IRISH MEDICINES BOARD ACT 1995

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

(S.I. No. 786 of 2007)

VPA: **10007/022/002**
Case No: 7003707

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:

Boehringer Ingelheim Ltd

Ellesfield Avenue, **Bracknell**, **Berkshire RG12 8YS**, **England**

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:

Trinacol Solution for Injection

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 **14/01/2008**.

Signed on behalf of the Irish Medicines Board

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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

Trinacol Solution for Injection

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:	
Active substances	
Sulphadiazine	200 mg
Trimethoprim	40 mg
Chlorocresol	1 mg as antimicrobial preservative
Sodium Formaldehyde Sulphoxylate dihydrate	1 mg as antioxidant

For a full list of excipients see section 6.1.

3 PHARMACEUTICAL FORM

Solution for injection.
A clear yellow aqueous solution.

4 CLINICAL PARTICULARS

4.1 Target Species

For use in cattle, pigs and dogs.

4.2 Indications for use, specifying the target species

Trinacol is indicated in the treatment of acute, subacute and chronic conditions of bacterial origin in cattle, pigs and dogs.

The therapeutic spectrum includes both Gram-negative and Gram-positive bacteria including *Streptococci, Staphylococci, Actinobacilli, Actinomycae, Salmonella, Pasteurella, Pneumococci, Proteus, E. Coli, Corynebacteria, Vibrio, Bordetella, Brucella, Klebsiellae and Haemophilae.*

4.3 Contraindications

Injections should not be given by routes other than those recommended. Not to be administered intraperitoneally.

Do not administer to animals with known sulphonamide sensitivity, severe liver parenchymal damage, or blood dyscrasias.

4.4 Special warnings for each target species

None known.

4.5 Special precautions for use

Special precaution(s) for use in animals

Adequate drinking water should be available during the therapeutic effect of the product.

Special precautions to be taken by the person administering the veterinary medicinal product to animals

Care must be taken to avoid accidental self injection.

4.6 Adverse reactions (frequency and seriousness)

Anaphylactic shock, potentially fatal, has been observed on occasions following administration of potentiated sulphonamide preparations particularly by intravenous route. Veterinary surgeons should be mindful of this possibility during the injection process. For intravenous administration the product should be warmed to body temperature and injected slowly over as long a period as is reasonably practical. At the first sign of intolerance the injection should be interrupted and shock treatment initiated.

Intravenous administration should only be used with extreme caution and only if therapeutically justified.

Local reaction characterised by swelling and/or hardness may be observed at the injection site following treatment. These lesions are of a transient nature, resolving within one week after treatment.

4.7 Use during pregnancy, lactation or lay

Trinacol can be safely administered to pregnant and lactating animals.

4.8 Interaction with other medicinal products and other forms of interaction

None known.

4.9 Amounts to be administered and administration route

Dogs: 1 ml per 8 kg body weight daily (equivalent to 30 mg combined actives per kg) by subcutaneous injection only
The recommended site in dogs is the loose skin at the top of the neck.

Cattle and Pigs: 1 ml per 16 kg body weight daily (equivalent to 15 mg combined actives per kg) by intramuscular or slow intravenous injection.

Maximum recommended volume to be administered at a single intramuscular site: 15 ml of product.

For all species a single injection may be sufficient in uncomplicated conditions, but in severe infections treatment may be repeated until two days after the symptoms have been resolved up to a maximum of five days.

An appropriately graduated syringe must be used to allow accurate administration of the required dose. This is particularly important when injecting small volumes.

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

Not applicable

4.11 Withdrawal Period(s)

Animals may not be slaughtered for human consumption during treatment
Meat and Offal:
Cattle: 12 days
Pigs: 20 days
Milk: 48 hours

5 PHARMACOLOGICAL or IMMUNOLOGICAL PROPERTIES

Pharmacotherapeutic group: Antibacterials for systemic use; Sulfadiazine + Trimethoprim
ATC Vet code : QJ01EW10

5.1 Pharmacodynamic properties

Trinacol is a broad spectrum antibacterial active against both Gram-negative and Gram-positive bacteria including *Streptococci, Staphylococci, Actinobacilli, Actinomycae, Salmonella, Pasteurella, Pneumococci, Proteus, E. Coli, Corynebacteria, Vibrio, Bordetella, Brucella, Klebsiellae and Haemophilae*
Sulfadiazine (SDZ) inhibits the incorporation of para-aminobenzoic acid into folic acid and trimethoprim (TMP) inhibits the enzyme dihydrofolate reductase (DHFR) which converts dihydrofolic acid into tetrahydrofolic acid. TMP and SDZ act together synergistically with a double-blockade mode of action. The combination is bactericidal, inhibiting sequential steps in the synthesis of purines which are required for DNA synthesis. TMP/SDZ combinations have a broad bactericidal action against many gram-positive and gram-negative aerobic bacteria, a large proportion of anaerobic bacteria, chlamydia, and protozoa.

5.2 Pharmacokinetic properties

Sulfadiazine is moderately well absorbed after oral administration (rapidly by pigs but more slowly by cattle), is protein bound only to a limited extent and is well distributed. Metabolism occurs in the liver and the major products are acetylated derivatives which are excreted mainly by glomerular filtration. The plasma half lives in cattle, pigs and dogs are 2 – 3 and 4 hours respectively. Trimethoprim is a weak base with low water solubility. It is readily absorbed from the gastro-intestinal tract, although it is degraded in the rumen. Trimethoprim is about 65% protein bound but, being lipid soluble, readily penetrates cellular barriers to become widely distributed. It is partly oxidised and conjugated in the liver and the metabolities, plus unchanged Trimethoprim are excreted in the urine. The degree of metabolism varies: 80% in the dog and almost 100% in the cow. The half-life is also variable: 2 hours in the pig and 1 hour in the cow.
Given the wide interspecies variability in the half-life of both actives, it is not possible to attain pharmacokinetic matching of the two compounds, but there is evidence that synergism occurs over a wide range of dose ratios. The combination of 1 : 5 Trimethoprim:Sulfadiazine is well documented for veterinary use.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Chlorocresol
Sodium Formaldehyde Sulphoxylate Dihydrate
Disodium edetate dihydrate
Sodium hydroxide
N-methyl pyrrolidone
Water for injection

6.2 Incompatibilities

None known.

6.3 Shelf-life

Shelf life of the veterinary medicinal product as packaged for sale : 2 years.
Shelf life after first opening the immediate packaging : 28 days.

6.4 Special precautions for storage

Do not store above 25º C.
Do not freeze. Protect from light.
Crystallisation of the product at low temperatures can be reversed by gentle warming.

6.5 Nature and composition of immediate packaging

Cardboard box containing a 100 ml amber type II glass vial sealed with nitryl rubber bungs.

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

Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal products should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

Boehringer Ingelheim Limited,
Ellesfield Avenue,
Bracknell,
Berkshire,
RG12 8YS,
United Kingdom.

8 MARKETING AUTHORISATION NUMBER(S)

VPA 10007/022/002

9 DATE OF THE FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

14th January 2008

10 DATE OF REVISION OF THE TEXT