

Summary of Product Characteristics

1 NAME OF THE VETERINARY MEDICINAL PRODUCT

Cobactan 4.5% w/v powder and solvent for solution for injection for horse and cattle.

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 (E1519) 10 mg

Each ml of the reconstituted solution contains:

Active substance:

Cefquinome (as sulphate) 45 mg

Excipient:

Benzyl alcohol (E1519) 10 mg

For a full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Powder and solvent for solution for injection.

White to pale yellowish-white crystalline powder and clear colourless solvent.

4 CLINICAL PARTICULARS

4.1 Target Species

Horse (adult and foal) and cattle (adult and calf).

4.2 Indications for use, specifying the target species

For the treatment of bacterial infections in horses and cattle caused by the following Gram positive and Gram negative microorganisms sensitive to cefquinome:

Horses:

- Respiratory diseases caused by *Streptococcus equi* subsp. *zooepidemicus*

Foals:

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

Cattle:

- Respiratory diseases caused by *Pasteurella multocida* and *Mannheimia haemolytica*
- Digital dermatitis, infectious bulbar necrosis and acute interdigital necrobacillosis (foul in the foot)
- Acute *E. coli* mastitis with signs of systemic involvement

Calves:

- *E. coli* septicaemia

4.3 Contraindications

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

Do not use in poultry (including eggs) due to risk of spread of antimicrobial resistance to humans.

4.4 Special warnings for each target species

None.

4.5 Special precautions for use

Special precautions for use in animals

Cobactan 4.5% selects for resistant strains such as bacteria carrying extended spectrum betalactamases (ESBL) which may constitute a risk to human health if these strains disseminate to humans e.g. via food. For this reason, Cobactan 4.5% should be reserved for the treatment of clinical conditions which have responded poorly, or are expected to respond poorly (refers to very acute cases when treatment must be initiated without bacteriological diagnosis), to first line treatment. Official, national and regional antimicrobial policies should be taken into account when the product is used. Increased use, including use of the product deviating from the instructions given in the SPC, may increase the prevalence of such resistance. Whenever possible, Cobactan 4.5% should only be used based on susceptibility testing.

Cobactan 4.5% is intended for treatment of individual animals. Do not use for disease prevention or as a part of herd health programmes. Treatment of groups of animals should be strictly limited to ongoing disease outbreaks according to the approved conditions of use.

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. In horses, occasionally slight transient reactions may occur at the injection site. In cattle, use of the product may result in localized tissue reaction. Tissue lesions are repaired 15 days after the last injection.

4.7 Use during pregnancy, lactation or lay

There is no information on reproductive toxicity (incl. teratogenicity) in horses and cattle. 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.

Target species	Indication	Dosage	Frequency and Duration
Horses	Respiratory diseases 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.
Foals	severe bacterial infections with a high risk of septicaemia in which <i>E. 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.
Cattle	Respiratory diseases caused by <i>Pasteurella multocida</i> and <i>Mannheimia haemolytica</i>	1 mg cefquinome/kg bodyweight (1 ml reconstituted solution/45 kg bodyweight)	Once daily for 3 to 5 consecutive days
	Digital dermatitis, infectious bulbar necrosis and acute interdigital necrobacillosis (foul in the foot)		
	Acute <i>E. coli</i> mastitis with signs of systemic involvement	1 mg cefquinome/kg bodyweight (1 ml reconstituted solution/45 kg bodyweight)	Once daily for 2 consecutive days
Calves	<i>E. coli</i> septicaemia	2 mg cefquinome/kg bodyweight (2 ml reconstituted solution/45 kg bodyweight)	Once daily for 3 to 5 consecutive days

In cattle and calves treatments will be given by intramuscular injection, and restricted to 10 ml per injection site. In horses and foals the injections can be given either intramuscularly or intravenously. It is recommended to administer the product into different injection sites, in cattle preferably into the neck, respectively the cervical region. 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 20 mg/kg in cattle, 1 mg/kg in horses and 3 mg/kg in foals twice daily have been well tolerated.

4.11 Withdrawal Period(s)

Horse

Meat: 4 days

Not to be used in horses producing milk for human consumption.

Cattle

Meat: 2 days

Milk: 36 hours (3 milkings)

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 bactericidal and 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 *Streptococcus equi* subsp. *Zooepidemicus*, *Escherichia coli*, *Pasteurella multocida*, *Mannheimia haemolytica* and *Fusobacterium spp.*

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 µg/mL for *S. equi* subsp. *zooepidemicus* and from 0.032 to 2 µg/mL for *E. coli*. The MIC₉₀ was 0.032 µg/mL for *S. equi* subsp. *zooepidemicus* and 0.125 µg/mL for *E. coli*.

Since 1994, bacterial isolates from cattle in Germany, France, United Kingdom, the Netherlands, Spain, Italy, Belgium and Ireland have been regularly tested on their susceptibility against cefquinome. Investigations which have been done between 2000 and 2004 on 304 *Mannheimia haemolytica* and *Pasteurella multocida* isolates have shown a susceptibility rate of 100 % with a MIC of ≤ 0.008 to 0.125 µg/ml (limiting concentration for susceptibility: 2 µg/ml).

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. However, some extended spectrum beta-lactamases (ESBL) can hydrolyse cefquinome and cephalosporins of other generations. The potential for resistance development against cefquinome is rather low. High-level resistance to cefquinome would require the coincidence of two genetic modifications, i.e. hyperproduction of specific β-lactamases as well as decreased membrane permeability.

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 µg/ml are reached within one hour after intramuscular administration at the dose of 1 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 young foals peak serum concentrations of about 1.8 µg/ml are reached in less than 1 hour after intramuscular administration at the dose of 1 mg cefquinome/kg bodyweight. Bioavailability is 87%. For adult horses, the period of time that plasma concentrations were above MIC (T>MIC) for *Streptococcus equi* subsp. *zooepidemicus* (MIC = 0.032) were 55.4% and 49.6% of the treatment interval for the IM and IV route, respectively.

In cattle peak serum concentrations of about 2 µg/ml are reached within less than 1 hour after intramuscular administration at the dose of 1 mg cefquinome/kg bodyweight. Cefquinome has a relatively short half-life (2.5 hours), is <5 % protein bound and excreted unchanged in the urine.

Cefquinome is not resorbed after oral administration.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Benzyl alcohol (E1519)
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 crystalline 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 crystalline 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 veterinary medicinal product or waste materials derived from such veterinary medicinal product should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

Intervet Ireland Ltd.,
Magna Drive,
Magna Business Park,
Citywest Road,
Dublin 24,
Ireland.

8 MARKETING AUTHORISATION NUMBER(S)

VPA: 10996/209/001

9 DATE OF THE FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

24th February 2012

10 DATE OF REVISION OF THE TEXT

May 2012