

IRISH MEDICINES BOARD ACT 1995

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

(S.I. No. 786 of 2007)

VPA: **10996/197/001**
Case No: 7003468

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:

Intervet Ireland Limited

Magna Drive, Magna Business Park, 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:

Cephaguard IV IM 4.5% powder and solvent for 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 revoked, shall continue in force from **31/01/2008** until .

Signed on behalf of the Irish Medicines Board

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

Cephaguard IV IM 4.5% powder and solvent for solution for injection

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

1 vial with powder contains:

30 ml-vial: 1.35 g cefquinome (as sulphate)

100 ml-vial 4.5 g cefquinome (as sulphate)

1 ml solvent contains:

Preservative: Benzyl alcohol 10 mg

Each ml of the reconstituted solution contains:

Active substance:

Cefquinome (as sulphate) 45 mg

Excipient:

Benzyl alcohol 10 mg

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Powder and solvent for solution for injection

4 CLINICAL PARTICULARS

4.1 Target Species

Horse (adult and foal)

4.2 Indications for use, specifying the target species

For the treatment of:

Respiratory diseases in horses caused by *Streptococcus equi* subsp. *zooepidemicus*

Severe bacterial infections with a high risk of septicaemia in foals in which *Escherichia coli* is involved

4.3 Contraindications

Do not use in animals which are known to be hypersensitive to cephalosporin antibiotics or other β -lactam antibiotics.

4.4 Special warnings for each target species

The safety of Cobactan 4.5% has not been determined in horses intended for breeding.

4.5 Special precautions for use

Special precautions for use in animals

Use of the product should be based on susceptibility testing and take into account official and local antimicrobial policies.

Inappropriate use of the product may increase the prevalence of bacteria resistant to cefquinome and may decrease the effectiveness of treatment with cephalosporins, due to the potential for cross-resistance.

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

Penicillins and cephalosporins may cause hypersensitivity (allergy) following injection, inhalation, ingestion or skin contact. Hypersensitivity to penicillins may lead to cross sensitivity to cephalosporins and vice versa. Allergic reactions to these substances may occasionally be serious.

1. Do not handle this product if you know you are sensitized, or if you have been advised not to work with such preparation.
2. Handle this product with great care to avoid exposure, taking all recommended precautions.
3. If you develop symptoms following exposure such as a skin rash, you should seek medical advice and show the doctor this warning. Swelling of the face, lips or eyes or difficulty with breathing, are more serious symptoms and require urgent medical attention.

In case of accidental contact with eyes, rinse immediately with copious amounts of water. Accidental spillage on the skin should be washed off immediately with soap and water. In case of accidental self-injection, seek medical advice immediately and show the package leaflet or the label to the physician.

4.6 Adverse reactions (frequency and seriousness)

Hypersensitivity reactions to cephalosporins occur rarely.
Occasionally slight transient reactions may occur at the injection site.

4.7 Use during pregnancy, lactation or lay

There is no information on reproductive toxicity (incl. teratogenicity) in horses. Laboratory studies in rats and rabbits have not shown any teratogenic, foetotoxic or maternotoxic effects. Use only according to the benefit/risk assessment by the responsible veterinarian.

4.8 Interaction with other medicinal products and other forms of interaction

See section 5.1 with regard to cross-resistance.
No interactions were seen during the clinical field trials

4.9 Amounts to be administered and administration route

Reconstitute the solution for injection by adding the whole content of the solvent vial. After reconstitution, shake the vial well before use. Do not use another solvent (e.g. water for injection). Swab the rubber stopper before removing each dose. Use a dry sterile needle and syringe. An appropriately graduated syringe must be used to allow accurate administration of the required dose volume. The rubber stopper may be punctured up to 20 times.

Indication	Dose	Frequency and Duration
Respiratory diseases in horses caused by <i>Streptococcus equi</i> subsp. <i>zooepidemicus</i>	1 mg cefquinome/kg bodyweight (1 mL reconstituted solution /45 kg bodyweight)	Once daily for 5 to 10 consecutive days. Stop treatment 2 days beyond cessation of clinical signs.*
Severe bacterial infections with a high risk of septicaemia in foals in which <i>Escherichia coli</i> is involved	1 mg cefquinome/kg bodyweight (1 mL reconstituted solution / 45 kg bodyweight)	Twice daily for 6 to 14 consecutive days. Stop treatment 3 days beyond cessation of clinical signs.*

* If no response is seen in 3-4 days, the diagnosis should be redetermined.

All treatments will be given by intravenous or intramuscular injections. It is recommended to administer the product into different injection sites. In foals, it is recommended to start the treatment with intravenous injections for 3 days and to follow with intramuscular injections.

To ensure the correct dosage and to avoid possible underdosing, the bodyweight should be determined as accurately as possible.

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

Doses of 1 mg/kg in horses and 3 mg/kg in foals twice daily have been well tolerated.

4.11 Withdrawal Period(s)

Meat: 4 days
Not allowed for use in lactating mares producing milk for human consumption.

5 PHARMACOLOGICAL or IMMUNOLOGICAL PROPERTIES

Pharmacotherapeutic group: other beta-lactam antibacterials
ATCvet code: QJ01DE90

5.1 Pharmacodynamic properties

Cefquinome is an antibacterial of the cephalosporin group which acts by inhibition of cell wall synthesis. It is characterised by its broad therapeutic spectrum of activity and a high stability against penicillinases and beta-lactamases.

In vitro activity has been demonstrated against common Gram positive and Gram negative bacteria including *Escherichia coli*, *Streptococcus equi* subsp. *zooepidemicus*, *Klebsiella pneumoniae*, *Enterobacter spp.*, *Staphylococcus aureus*, *Streptococcus equi* subsp. *equi*, *Clostridium perfringens* and *Actinobacillus equuli*.

A total of 162 bacterial isolates were collected from adult horses and foals with diseases corresponding to the indications for use in Germany, France, United Kingdom, Hungary and the Netherlands between 1999 and 2005.

These pathogens were found to be susceptible to cefquinome with MIC levels ranging from < 0.008 to $0.25 \mu\text{g/mL}$ for *S. equi* subsp. *zooepidemicus* and from 0.032 to $2 \mu\text{g/mL}$ for *E. coli*. The MIC_{90} was $0.032 \mu\text{g/mL}$ for *S. equi* subsp. *zooepidemicus* and $0.125 \mu\text{g/mL}$ for *E. coli*.

Cefquinome as a fourth generation cephalosporin combines high cellular penetration and β -lactamase stability. In contrast to cephalosporins of previous generations, cefquinome is not hydrolysed by chromosomally-encoded cephalosporinases of the Amp-C type or by plasmid mediated cephalosporinases of some enterobacterial species.. Resistance mechanism in Gram negative organisms due to extended spectrum beta-lactamases (ESBL) and in Gram-positive organisms due to alteration of penicillin binding proteins (PBPs) may lead to cross-resistance.

5.2 Pharmacokinetic properties

In horses peak serum concentrations of about $2.5 \mu\text{g/mL}$ are reached within one hour after intramuscular administration at the dose of $1 \text{ mg cefquinome/kg bodyweight}$. Cefquinome has a plasma half-life of 2 hours in adult horses and 1.4 hour in foals and is bound to plasma proteins at $< 5\%$. Bioavailability following intramuscular administration is almost 100%.

In foals peak serum concentrations of about $1.8 \mu\text{g/mL}$ in less than 1 hour after intramuscular administration at the dose of $1 \text{ mg cefquinome/kg bodyweight}$. Bioavailability is 87%. For adult horses, the period of time that plasma concentrations were above MIC ($T > \text{MIC}$) for *Streptococcus equi* subsp. *zooepidemicus* ($\text{MIC} = 0.032$) were 55.4% and 49.6% of the treatment interval for the IM and IV route, respectively.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Benzyl alcohol
Disodium phosphate dihydrate
Water for injection

6.2 Incompatibilities

In the absence of compatibility studies, this veterinary medicinal product must not be mixed with other veterinary medicinal products.

6.3 Shelf-life

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

Powder: 2 years

Solvent: 3 years

Note: This shelf life relates to single vials of powder and solvent. The common carton box for powder and solvent vials bears the shorter shelf life of 2 years.

Shelf-life after dilution or reconstitution according to directions:

10 days when stored in a refrigerator (2°C – 8°C)

After this time, product remaining in the container should be discarded.

6.4 Special precautions for storage

Powder and solvent:

This veterinary medicinal product does not require any special storage conditions.

Reconstituted solution:

Store in a refrigerator (2°C – 8°C).

6.5 Nature and composition of immediate packaging

30 mL type II (Ph. Eur.) glass vials sealed with bromobutyl rubber stoppers containing 1.35 g cefquinome (as sulphate) as crystallised powder

30 mL type I (Ph. Eur.) glass vials sealed with bromobutyl rubber stoppers containing 29 mL solvent

100 mL type II (Ph. Eur.) glass vials sealed with bromobutyl rubber stoppers containing 4.5 g cefquinome (as sulphate) as crystallised powder

100 mL type I (Ph. Eur.) glass vials sealed with bromobutyl rubber stoppers containing 96 mL solvent

For all vials, the stoppers are covered by aluminium caps.

Pack sizes:

Box of one 30 mL powder vial bundled with a box of one 30 mL solvent vial

Box of one 100 mL powder vial bundled with a box of one 100 mL solvent vial

Box containing one 30 mL powder vial and one 30 mL solvent vial

Box containing one 100 mL powder vial and one 100 mL solvent vial

Not all pack sizes may be marketed.

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

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

7 MARKETING AUTHORISATION HOLDER

Intervet Ireland Limited
Magna Drive
Magna Business Park
Dublin 24
Ireland

8 MARKETING AUTHORISATION NUMBER(S)

VPA 10996/197/1

9 DATE OF THE FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

21st December 2005

10 DATE OF REVISION OF THE TEXT

30th January 2008