1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Cepravin Dry Cow 250 mg intramammary suspension for cattle

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 3 g syringe contains:

Active substance:
Cefalonium (as cefalonium dihydrate) 250 mg

Excipients:

Qualitative composition of excipients and other constituents
Aluminium distearate
Liquid paraffin

White to cream coloured suspension.

3. CLINICAL INFORMATION

3.1 Target species

Cattle (dairy cows at drying-off).

3.2 Indications for use for each target species

For routine dry cow therapy to treat existing sub-clinical infections and to prevent new infections which occur during the dry period.

3.3 Contraindications

Do not use in lactating cows.
Do not use within 54 days of calving.
Do not use in cases of hypersensitivity to cephalosporins, other β-lactam antibiotics or to any of the excipients.

3.4 Special warnings

None.

3.5 Special precautions for use

Special precautions for safe use in the target species:

- If the product is used in heifers during their first pregnancy the same precautions should be observed as in cows, i.e., infusions should be given not less than 54 days before calving and milk discarded for the statutory four days after calving.
- It is unlikely that antibiotic treatment alone will control Summer Mastitis and therefore other measures should be implemented as part of routine management. These measures include:
  - Practising some form of fly control on the farm.
  - Avoiding pasturing cattle on wet or wooded fields which are known to be associated with Summer Mastitis.
  - Post-infusion teat dipping of cows and heifers receiving prophylactic intramammary infusions for the disease.
  - Prompt attention to teat injuries or sores as these rapidly attract flies.

- Farms with an intractable problem should consider changing the calving pattern to avoid having animals at risk during the summer months.

Use of the product should be based on susceptibility testing of the bacteria isolated from milk samples from the animal. If this is not possible, therapy should be based on local (regional, farm level) epidemiological information about susceptibility of the target bacteria. Use of the product deviating from the instructions given in the SPC may increase the prevalence of bacteria resistant to cefalonium and may decrease the effectiveness of treatment with other beta lactams.
Dry cow therapy protocols should take local and national policies on antimicrobial use into consideration and undergo regular veterinary review.
The feeding to calves of milk containing residues of cefalonium that could select for antimicrobial-resistant bacteria (e.g. production of beta-lactamases) should be avoided up to the end of the milk withdrawal period, except during the colostral phase.
The efficacy of the product is only established against the pathogens mentioned in section 4.2. Consequently, serious acute mastitis (potentially fatal) due to other pathogen species, particularly *Pseudomonas aeruginosa*, can occur after drying off. Good hygiene practices should be thoroughly respected in order to reduce this risk.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:
Wash hands after use.
Penicillin and cefalosporins may cause sensitisation (allergy) following injection, inhalation, ingestion or skin contact. Sensitivity to penicillin may lead to cross-sensitivity to cefalosporin and vice versa. Allergic reactions to these substances may occasionally be serious.
Do not handle this product if you know you are sensitised, or if you have been advised not to work with such preparations.
Handle this product with great care to avoid exposure, taking all recommended precautions.
If you develop symptoms following exposure such as a skin rash you should seek medical advice and show the package leaflet or the label to the physician. Swelling of the face, lips or eyes or breathing difficulties are more serious symptoms and require urgent medical attention.

Special precautions for the protection of the environment:
Not applicable.

3.6 Adverse events

None known.

Reporting adverse events is important. It allows continuous safety monitoring of a veterinary medicinal product. Reports should be sent, preferably via a veterinarian, to either the marketing authorisation holder or the national competent authority via the national reporting system. See the package leaflet for respective contact details.

3.7 Use during pregnancy, lactation or lay

Pregnancy and lactation:
The veterinary medicinal product is intended for use during the last trimester of pregnancy once the lactating cow has been dried off.
There is no adverse treatment effect on the foetus.
Do not use in cows that are lactating.

3.8 Interaction with other medicinal products and other forms of interaction

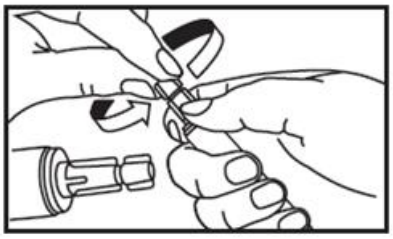
None known.

3.9 Administration routes and dosage

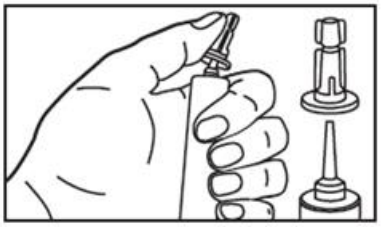
Intramammary use.
The contents of one syringe should be infused into the teat canal of each quarter immediately after the last milking of the lactation. Before infusion, the teat should be thoroughly cleaned and disinfected. Avoid contamination of the nozzle after removing the cap. Do not bend the nozzle. After infusion it is advisable to dip the teats in an antiseptic preparation specifically designed for this purpose. The syringe must only be used once.

1. After milking is complete thoroughly clean and disinfect the end of the teat (e.g. with the cleaning towel provided).

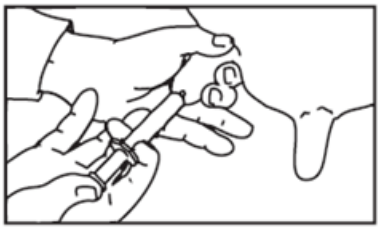
2.(i) **Option 1: For short nozzle intramammary administration** hold the barrel of the syringe and the base of the cap in one hand and twist off the small upper part of the cap above the indent mark (the base portion of the cap remains on the syringe). Take care not to contaminate the short exposed part of the nozzle.



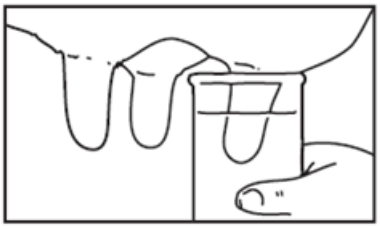
(ii) **Option 2: For full nozzle intramammary administration** remove the cap fully by holding the barrel of the syringe firmly on one hand and with the thumb push up and along the length of the cap until the cap clicks off. Take care not to contaminate the nozzle.



3. Insert the nozzle into the teat canal and apply steady pressure on the syringe plunger until the full dose has been delivered. Holding the end of the teat with one hand, gently massage upwards with the other to aid dispersion of the antibiotic into the quarter.



4. Finally immerse the teats in a teat dip.



3.10 Symptoms of overdose (and where applicable, emergency procedures and antidotes)

Repeated doses in cattle on three consecutive days did not demonstrate or produce any adverse effects.

3.11 Special restrictions for use and special conditions for use, including restrictions on the use of antimicrobial and antiparasitic veterinary medicinal products in order to limit the risk of development of resistance

Not applicable.

3.12 Withdrawal periods

Meat and offal: 21 days.

Milk: Milk for human consumption may only be taken 96 hours after calving.
If calving occurs before 54 days after treatment, the absence of antibiotic should be confirmed by testing before the milk is used for human consumption.
Milk for human consumption may be taken after 54 days plus 96 hours after treatment.

In cows suffering from hypocalcaemia, it may be necessary to discard milk for a longer period.

4. PHARMACOLOGICAL INFORMATION

4.1 ATCvet code: QJ51DB90

4.2 Pharmacodynamics

The cefalosporins are a family of drugs which are similar in chemical structure to the penicillins. The major difference being that penicillins are based on a β-lactam ring fused with a dihydrothiazine ring and cefalosporins on a β-lactam ring fused with a thiazolidone ring. The two families of antibiotics are collectively known as β-lactams.

Both cefalosporins and penicillins kill susceptible bacteria and the mode of action of the individual antibiotics of both families is the same.

The cell wall of bacteria is essential for their normal growth and development. Peptidoglycan is a heteropolymeric component of the cell wall which gives it rigidity. Peptidoglycan consists of glycan chains which are linear strands of two alternating amino sugars (N-acetylglucosamine and N-acetylmuramic acid) that are linked by peptide chains.
Cefalonium and other β-lactams act by inhibiting the enzyme transpeptidase, usually following interaction with penicillin binding protein (PBP), which is responsible for the final stage of peptidoglycan synthesis. This inhibition of cell wall synthesis produces unstable forms of the bacterium during reproduction and these unstable forms lyse.
Therefore, these antibiotics are bactericidal in their mode of action.

β-lactam antibiotics cannot kill or even inhibit all bacteria as there are various methods by which bacteria become resistant. These mechanisms include non-susceptible PBPs, failure of the antibiotic to penetrate to the site of action and production of β-lactamase enzymes. These enzymes hydrolyse the β-lactam ring producing an inactive derivative.
Cefalosporins in general are not susceptible to the actions of β-lactamase enzymes, especially when compared with penicillin, ampicillin or amoxicillin.

The penicillins and cefalosporins have a high therapeutic index in both animals and man. The reason for this probably relates to their highly specific mode of action in attacking the bacterial cell wall. As mammalian cells do not have an outer cell wall like that found in bacteria the β-lactams are without effect on mammalian cell division. The most common adverse effect of the cefalosporins is a hypersensitivity reaction which in most cases manifests as maculopapular skin rashes after several days of therapy. They may be accompanied by eosinophilia and fever.
Anaphylactic reactions are rare with the cefalosporins. There are no data available specifically on the effects of cefalonium in man.

Cefalonium is a broad spectrum cefalosporin antibiotic which has bactericidal activity against the majority of organisms associated with bovine mastitis. The antibacterial activity is not impaired in the presence of milk.

Cefalonium is active against non-β-lactamase and β-lactamase producing organisms:

Trueperella pyogenes	*Citrobacter* spp.
Staphylococcus aureus	*Enterobacter* spp.
Penicillin resistant strains of *Staphylococcus aureus*	*Escherichia coli*
Streptococcus dysgalactiae	*Klebsiella* spp.
Streptococcus uberis	*Proteus* spp.
Streptococcus agalactiae	
Corynebacterium ulcerans	

Effective levels of cefalonium are maintained in most quarters for up 10 weeks after infusion of the veterinary medicinal product.
Cattle treated with the veterinary medicinal product have a lower incidence of *Streptococcus uberis* infection during the dry period and the immediate post-calving period, with accompanying lower somatic cell counts.

4.3 Pharmacokinetics

The serum pharmacokinetics of cefalonium have not been investigated in definitive studies so the serum half-life is not known. Some work in dogs has shown that the drug is absorbed following oral administration.

Pharmacokinetics of cefalonium in the target species has only been investigated following intramammary administration. Studies were originally conducted using the veterinary medicinal product containing non-radiolabelled cefalonium. The presence of cefalonium and/or its biologically active metabolites was detected in urine or serum using a microbiological assay.

These original studies have been supplemented by a new study using C-14 radiolabelled cefalonium incorporated into the veterinary medicinal product formulation. In this study the serum, urine, faeces, tissue and milk were examined for the presence of radiochemical content. The results showed that cefalonium was extensively but slowly absorbed from the udder and excreted primarily in the urine. Between 7 and 13% of the radioactivity was eliminated in urine on each of the first three days post dosing whilst daily excretion in faeces was < 1% over the same period.
Mean blood concentration of radioactivity remained fairly constant during approximately 10 days after dosing which is consistent with slow but prolonged absorption of cefalonium from the udder. Plasma levels of radioactivity were generally higher than those found in blood indicating limited uptake of cefalonium and its metabolites into blood cells.

The results of the earlier work support the conclusion of the radiolabelled work. In these 2 studies the veterinary medicinal product was given as a single infusion to 4 and 2 cows respectively. In one of the studies 2 additional cows were given repeated infusions of the formulation for 3 days. Antibiotic activity was detected in urine at concentrations which indicated rapid and significant absorption from the udder. Absorption and elimination of cefalonium and its metabolites was however more rapid in the older studies.

There are no data on the pharmacokinetics of cefalonium in humans. However, cefalonium is structurally related to cefaloridine, differing only by the presence of a carbamoyl moiety at the para-position of the pyridine ring.

Cefaloridine is used in man and administered by the parenteral route. The half-life is about 1-1.5 hours and only about 20% is bound to plasma proteins. It is reported to be poorly absorbed after oral administration. Given the similarity in structures, cefalonium probably has similar properties.

Many cefalosporins are eliminated unchanged in urine by humans and laboratory animals. It is therefore very likely that most of the radioactivity in urine at early time points will be present as unchanged cefalonium. Results from the new study in cows show however that this is not the situation with milk. For the early milkings post calving the concentration of cefalonium in milk accounts for only a small proportion of the total radioactive residue. This indicates that any metabolism/degradation

takes place within the udder. However, in addition to analysis for cefalonium concentrations milk samples were also analysed for microbiological residues using a validated method. It was determined that the metabolites/degradation products had no antibiotic activity.

5. PHARMACEUTICAL PARTICULARS

5.1 Major incompatibilities

None known.

5.2 Shelf life

Shelf-life of the veterinary medicinal product as packaged for sale: 3 years.
Shelf life after first opening the immediate packaging: use immediately.

5.3 Special precautions for storage

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

5.4 Nature and composition of immediate packaging

Single dose 3 g white polyethylene nozzled syringes with red indented polyethylene caps.
Carton box containing 20 syringes and cleaning towels.
Plastic bucket containing 200 syringes (10 boxes of 20 syringes and cleaning towels).
Plastic bucket of 144 ~~intramammary~~ syringes with cleaning towels.

Not all pack sizes may be marketed.

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

Medicines should not be disposed of via wastewater or household waste.
Use take-back schemes for the disposal of any unused veterinary medicinal product or waste materials derived thereof in accordance with local requirements and with any national collection systems applicable to the veterinary medicinal product concerned.

6. NAME OF THE MARKETING AUTHORISATION HOLDER

Intervet Ireland Limited

7. MARKETING AUTHORISATION NUMBER(S)

VPA 10996/224/001

8. DATE OF FIRST AUTHORISATION

Date of first authorisation: 01 October 1988

9. DATE OF THE LAST REVISION OF THE SUMMARY OF THE PRODUCT CHARACTERISTICS

10. CLASSIFICATION OF VETERINARY MEDICINAL PRODUCTS

Veterinary medicinal product subject to prescription.

Detailed information on this veterinary medicinal product is available in the Union Product Database (https://medicines.health.europa.eu/veterinary).

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

CARTON BOX or BUCKET

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Cepravin Dry Cow 250 mg intramammary suspension for cattle

2. STATEMENT OF ACTIVE SUBSTANCES

Each 3 g syringe contains: 250 mg cefalonium (as cefalonium dihydrate).

3. PACKAGE SIZE

20 syringes.
200 syringes (10 x 20 syringes)
144 ~~intramammary~~ syringes with cleaning towels

4. TARGET SPECIES

Cattle (dairy cows at drying-off).

5. INDICATIONS

6. ROUTES OF ADMINISTRATION

Intramammary use.

7. WITHDRAWAL PERIODS

Meat and offal: 21 days.

Milk: Milk for human consumption may only be taken 96 hours after calving.
If calving occurs before 54 days after treatment, the absence of antibiotic should be confirmed by testing before the milk is used for human consumption.
Milk for human consumption may be taken after 54 days plus 96 hours after treatment.

In cows suffering from hypocalcaemia, it may be necessary to discard milk for a longer period.

8. EXPIRY DATE

Exp. {mm/yyyy}

Shelf life after first opening the immediate packaging: use immediately.

9. SPECIAL STORAGE PRECAUTIONS

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

10. THE WORDS "READ THE PACKAGE LEAFLET BEFORE USE"

Read the package leaflet before use.

11. THE WORDS "FOR ANIMAL TREATMENT ONLY"

For animal treatment only.

12. THE WORDS "KEEP OUT OF THE SIGHT AND REACH OF CHILDREN"

Keep out of the sight and reach of children.

13. NAME OF THE MARKETING AUTHORISATION HOLDER

Intervet Ireland Ltd.

14. MARKETING AUTHORISATION NUMBERS

VPA10996/224/001

15. BATCH NUMBER

Lot {number}

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

SYRINGE LABEL

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Cepravin Dry Cow

2. QUANTITATIVE PARTICULARS OF THE ACTIVE SUBSTANCES

250 mg cefalonium (as cefalonium dihydrate) /3 g syringe.

3. BATCH NUMBER

Lot {number}

4. EXPIRY DATE

Exp. {mm/yyyy}

B. PACKAGE LEAFLET

PACKAGE LEAFLET

1. Name of the veterinary medicinal product

Cepravin Dry Cow 250 mg intramammary suspension for cattle

2. Composition

Each 3 g syringe contains:

Active substance:
Cefalonium (as cefalonium dihydrate) 250 mg

White to cream coloured intramammary suspension.

3. Target species

Cattle (dairy cows at drying-off).

4. Indications for use

For routine dry cow therapy to treat existing sub-clinical infections and to prevent new infections which occur during the dry period.

5. Contraindications

Do not use in lactating cows.
Do not use within 54 days of calving.
Do not use in cases of hypersensitivity to cephalosporins, other β-lactam antibiotics or to any of the excipients.

6. Special warnings

Special precautions for safe use in the target species:

- If the product is used in heifers during their first pregnancy the same precautions should be observed as in cows, i.e. infusions should be given not less than 54 days before calving and milk discarded for the statutory four days after calving.
- It is unlikely that antibiotic treatment alone will control Summer Mastitis and therefore other measures should be implemented as part of routine management.
  These measures include:
  - Practising some form of fly control on the farm.
  - Avoiding pasturing cattle on wet or wooded fields which are known to be associated with Summer Mastitis.
  - Post-infusion teat dipping of cows and heifers receiving prophylactic intramammary infusions for the disease.
  - Prompt attention to teat injuries or sores as these rapidly attract flies.
  - Farms with an intractable problem should consider changing the calving pattern to avoid having animals at risk during the summer months.

Use of the product should be based on susceptibility testing of the bacteria isolated from the animal. If this is not possible, therapy should be based on local (regional, farm level) epidemiological information about susceptibility of the target bacteria.

Use of the product deviating from the instructions given in the SPC may increase the prevalence of bacteria resistant to cefalonium and may decrease the effectiveness of treatment with other beta lactams.
Dry cow therapy protocols should take local and national policies on antimicrobial use into consideration and undergo regular veterinary review.
The feeding to calves of milk containing residues of cefalonium that could select for antimicrobial-resistant bacteria (e.g. production of beta-lactamases) should be avoided up to the end of the milk withdrawal period, except during the colostral phase.
The efficacy of the product is only established against the pathogens mentioned in Section 17 Other information, serious acute mastitis (potentially fatal) due to other pathogen species, particularly *Pseudomonas aeruginosa*, can occur after drying off. Good hygienic practices should be thoroughly respected in order to reduce this risk.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:
Wash hands after use.
Penicillin and cefalosporins may cause sensitisation (allergy) following injection, inhalation, ingestion or skin contact.
Sensitivity to penicillin may lead to cross- sensitivity to cefalosporin and vice versa.
Allergic reactions to these substances may occasionally be serious.
Do not handle this product if you know you are sensitised, or if you have been advised not to work with such preparations.
Handle this product with great care to avoid exposure, taking all recommended precautions.
If you develop symptoms following exposure such as a skin rash you should seek medical advice and show the package leaflet or the label to the physician.
Swelling of the face, lips or eyes or difficulty breathing are more serious symptoms and require urgent medical attention.

Pregnancy and lactation:
The veterinary medicinal product is intended for use during the last trimester of pregnancy once the lactating cow has been dried off. There is no adverse treatment effect on the foetus.
Do not use in lactating cows.

Interaction with other medicinal products and other forms of interaction:
None known.

Overdose:
Repeated doses in cattle on three consecutive days did not demonstrate or produce any adverse effects.

7. Adverse events

None known.

Reporting adverse events is important. It allows continuous safety monitoring of a product. If you notice any side effects, even those not already listed in this package leaflet, or you think that the medicine has not worked, please contact, in the first instance, your veterinarian. You can also report any adverse events to the marketing authorisation holder using the contact details at the end of this leaflet, or via your national reporting system: www.hpra.ie

8. Dosage for each species, routes and method of administration

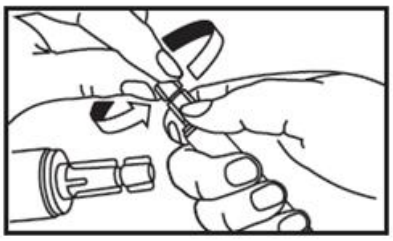
Intramammary use.
The contents of one syringe should be infused into the teat canal of each quarter immediately after the last milking of the lactation.

9. Advice on correct administration

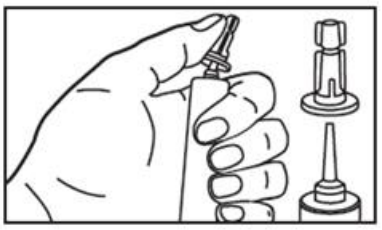
Before infusion, the teat should be thoroughly cleaned and disinfected.
Avoid contamination of the nozzle after removing the cap. Do not bend the nozzle. After infusion it is advisable to dip the teats in an antiseptic preparation specifically designed for this purpose. The syringe must only be used once.

1. After milking is complete thoroughly clean and disinfect the end of the teat (e.g. with the cleaning towel provided).

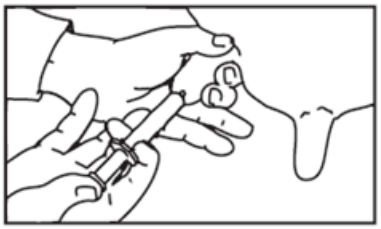
2.(i) **Option 1: For short nozzle intramammary administration** hold the barrel of the syringe and the base of the cap in one hand and twist off the small upper part of the cap above the indent mark (the base portion of the cap remains on the syringe). Take care not to contaminate the short exposed part of the nozzle.



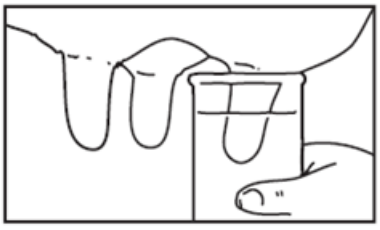
(ii) **Option 2: For full nozzle intramammary administration** remove the cap fully by holding the barrel of the syringe firmly on one hand and with the thumb push up and along the length of the cap until the cap clicks off. Take care not to contaminate the nozzle.



3. Insert the nozzle into the teat canal and apply steady pressure on the syringe plunger until the full dose has been delivered. Holding the end of the teat with one hand, gently massage upwards with the other to aid dispersion of the antibiotic into the quarter.



4. Finally immerse the teats in a teat dip.



10. Withdrawal periods

Meat and offal: 21 days.

Milk: Milk for human consumption may only be taken 96 hours after calving.
If calving occurs before 54 days after treatment, the absence of antibiotic should be confirmed by testing before the milk is used for human consumption. Milk for human consumption may be taken

after 54 days plus 96 hours after treatment.

In cows suffering from hypocalcaemia, it may be necessary to discard milk for a longer period.

11. Special storage precautions

Keep out of the sight and reach of children.

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

Do not use after the expiry date stated which is stated on the label/carton/bucket after Exp.
The expiry date refers to the last day of that month.
Shelf life after first opening the immediate packaging: use immediately.

12. Special precautions for disposal

Medicines should not be disposed of via wastewater or household waste.
Use take-back schemes for the disposal of any unused veterinary medicinal product or waste materials derived thereof in accordance with local requirements and with any national collection systems applicable to the veterinary medicinal product concerned.
Ask your veterinary surgeon or pharmacist how to dispose of medicines no longer required.

13. Classification of veterinary medicinal products

Veterinary medicinal product subject to prescription.

14. Marketing authorisation numbers and pack sizes

VPA10996/224/001

Single dose 3 g white polyethylene nozzled syringes with red indented polyethylene caps. Carton box containing 20 syringes and cleaning towels.
Plastic bucket containing 200 syringes (10 boxes of 20 syringes and cleaning towels).
Plastic bucket of 144 ~~intramammary~~ syringes with cleaning towels.

Not all pack sizes may be marketed.

15. Date on which the package leaflet was last revised

Detailed information on this veterinary medicinal product is available in the Union Product Database (https://medicines.health.europa.eu/veterinary).

16. Contact details

Marketing authorisation holder and contact details to report suspected adverse reactions:
Intervet Ireland Ltd
Magna Drive
Magna Business Park
Dublin 24

Ireland
Tel.: +353 (0)1 2970220

Manufacturer responsible for batch release:
TriRx Segré
La Grindolière
Zone Artisanale
Segré
49500 Segré-en-Anjou Bleu
France

Intervet International GmbH
Feldstrasse 1a
85716 Unterschleissheim
Germany

17. Other information

Pharmacodynamics
The cephalosporins are a family of drugs which are similar in chemical structure to the penicillins. The major difference being that penicillins are based on a β -lactam ring fused with a dihydrothiazine ring and cephalosporins on a β-lactam ring fused with a thiazolidone ring. The two families of antibiotics are collectively known as β -lactams.
Both cephalosporins and penicillins kill susceptible bacteria and the mode of action of the individual antibiotics of both families is the same.
The cell wall of bacteria is essential for their normal growth and development. Peptidoglycan is a heteropolymeric component of the cell wall which gives it rigidity. Peptidoglycan consists of glycan chains which are linear strands of two alternating amino sugars (N-acetylglucosamine and N-acetylmuramic acid) that are linked by peptide chains.
Cefalonium and other β -lactams act by inhibiting the enzyme transpeptidase, usually following interaction with penicillin binding protein (PBP), which is responsible for the final stage of peptidoglycan synthesis. This inhibition of cell wall synthesis produces unstable forms of the bacterium during reproduction and these unstable forms lyse.
Therefore, these antibiotics are bactericidal in their mode of action.
β -Lactam antibiotics cannot kill or even inhibit all bacteria as there are various methods by which bacteria become resistant. These mechanisms include non-susceptible PBPs, failure of the antibiotic to penetrate to the site of action and production of β-lactamase enzymes. These enzymes hydrolyse the β -lactam ring producing an inactive derivative.
Cephalosporins in general are not susceptible to the actions of β-lactamase enzymes, especially when compared with penicillin, ampicillin or amoxicillin.
The penicillins and cephalosporins have a high therapeutic index in both animals and man. The reason for this probably relates to their highly specific mode of action in attacking the bacterial cell wall. As mammalian cells do not have an outer cell wall like that found in bacteria the β-lactams are without effect on mammalian cell division. The most common adverse effect of the cephalosporins is a hypersensitivity reaction which in most cases manifests as maculopapular skin rashes after several days of therapy. They may be accompanied by eosinophilia and fever.
Anaphylactic reactions are rare with the cephalosporins. There are no data available specifically on the effects of cefalonium in man.
Cefalonium is a broad spectrum cephalosporin antibiotic which has bactericidal activity against the majority of organisms associated with bovine mastitis. The antibacterial activity is not impaired in the presence of milk.
Cefalonium is active against non-β-lactamase and β-lactamase producing organisms:

Trueperella pyogenes	*Citrobacter* spp.
Staphylococcus aureus	*Enterobacter* spp.
Penicillin resistant strains of *Staphylococcus aureus*	*Escherichia coli*
Streptococcus dysgalactiae	*Klebsiella* spp.

Streptococcus uberis *Proteus* spp.
Streptococcus agalactiae
Corynebacterium ulcerans
Effective levels of cefalonium are maintained in most quarters for up 10 weeks after infusion of the veterinary medicinal product.
Cattle treated with the veterinary medicinal product have a lower incidence of *Streptococcus uberis* infection during the dry period and the immediate post-calving period, with accompanying lower somatic cell counts.

Pharmacokinetics
The serum pharmacokinetics of cefalonium have not been investigated in definitive studies so the serum half-life is not known. Some work in dogs has shown that the drug is absorbed following oral administration.
Pharmacokinetics of cefalonium in the target species has only been investigated following intramammary administration. Studies were originally conducted using the veterinary medicinal product containing non-radiolabelled cefalonium. The presence of cefalonium and/or its biologically active metabolites was detected in urine or serum using a microbiological assay.
These original studies have been supplemented by a new study using C-14 radiolabelled cefalonium incorporated into the veterinary medicinal product formulation. In this study the serum, urine, faeces, tissue and milk were examined for the presence of radiochemical content. The results showed that cefalonium was extensively but slowly absorbed from the udder and excreted primarily in the urine. Between 7 and 13% of the radioactivity was eliminated in urine on each of the first three days post dosing whilst daily excretion in faeces was < 1% over the same period.
Mean blood concentration of radioactivity remained fairly constant during approximately 10 days after dosing which is consistent with slow but prolonged absorption of cefalonium from the udder. Plasma levels of radioactivity were generally higher than those found in blood indicating limited uptake of cefalonium and its metabolites into blood cells.
The results of the earlier work support the conclusion of the radiolabelled work. In these 2 studies the veterinary medicinal product was given as a single infusion to 4 and 2 cows respectively. In one of the studies 2 additional cows were given repeated infusions of the formulation for 3 days. Antibiotic activity was detected in urine at concentrations which indicated rapid and significant absorption from the udder. Absorption and elimination of cefalonium and its metabolites was however more rapid in the older studies.
There are no data on the pharmacokinetics of cefalonium in humans. However, cefalonium is structurally related to cefaloridine, differing only by the presence of a carbamoyl moiety at the para-position of the pyridine ring.
Cefaloridine is used in man and administered by the parenteral route. The half-life is about 1-1.5 hours and only about 20% is bound to plasma proteins. It is reported to be poorly absorbed after oral administration. Given the similarity in structures, cefalonium probably has similar properties.
Many cephalosporins are eliminated unchanged in urine by humans and laboratory animals. It is therefore very likely that most of the radioactivity in urine at early time points will be present as unchanged cefalonium. Results from the new study in cows show however that this is not the situation with milk. For the early milkings post calving the concentration of cefalonium in milk accounts for only a small proportion of the total radioactive residue. This indicates that any metabolism/degradation takes place within the udder. However, in addition to analysis for cefalonium concentrations milk samples were also analysed for microbiological residues using a validated method. It was determined that the metabolites/degradation products had no antibiotic activity.

POM (Prescription Only)