 (1%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Changes in manure</td>
<td>1 (1%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Hypersensitivity</td>
<td>1 (1%)</td>
<td>0 (0%)</td>
</tr>
</tbody>
</table>

Horses with elevated SDH, hypoalbuminemia, prolonged PT, or prolonged APTT did not show associated clinical signs. One horse exhibited an exacerbation of pre-existing hypoalbuminemia after treatment; this horse also showed concurrent elevation in SDH. Two horses that received Zimeta were diagnosed with gastric ulcers. One horse that received 4 doses of Zimeta was diagnosed with grade IV evidence of gastric ulceration and hypoproteinemia of the mucosa of the right dorsal colon on post-mortem examination which was performed following euthanasia due to illness unrelated to treatment (septic arthritis and cellulitis). This horse was previously treated with a different NSAID prior to enrollment in the study. A second horse that enrolled in the study due to a mandibular facial wound, and received two doses of Zimeta, was diagnosed with grade IV evidence of BWS-4 ulcers 4 days following completion of the field study. In the field study, Zimeta was used concomitantly with other therapies, including antibiotics and sedatives.

Information for Owners or Person Treating Horse: A Client Information Sheet should be provided to the person treating the horse. Treatment administration and caretakers should be aware of the potential for adverse reactions and the clinical signs associated with NSAID intolerance. Adverse reactions may include colic, diarrhea, and decreased appetite. Serious adverse reactions can occur without warning and, in some situations, result in death. Clients should be advised to discontinue NSAID therapy and contact their veterinarian immediately if any signs of intolerance are observed.

Clinical Pharmacology: Dipyrone is a water soluble pyrazoline derivative that is immediately Hydrolyzed to 4-methylaminopyrazine (4-MAA) following administration by any route. In most species, including the horse, 4-MAA is the molecule assayed for pharmacodynamic activity, as dipyrone is present for an extremely short period of time. In horses, 4-MAA is further metabolized by the liver to secondary metabolites that primarily undergo renal excretion. 4-MAA is also the molecule associated with clinical efficacy in humans. The mechanism of action to reduce pyresia has not been fully characterized.
Tell your veterinarian if your horse has ever had the following medical problems:

- Any side effects from taking Zimet® (dipyrone injection) or other NSAIDs
- Any increased rectal temperature, Hoarse, unusual irritability, or known kidney disease
- Any known liver disease
- Any known stomach or gastrointestinal ulcers

Tell your veterinarian if you plan to breed your horse, or if your mare is pregnant or nursing a foal.

WHAT ARE THE POSSIBLE SIDE EFFECTS THAT MAY OCCUR IN MY HORSE DURING ZIMETA THERAPY?

Zimeta, like other NSAIDs, may cause some side effects in individual horses. Serious side effects associated with NSAID therapy can occur with or without warning. Look for the following side effects that may indicate that your horse is having a problem with Zimeta or may have another medical problem:

- Change in eating or drinking habits (frequency or amount consumed)
- Change in urination
- Unexpected weight loss
- Change in behavior, such as depression
- Change in manure, such as diarrhea
- Unexplained bleeding

It is important to stop therapy and contact your veterinarian if you think your horse has a medical problem or side effect while taking Zimeta. If you have additional questions about possible side effects, talk with your veterinarian or call Dechra Veterinary Products at 1-866-933-2472.

CAN ZIMETA BE GIVEN WITH OTHER MEDICATIONS?

Zimeta should not be given at the same time as with other NSAIDS (for example, aspirin, phenylbutazone, diclofenac, ketoprofen, f Rican, or f Rocoxib) or systemic corticosteroids (for example, prednisolone, dexamethasone, or triamcinolone). Consult your veterinarian before giving Zimeta to your horse if you are giving other medications.

WHAT SHOULD I KNOW ABOUT ZIMETA?

- Zimeta is available as a 500 mg/mL solution in a 100 mL, and 30°C (59° and 86°F). Protect from light. Multi-dose vial. Use within 30 days of first puncture.

HOW TO GIVE ZIMETA TO YOUR HORSE

- Administer Zimeta by intravenous injection. Zimeta should not be given by any other route.
- Dose your horse based on body weight. Duration of therapy should be based upon degree of fever. Consult your veterinarian or call Dechra Veterinary Products at 1-866-933-2472.

THERAPY

Dose and Duration.

As with all prescribed medicines, Zimeta should only be given to the horse for which it is prescribed. Consult your veterinarian if you have any questions or concerns about Zimeta or try to understand the reason for treatment.

DO WHAT I DO IN CASE MY HORSE RECEIVES MORE THAN THE PRESCRIBED AMOUNT OF ZIMETA?

Consult your veterinarian if your horse receives more than the prescribed amount of Zimeta.

WHAT ELSE SHOULD I KNOW ABOUT ZIMETA?

This sheet provides a summary of information about Zimeta (dipyrone injection) and general information about NSAIDs. If you have any questions or concerns about Zimeta or try to understand the reason for treatment.

With all prescribed medicines, Zimeta should only be given to the horse for which it is prescribed. It should be given to your horse only for the condition for which it is prescribed, at the prescribed dose and duration.

It is important to periodically discuss your horse’s response to Zimeta with your veterinarian. Your veterinarian will determine if your horse is responding as expected and if your horse should continue receiving Zimeta.

Manufacturered for:

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Metachloroxizine-Related Committee for Veterinary Medicinal Products. The European Agency for the Evaluation of Medicinal Products. June 2003. EMA/MRL/678/03-Final