DIP3-MY

Penstrep-400

NAME PRODUCT
Penstrep-400
Suspension for injection

PRODUCT DESCRIPTION
White suspension.

QUALITATIVE AND QUANTITATIVE COMPOSITION PER ML
Active ingredients:
Benzylpenicillin procaine ..... 200 000 IU
Dihydrostreptomycin sulfate ..... 200 mg
Preservatives:
Sodium methyl-p-hydroxybenzoate ..... 1.72 mg
Sodium propyl-p-hydroxybenzoate ..... 0.12 mg

TARGET SPECIES
Horses, cattle, sheep, pigs, dogs and cats.

PHARMACODYNAMICS PROPERTIES AND PHARMACOKINETIC DATA
Procaine benzylpenicillin: antibiotic betalactam that is contained within the natural penicillins of group G, exclusively parenteral administration and reduced spectrum. It has a fundamentally bactericidal action against the majority of Gram + bacteria and against a limited number of Gram - bacteria (especially in the urinary medium), as well as against certain spirochetes and actinomycetes, including the following microorganisms in its spectrum of action:

Gram-positive:
Corynebacterium spp., Streptococcus spp., *Staphylococcus* spp., *Clostridium* spp., *Bacillus anthracis*, *Erisypelotrix* spp., *Nocardia* spp., *Listeria* spp., *Vibrio* spp., *Actinomyces* spp.

Gram-negative:
Fusobacterium necrophorum, *Pasteurella* spp., *Haemophilus* spp., *Actinobacillus* spp., *Proteus* spp., *Neisseria* spp.

Other:
Some Rickettsias, *Leptospira* spp., Espiroquetas (*Borrelia, Treponema*).

Dihydrostreptomycin: bactericidal aminoglycoside antibiotic, active against Gram-negative bacteria and some Gram-positive, including in their spectrum of action:
Escherichia coli, *Klebsiella* spp., *Shigella* sp., *Proteus* spp., (some species), *Salmonella* spp. (some species), *Yersinia* spp., *Pasteurella* spp. (some species), strains of *Actinomyces bovis*, *Leptospira* spp., *Mycobacterium* spp., *Haemophilus* spp., *Brucella* spp., *Campylobacter fetus*.
The association of both compounds achieves a bactericidal effect of Gram-positive and Gram-negative bacteria.

Mode of action: procaine benzylpenicillin works by blocking the biosynthesis of the bacterial wall. It is fixed by covalent union after the opening of the beta-lactam nucleus, on certain enzymatic proteins PBP (transpeptidases). Penicillin is only active on bacteria in the multiplication phase. Dihydrostreptomycin works by binding to the 30S unit of ribosomes. Above all, it prevents the initiation phase, disturbing the ordering of the messenger RNA and causing an incorrect reading of the genetic code by the transfer RNA. It also disturbs the permeability of the bacterial membrane. With the association of both compounds, a synergism is achieved due to a first effect of penicillin on the bacterial cell wall, allowing dihydrostreptomycin to penetrate more easily into the cell, therefore increasing the effectiveness of the two compounds separately.

Resistance: some previously mentioned microorganisms become resistant to the product by producing beta-lactamases, which break the beta-lactam ring of penicillins, making them inactivated. In addition, there is cross-resistance with other aminoglycosides such as streptomycin, neomycin, gentamicin and kanamycin.

Pharmacokinetics: after intramuscular administration, benzylpenicillin is released over a long period from the injection site, producing a maximum concentration in the blood within 1-3 hours of administration (depending on species). It is weakly bound to plasma proteins in a production of 45 to 65% and therapeutic blood levels persist 24 hours. Dihydrostreptomycin, however, is rapidly absorbed from the point of inoculation, reaching the highest concentrations in the blood after 1 hour, being absorbed approximately 2 times faster than benzylpenicillin, its biological half-life being half that of the latter.
The optimal pH of activity of benzylpenicillin is slightly acidic, 5.5 to 6.5. It is widely distributed throughout the body, but the concentration in the different body tissues differs, reaching significant amounts of the drug in the lung, kidney, liver, skin, and intestinal contents, and low concentrations are observed in poorly vascularized areas, such as cornea, cartilage, and bones. The inflammatory state allows its diffusion into pleural, pericardial, peritoneal, and synovial fluids, as well as into cerebrospinal fluid and abscesses. It crosses the placenta and slowly enters the fetal circulation from the mother. It is partially metabolized to peniciloic acid, but for the most part (90%) it is excreted in the urine in unchanged form.
It also appears in small amounts in the milk of lactating females. With respect to dihydrostreptimycin, it is preferentially distributed in the extracellular spaces of the body and is hardly bound to plasma proteins (less than 10%), minimally penetrating most tissues except the kidney (relatively small volume of distribution: 0, 35 L. 0.45 kg). Good concentrations are obtained in the fluids of the body cavities, especially if there is inflammation. It crosses the blood-brain and placental barriers, as well as joints and the eyeball, but does not achieve therapeutic concentrations in them, nor does it achieve bronchial secretions, intestinal fluid, prostate secretions, bile, and milk. Is excreted in 50 - 60% the urine, unchanged, and 2 - 5% is eliminated in bile.

INDICATIONS FOR USE, SPECIFYING THE TARGET SPECIES
Treatment of bacterial infections, postoperative and/or secondary to viral infections, caused by germs sensitive to the association, such as:
Horses:
- Metritis.
- Pneumonia and bronchopneumonia.
- Papera.

Cattle and sheep:
- Skin abscesses.
- Actinomycosis.
- Foot conditions.
- Arthritis.
- Anthrax.
- Leptospirosis.
- Mamitis.
- Metritis.
- Pneumonia and bronchopneumonia.

Swine:
- Arthritis.
- Abortion (by Brucellas, Leptospiras and other sensitive germs).
- Leptospirosis.
- Mal rojo.
- Pneumonia and bronchopneumonia.
- MMA syndrome.

Dogs and cats:
- Arthritis
- Genito-urinary infections
- Pneumonia
- Tracheobronchitis
- Peritonitis

Manufactured by:
Interchemie Werken de Adelaar Eesti AS
Vanapere tee 14, Püünsi village, Viimsi municipality,
Harju country, 74013 ESTONIA

Holland

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CONTRAINDICATIONS
Do not administer in:
- animals with hypersensitivity to penicillins and/or aminoglycosides.
- animals with renal failure, liver disease, heart disease or with cochleovestibular lesions.
- animals under 1 month old.
- rabbits, guinea pigs and hamsters.

SPECIAL WARNINGS FOR EACH TARGET SPECIES
Do not administer to horses whose meat is intended for human consumption.

SPECIAL SAFETY PRECAUTIONS TO BE TAKEN BY THE PERSON MANAGING OR HANDLING THE PRODUCT
Have not been described.

SPECIAL PRECAUTIONS FOR USE
- Maintain aseptic conditions during the administration of the preparation, previously disinfecting the injection area with alcohol.
- Do not administer subcutaneously, intravenously or in the vicinity of an important nerve.
- Administer with caution in animals with a history of allergies.
- Monitor renal function during treatment, especially in young animals.
- Avoid prolonged treatments, especially in carnivores.

INTERACTION WITH OTHER MEDICAMENTS AND OTHER FORMS OF INTERACTION
Do not administer in conjunction with:
- Bacteriostatic antibiotics and other aminoglycosides, due to their antagonism.
- Pentobarbital and inhalation anesthetics, due to the risk of vascular depression.
- Muscle relaxants, due to the risk of neuromuscular blockade.
- Others: heparin, calcium gluconate, riboflavin, triamcinolone, indomethacin, phenylbutazone, salicylates and other weak acids.

INCOMPATIBILITIES
Benzylpenicillin is incompatible with acids, even weak (maximum solution stability is at pH 6.5), alkalis, oxidizers in general, sodium sulfonamides, silver salts, mercury, copper, iron, aluminum and bismuth (precipitation), lead, nickel and zinc (inactivation). Iodine and iodides, sulfides, primary amines, quinine salts, procaine, ephedrine, tetracycline and oxytetracycline hydrochloride (precipitation), vitamin B_1, chloramphenicol, glucose.

USE DURING PREGNANCY AND LACTATION
Do not administer in pregnant females, because there is a risk of fetal cochleovestibular toxicity.

ADVERSE REACTIONS (FREQUENCY AND SERIOUSNESS)
Allergic or anaphylactic reactions: occur in hypersensitive animals, and are sometimes severe, usually lasting between 2 and 4 hours. Older dogs and bovids tend to be more predisposed, and their symptoms are salivation, tremors, vomiting, labored breathing and skin edema, in some areas of the body. In severe cases, administration will be abolished and epinephrine and/or corticosteroids applied immediately.

Pigs and fattening pigs: occasionally, and in stressful situations, transient fever, vomiting, incoordination, tremors and apathy may occur.

White-coated horses and thin skin: skin and cardinal plaques can be seen at the point of application, with local edema and muscle pain.

OVERDOSE (SYMPTOMS, EMERGENCY MEASURES, ANTIDOTES)
Curariform toxicity due to accidental intoxication: symptoms include restlessness, respiratory distress, loss of consciousness and sometimes death from respiratory failure and vasomotor depression. In these cases, administration of the drug will be discontinued and manmade breathing, as well as antihistamines and calcium salts will be applied slowly through IV.

Ototoxicity: (mainly in cats): as a species particularly sensitive to dihydrostreptomycin, especially in prolonged treatments. Symptoms include loss of balance and hearing, ataxia and progressive rotary nystagmus loss. In these cases, administration of the medicinal product will be discontinued. However, recovery is slow and gradual, and in some cases the damage is permanent.

Nephrotoxicity: albuminuria, cylinder, enzymatic and anuria are usually observed.

WITHDRAWAL PERIODS
Meat : 30 days.
Milk : 3 days.

Not allowed for use in horses whose meat is intended for human consumption.

AMOUNTS TO BE ADMINISTERED AND ADMINISTRATION ROUTE
Intramuscular route.

Cattle, sheep, pigs and horses:
6000 - 12000 IU of procaine benzylpenicillin + 6 - 12 mg of dihydrostreptomycin/kg b.w. and day (equivalent to 0.3 - 0.6 ml of Penstrep-400 for every 10 kg of live weight).

Dogs and cats:
10000 - 20000 IU procaine benzylpenicillin + 10 - 20 mg dihydrostreptomycin/kg b.w. and day (equivalent to 0.5 - 1 ml of Penstrep-400 for every 10 kg of live weight).
Continue treatment until 1 or 2 days after remission of symptoms.

STORAGE INSTRUCTIONS
Storage: Store at 2 - 8 °C.
Shelf life: 24 months.
Shelf life after first opening of container: 28 days.

PACKAGING
50 and 100 ml of clear type II glass injection vials closed with a rubber stopper and an aluminium cap.

Keep out of reach of children / Jauhkan dari Kanak-Kanak!

MARKETING AUTHORIZATION HOLDER
Danberg (M) Sdn Bhd (58493-A),
Lot 1, Jalan Bursa 23/4, Seksyen 23,
40300 Shah Alam, Selangor, Malaysia

Controlled Medicine / Ubat Terkawal

- Product Registration No. -

DATE OF REVISION
17 June 2021

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