SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

COBACTAN 2.5% w/v suspension for injection for cattle and pigs

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

1 ml suspension for injection contains:

Active substance:

Cefquinome (as sulfate) 25 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 and pigs

4.2 Indications for use, specifying the target species

For the treatment of bacterial infections in cattle and pigs caused by the Gram positive and Gram negative microorganisms sensitive to cefquinome.

Cattle:
Respiratory disease 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 in calves

Pigs:
For the treatment of bacterial infections of the lungs and respiratory tract caused by *Pasteurella multocida, Haemophilus parasuis, Actinobacillus pleuropneumoniae, Streptococcus suis* and other cefquinome-sensitive organisms

Mastitis-Metritis-Agalactia syndrome (MMA) with involvement of *E.coli, Staphylococcus spp., Streptococcus spp*. and other cefquinome sensitive organisms

Piglets:
Reduction of mortality in cases of meningitis caused by *Streptococcus suis*.
For the treatment of:
Arthritis caused by *Streptococcus ssp., E. coli* and other cefquinome-sensitive organisms.
Epidermitis (mild or moderate lesions) caused by *Staphylococcus hyicus.*

4.3 Contraindications

Do not use Cobactan 2.5% in animals, which are known to be hypersensitive to ß-lactam antibiotics.
Do not administer to animals less than 1.25 kg body weight.
Do not use in poultry (including eggs) due to risk of spread of antimicrobial resistance to humans.

4.4 Special warnings <for each animal target species>

None

4.5 Special precautions for use

i. Special precautions for use in animals

Cobactan 2.5% 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 2.5% 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 2.5% should only be used based on susceptibility testing.

Cobactan 2.5% 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 restricted to ongoing disease outbreaks according to the approved conditions of use.

User Warnings

1. Do not handle this veterinary medicinal product if you know you are sensitized, or if you have been advised not to work with such preparation.
2. Handle this veterinary medicinal 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.
4. 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.

4.6 Adverse reactions (frequency and seriousness)

Use of the veterinary medicinal product may result in localized tissue reaction. Tissue lesions are repaired 15 days after the last administration of the veterinary medicinal product.
Hypersensitivity reactions to cephalosporins occur rarely.

4.7 Use during pregnancy and lactation

There is no available information indicating reproductive toxicity in cattle or pigs. In reproduction toxicity studies in laboratory animals cefquinome did not reveal any effect on reproduction or teratogenic potential.

Use only accordingly to the benefit/risk assessment by the responsible veterinarian.

4.8 Interaction with other medicinal products and other forms of interaction

It is known that a cross sensitivity to cephalosporin exists for bacteria sensitive to the cephalosporin group.

Due to undesirable pharmacodynamic interaction, do not apply cefquinome simultaneously with pharmaceuticals acting bacteriostatically.

4.9 Amounts to be administered and administration route

Species	Indication	Dosage	Frequency
Cattle	Respiratory disease caused by *Pasteurella multocida* and M. haemolytica Digital dermatitis, infectious bulbar necrosis and acute interdigital necrobacillosis (foul in the foot)	1 mg cefquinome/kg bw (2 ml/50 kg bw)	Once daily for 3 or 5 consecutive days
	Acute *E. coli* mastitis with signs of systemic involvement	1 mg cefquinome/kg bw (2 ml/50 kg bw)	Once daily for 2 consecutive days
Calves	*E. coli* septicaemia	2 mg cefquinome/kg bw (4 ml/50 kg bw)	Once daily for 3 or 5 consecutive days
Pigs	Respiratory disease	2 mg cefquinome/kg bw (2 ml/25 kg bw)	Once daily for 3 consecutive days.
	MMA	2 mg cefquinome/kg bw (2 ml/25 kg bw)	Once daily for 2 consecutive days.
Piglets	Meningitis Arthritis Epidermitis	2 mg cefquinome/kg bw (2 ml/25 kg bw)	Once daily for 5 consecutive days

All treatments to be given by intramuscular injection. Studies have indicated the advisability of giving second and subsequent injections at a different injection site. The preferred injection site is in muscular tissue in the mid neck'

To ensure a correct dosage, body weight should be determined as accurately as possible to avoid underdosing.

Shake the vial well before using.

The veterinary medicinal product does not contain an antimicrobial preservative. Swab the septum 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. This is particularly important when injecting small volumes, for example when treating piglets. The cap may be safely punctured up to 25 times. The 50ml vial should be used for treating small piglets. When treating groups of animals, use a draw-off needle.

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

Overdoses of 20 mg/kg/day in cattle and 10 mg/kg/day in pigs and piglets have been well tolerated.

4.11 Withdrawal periods

Species	Product	Withdrawal Period
Cattle	Meat and offal	5 days
Cattle	Milk	24 hours
Pigs	Meat and offal	3 days

5. PHARMACOLOGICAL PROPERTIES

Pharmaceutic group: Cephalosporins and related substances
ATCvet code: QJ01DE90

The antibacterial drug cefquinome is a broad-spectrum cephalosporin of the fourth-generation which acts by inhibition of the cell wall synthesis. It is bactericidal and is characterized by its broad therapeutic spectrum of activity and a high stability against penicillinases and beta-lactamases.

5.1 Pharmacodynamic properties

In vitro activity has been demonstrated against common Gram positive and Gram negative bacteria including *Escherichia coli*, Citrobacter spp., Klebsiella spp., *Mannheimia haemolytica*, *Pasteurella multocida*, Proteus spp., Salmonella spp., *Serratia marcescens*, *Haemophilus somnus*, *Arcanobacterium pyogenes*, Bacillus spp., Corynebacterium spp., Staphylococcus spp., Streptococcus spp., Bacteroides spp., Clostridium spp., Fusobacterium spp., Prevotella spp., Actinobacillus spp. and *Erysipelothrix rhusiopathiae*.
Bacterial strains were isolated between 1999 and 2002 from cattle and pigs presenting diseases corresponding to target indications in Germany, France, The Netherlands and United Kingdom. From a sample of more than 350 isolates, 97.7% were found to be susceptible to cefquinome (resistance breakpoint of 4 µg/mL). These susceptible strains had MIC levels ranging from < 0.004 to 2 µg/mL.

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 ß-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 ß-lactamases as well as decreased membrane permeability.

5.2 Pharmacokinetic particulars

In cattle peak serum concentrations of about 2 µg/ml are reached within 1.5-2 hours after intramuscular or subcutaneous administration at the dose of 1 mg/kg. Cefquinome has a relatively short half-life (2.5 hours), is < 5 % protein bound and excreted unchanged in the urine. Cefquinome is not absorbed after oral administration.
In pigs or piglets, at 2 mg/kg dosage, maximum serum concentrations of around 5 µg/ml are measured within 15 to 60 minutes after intramuscular injection. The average half-life is about 9 hours.
Cefquinome binds poorly to plasma proteins and therefore penetrates into the cerebrospinal fluid (CSF) and the synovial fluid in pigs. The concentration profile is similar between the synovial fluid and the plasma. The concentrations reached in the CSF 12 hours after treatment are similar to those in plasma.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Ethyl oleate

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 of the immediate packaging: 28 days

6.4. Special precautions for storage

Do not store above 25°C. Protect from light.

6.5 Nature and composition of immediate packaging

Carton containing one 50ml or 100ml colourless glass bottle, type II with a grey epichlorhydrine rubber stopper, fluoro polymer coated, type I closure and sealed with aluminum caps.

Not all pack sizes may be marketed.

6.6 Special precautions for the disposal of unused veterinary medicinal product or waste materials derived from the use of such products

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

7. MARKETING AUTHORISATION HOLDER

Marketing authorisation holder:
Intervet International B.V.
Wim de Körverstraat 35
5831 AN Boxmeer
The Netherlands

Represented by:

Intervet UK Ltd.
Walton Manor
Walton
Milton Keynes
MK7 7AJ

8. MARKETING AUTHORISATION NUMBER(S)

Vm 01708/4452

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date: 08 November 1993

10. DATE OF REVISION OF THE TEXT

Date: April 2012