

IRISH MEDICINES BOARD ACT 1995

EUROPEAN COMMUNITIES (ANIMAL REMEDIES) (No. 2) REGULATIONS 2007

(S.I. No. 786 of 2007)

VPA: **10277/041/001**
Case No: 7004650

The Irish Medicines Board in exercise of the powers conferred on it by Animal Remedies (No. 2) Regulations (S.I. No. 786 of 2007) hereby grants to:

Schering Plough Limited

Shire Park, Welwyn Garden City, Hertfordshire AL7 1TW, United Kingdom

an authorisation, subject to the provisions of the said Regulations and the general conditions of the attached authorisation, in respect of the Veterinary Medicinal Product:

Tribrissen Oral Paste

The particulars of which are set out in Part 1 and Part 2 of the said Schedule. The authorisation is also subject to any special conditions as may be specified in the said Schedule.

The authorisation, unless previously revoked, shall continue in force from **30/09/2008**.

Signed on behalf of the Irish Medicines Board

A person authorised in that behalf by the said Board.

(NOTE: From this date of effect, this authorisation replaces any previous authorisation in respect of this product which is now null and void.)

Part II

Summary of Product Characteristics

1 NAME OF THE VETERINARY MEDICINAL PRODUCT

Tribrissen Oral Paste.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 37.5 g of paste contains:

Active substances:

Sulfadiazine	12.5 g
Trimethoprim	2.5 g

Excipient:

Chlorocresol	0.075 g
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For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Oral paste

4 CLINICAL PARTICULARS

4.1 Target Species

Horses

4.2 Indications for use, specifying the target species

The product is recommended for the treatment of bacterial diseases in horses including.

Alimentary tract infections.

Upper and lower respiratory tract infections, including strangles.

Infected wounds and cellulitis.

Antibacterial medication in surgical cases where asepsis cannot be guaranteed.

4.3 Contraindications

Do not use in horses with known sulphonamide sensitivity, with severe liver parenchymal damage, nor with blood dyscrasias.

4.4 Special warnings for each target species

None.

4.5 Special precautions for use

Special precautions for use in animals

The same syringe should not be used to treat more than one animal unless the animals are either running together, or are on the same premises and in direct contact with each other.

Use of the product should be based on susceptibility testing of the bacteria isolated from the animal. If this is not possible, therapy should be based on local (regional, farm level) epidemiological information about susceptibility of the target bacteria.

Special Precautions to be taken by the Person Administering the Product to Animals

Not applicable.

4.6 Adverse reactions (frequency and seriousness)

None reported.

4.7 Use during pregnancy, lactation or lay

Studies have shown that no abnormalities were witnessed in foals, nor were there any adverse effects on reproductive function in mares.

4.8 Interaction with other medicinal products and other forms of interaction

None known.

4.9 Amounts to be administered and administration route

Dose: 30mg of combined active ingredients per kg bodyweight daily. This dose is provided by adjusting the screw-guage on the plunger of the syringe according to the bodyweight of the horse. Each division on the plunger provides sufficient paste to medicate 50 kg bodyweight. Each syringe provides a daily dose for a 500 kg horse.

The dose should be administered once daily for five days or until two days after symptoms have subsided, up to a maximum of five days.

Preferably treatment should be initiated using an injectable formulation containing sulfadiazine and trimethoprim which may be followed by administration of the oral paste.

Administration : Orally. Set the screw-guage at the appropriate mark on the plunger of the syringe and remove the cap from the nozzle. Introduce the nozzle end of the syringe at the corner of the mouth (*labial commissure*).

Depress the plunger so as to deposit the paste on the upper surface of the tongue. raising the horse's head by the hand under the chin sometimes assists the swallowing process.

To ensure a correct dosage, bodyweight should be determined as accurately as possible.

4.10 Overdose (symptoms, emergency procedures, antidotes), if necessary

There are no specific recommendations in the case of overdosage.

4.11 Withdrawal Period(s)

Meat and offal: 6 days

5 PHARMACOLOGICAL or IMMUNOLOGICAL PROPERTIES

Pharmacotherapeutic Group: Antibacterials for systemic use; Sulfadiazine and trimethoprim

ATCvet Code: QJ01 EW10.

5.1 Pharmacodynamic properties

Tribriksen Oral Paste is a broad spectrum antibacterial used for the treatment of a wide range of diseases and conditions of bacterial origin in horses.

The two active ingredients produce a sequential double blockade of bacterial synthesis of folic acid, giving a level of activity many times greater than either drug alone.

Folates are essential to the bacterial/protozoal cell for multiplication and survival.

-sulphadiazine prevents the bacterial/protozoal cell from synthesising folic acid

-trimethoprim prevents the conversion of folic acid to folinic acid in the bacterial/protozoal cell, by inhibiting the bacterial/protozoal enzyme-dihydrofolate reductase.

Trimethoprim-sulphonamide therapy was devised to take advantage of the discovery that although all cells use folinic acid in the production of purines, pathogenic bacteria and animal cells differ sharply in two aspects of folate metabolism.

1) Whereas pathogenic bacteria must synthesise folic acid from para -aminobenzoic acid, animal cells incorporate folic acid from the food; animals are not therefore directly affected by sulphonamide therapy, at therapeutic doses.

2) Dihydrofolate reductase is required by all cells for the reduction of folic to folinic acid but trimethoprim has a much greater affinity for the bacterial enzyme - up to 10,000 times greater - than for the dihydrofolate reductase of the animal cell; at therapeutic levels trimethoprim blocks folinic acid production in the bacterial cell without interrupting animal folate metabolism.

Because of their sequential action, trimethoprim and sulphonamides potentiate each other, greatly increasing their individual antibacterial effects. The action of this combination is bactericidal, whereas the components used separately are generally bacteriostatic. Potentiation is shown even against bacteria that are generally resistant to one or other of the components.

The *in vitro* activity covers most common Gram-positive and Gram-negative bacteria including: *Actinobacillus spp.*, *Actinomyces bovis*, *Bordetella spp.*, *Corynebacterium spp.*, *Escherichia coli*, *Fusobacterium necrophorum*, *Haemophilus spp.*, *Klebsiella spp.*, *Listeria monocytogenes*, *Nocardia spp.*, *Pasteurella spp.*, *Proteus spp.*, *Salmonella spp.*, *Staphylococcus spp.*, and *Streptococcus spp.* infections.

5.2 Pharmacokinetic properties

Four horses, two of which were fed and two fasted, were given oral doses (30mg/kg) of Tribriksen Oral Paste on three consecutive days. Serial blood samples were drawn and the trimethoprim (TMP) and sulphadiazine (SDZ) concentrations were measured by specific quantitative thin layer chromatographic assays. Food intake appeared to affect the pharmacokinetic profile, but only for the first day of treatment, when both TMP and SDZ were both absorbed more rapidly in fasted horses. For both groups, peak TMP and SDZ concentrations occurred generally within 3 hours after drug administration and were in the range of 0.36 to 3.71 mg/ml (mean= 1.58 ug/ml) for TMP and 4.8 to 18.8 ug/ml (mean = 10.5 ug/ml) for SDZ. The mean serum elimination half-lives of TMP and SDZ were found to be 2.4 hours and 7.4 hours respectively.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Glycerol
Polysorbate 20
Xanthan Gum
Chlorocresol
Purified Water

6.2 Incompatibilities

None known.

6.3 Shelf-life

Shelf-life of the veterinary medicinal product as packaged for sale: 5 years

6.4 Special precautions for storage

Do not store above 25°C.
Do not freeze.

6.5 Nature and composition of immediate packaging

High density polyethylene oral dosing syringe and piston closed with a high density polyethylene cap, push fit containing 37.5g of product. The dosing device has an integral dial-a-dose mechanism.

6.6 Special precautions for the disposal of unused veterinary medicinal products or waste materials

Any unused product or waste materials should be disposed of in accordance with national requirements

7 MARKETING AUTHORISATION HOLDER

Schering Plough Ltd.
Shire Park
Welwyn Garden City
Hertfordshire
AL7 1TW
England

8 MARKETING AUTHORISATION NUMBER(S)

VPA 10277/041/001

9 DATE OF THE FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

30th September 2008

10 DATE OF REVISION OF THE TEXT