IRISH MEDICINES BOARD ACT 1995

ANIMAL REMEDIES REGULATIONS, 2005

(S.I. No. 734 of 2005)

VPA: **10126/005/001**
Case No: 7002810

The Irish Medicines Board in exercise of the powers conferred on it by Animal Remedies Regulations (S.I. No. 734 of 2005) hereby grants to:

Bimeda Chemicals

Broomhill Road, **Tallaght**, **Dublin 24.**, **Ireland**

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:

Dipen 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.

Signed on behalf of the Irish Medicines Board

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A person authorised in that behalf by the said Board.

(NOTE: 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

Dipen Injection

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:		
Active Substances		
Procaine Benzylpenicillin	150.0	mg
Dihydrostreptomycin (as Dihydrostreptomycin Sulphate)	150.0	mg
Excipients		
Methyl Parahydroxybenzoate	1.0	mg
Sodium Formaldehyde Sulfoxylate	1.49	mg
Cetrimide	0.2	mg

For a full list of excipients see section 6.1.

3 PHARMACEUTICAL FORM

Suspension for injection.

4 CLINICAL PARTICULARS

4.1 Target Species

Cattle, Sheep and Pigs

4.2 Indications for use, specifying the target species

For the treatment of infections caused by organisms sensitive to penicillin and dihydrostreptomycin. These include both gram positive and gram negative organisms as follows:

Pasteurella spp.	*Actinomyces pyogenes*
Streptococci	*Bacillus anthracis*
Penicillinase negative Staphylococci	*Corynebacterium pseudotuberculosis*
Listeria spp.	*Corynebacterium renale*
Leptospira spp.	*Erysipelothrix rhusiopathie*

4.3 Contraindications

Do not use in animals with known hypersensitivity to the active ingredients.

Do not use in sheep producing milk for human consumption.

Do not use by the intravenous route.

4.4 Special warnings for each target species

Cattle and sheep: None.

Pigs: Occasionally in suckling and fattening pigs, administration of this product may cause a transient pyrexia, vomiting, shivering, listlessness and incoordination. Additionally in pregnant sows and gilts a vulval discharge which could be associated with abortion has been reported. Care should be taken not to overdose.

4.5 Special precautions for use

Special precaution(s) for use in animals

None.

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

Penicillins, cephalosporins and dihydrostreptomycin may cause sensitization following injection, inhalation, ingestion or skin contact. Sensitivity to penicillins may lead to cross sensitivity to cephalosporins and vice versa. Allergic reactions to these substances may occasionally be serious.

Do not handle this product if you know that you are sensitized, or if you have been advised not to work with such preparations.

Handle this product with care to avoid exposure.

If you develop symptoms such as a skin rash following exposure, seek medical advice and show this warning to the doctor. Swelling of the face, lips or eyes, or difficulty with breathing are more serious symptoms and require urgent medical attention.

4.6 Adverse reactions (frequency and seriousness)

Penicillins, cephalosporins and dihydrostreptomycin may cause sensitisation following injection, inhalation, ingestion or skin contact. Sensitivity to penicillins may lead to cross sensitivity to cephalosporins and vice versa. Allergic reactions to these substances may occasionally be serious.

4.7 Use during pregnancy, lactation or lay

Although the use of penicillin has been associated with the vulval discharge in pregnant sows and gilts, there is no evidence from the extensive use of Dipen Injection that this product presents any particular hazard to dam or foetus. Dipen Injection may therefore be used safely in pregnant sows and gilts.

Administration of Dipen to lactating animals may lead to the excretion of antibiotics in the milk. Milk from treated animals should be withheld from human consumption in accordance with the instructions at 4.11.

4.8 Interaction with other medicinal products and other forms of interaction

Dipen does not interact significantly with any of the other drugs commonly administered to cattle, sheep or pigs.

4.9 Amounts to be administered and administration route

For administration by intramuscular injection only.

Dosage: Not more than 20 ml to be injected at any one site; 2 ml per 50 kg bodyweight (equivalent to 6 mg procaine penicillin and 6 mg dihydrostreptomycin per kg). This dosage may be repeated at 24 hour intervals over the next two days.

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

Care should be taken not to overdose.

Overdosing may invalidate the stated meat and milk withholding times.

Tolerance studies have been conducted with Dipen Forte, which contains higher concentrations of both active ingredients at twice the recommended dosage rate in all three target species, without any ill-effects being observed.

4.11 Withdrawal Period(s)

Milking from lactating cows should be discarded during treatment and may only be taken for human consumption from 72 hours after the last injection.

Animals may not be slaughtered for human consumption during treatment. Animals must not be slaughtered for human consumption until the following times after the last treatment.

21 days	-	Cattle
28 days	-	Sheep
35 days	-	Pigs

5 PHARMACOLOGICAL or IMMUNOLOGICAL PROPERTIES

Dipen contains two active ingredients: Procaine Benzylpenicillin and Dihydrostreptomycin.

Procaine benzylpenicillin is a complex, sparingly soluble organic salt of benzylpenicillin. Use of the procaine salt is intended to delay absorption of the drug from the injection site and so give rise to a longer duration of action than would be expected from benzylpenicillin. In other respects, however, procaine benzylpenicillin shares the properties of benzylpenicillin. Penicillins act by interfering with microbial cell wall synthesis.

Dihydrostreptomycin is an aminoglycoside drug closely related to streptomycin. Aminoglycosides disturb the permeability of the bacterial cell membrane, by an effect exerted during cell wall development.

Both procaine benzylpenicillin and dihydrostreptomycin are narrow spectrum antibiotics which have a bacteriostatic effect at low concentrations but which are bactericidal at higher concentrations. Penicillin is active primarily against gram-positive bacteria, while dihydrostreptomycin is active mainly against gram-negative bacteria, giving the combination product broad-spectrum antibiotic effects. In some instances the antibacterial effect is further enhanced by synergism between the active ingredients.

Following intramuscular injection of Dipen, peak concentrations of both antibiotics in plasma are reached within 1 to 2 hours. Peak blood levels of penicillin achieved are 1.41 mcg/ml in cattle, 1.56 mcg/ml in sheep and 1.32 mcg/ml in pigs. For dihydrostreptomycin, the appropriate levels are 17.09 mcg/ml in cattle, 21.68 mcg/ml in sheep and 20.29mcg/ml in pigs. All of these levels are well in excess of the MICs for both antibiotics for the more sensitive organisms. Dihydrostreptomycin tends in most instances to have a longer plasma half-life than that of penicillin.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Methyl Parahydroxybenzoate
Sodium Formaldehyde Sulfoxylate USNF
Disodium Edetate
Povidone
Sodium Citrate
Monopotassium Phosphate
Antifoam M30
Cetrimide
Lecithin
Water for Injections

6.2 Incompatibilities

None known.

6.3 Shelf-life

Shelf-Life: 2 years.

In-use shelf-life: 28 days

6.4 Special precautions for storage

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

6.5 Nature and composition of immediate packaging

Clear, Type II glass vial sealed with a brombutyl rubber stopper with aluminium overseal, containing 100 ml of an off-white sterile aqueous suspension.

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

Unused product or waste material should be disposed of in accordance with current practice for pharmaceutical waste under national waste disposal regulations.

7 MARKETING AUTHORISATION HOLDER

Bimeda Chemicals,
Broomhill Road,
Tallaght,
Dublin 24.
(A division of Cross Vetpharm Group Ltd.).

8 MARKETING AUTHORISATION NUMBER(S)

VPA 10126/5/1

9 DATE OF THE FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

1st October 2002