SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Parofor crypto 140 000 IU/ml oral solution for pre-ruminant cattle

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

Active substance:

140 000 IU of paromomycin activity

Excipients:

Qualitative composition of excipients and other constituents	Quantitative composition if that information is essential for proper administration of the veterinary medicinal product
Methyl parahydroxybenzoate (E218)	1.0 mg
Propyl parahydroxybenzoate	0.1 mg
Sodium metabisulfite (E223)	4.0 mg

A clear yellow to amber solution.

3. CLINICAL INFORMATION

3.1 Target species

Cattle (pre-ruminant).

3.2 Indications for use for each target species

Reduction in the occurrence of diarrhoea due to diagnosed *Cryptosporidium parvum*.
Calves should only receive the veterinary medicinal product upon confirmation of cryptosporidial oocysts in their faeces and before the onset of diarrhoea.
Paromomycin reduces faecal oocyst shedding.

3.3 Contraindications

Do not use in cases of hypersensitivity to the active substance, to other aminoglycosides or to any of the excipients.
Do not use in cases with impaired function of the kidneys or liver.
Do not use in ruminating animals.

3.4 Special warnings

In field studies investigating the effect of the veterinary medicinal product on diarrhoea associated with cryptosporidiosis, 23% to 32% of calves in treated groups

presented with diarrhoea, in comparison to 53% to 73% of calves in untreated groups, during the 7-day treatment period.

3.5 Special precautions for use

Special precautions for safe use in the target species:
The use of the veterinary medicinal product should be combined with good management practices e.g. good hygiene, proper ventilation and no overstocking.
Repeated use of the veterinary medicinal product on farms should be avoided by improving management practices and through cleaning and disinfection.
Aminoglycosides are considered as critically important in human medicine. Use of the veterinary medicinal product deviating from the instructions given in the SPC may increase the prevalence of bacteria resistant to paromomycin and may decrease the effectiveness of treatment with aminoglycosides due to the potential for cross-resistance.
The safety of the veterinary medicinal product has not been investigated in animals less than 3 days of age.

Special precautions to be taken by the person administering the veterinary medicinal product to animals
This veterinary medicinal product contains paromomycin, which can cause allergic reactions in some people.
People with known hypersensitivity to paromomycin or any other aminoglycoside should avoid contact with the veterinary medicinal product.
Avoid contact with the skin and eyes.
In the event of accidental contact with the skin or eyes, rinse with plenty of clean water.
If you develop symptoms following exposure, such as skin rash, you should seek medical advice and show the package leaflet or the label to the physician. Swelling of the face, lips and eyes or difficulty in breathing are more serious symptoms and require urgent medical attention.
Personal protective equipment consisting of protective clothing and impervious gloves should be worn when handling the veterinary medicinal product.
Do not eat, drink and smoke when handling the veterinary medicinal product.
Do not ingest. In case of accidental ingestion, seek medical advice immediately and show the package leaflet or the label to the physician.
Wash hands after use.

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

3.6 Adverse events

Cattle:

Undetermined frequency (cannot be estimated from available data)	Nephropathy (nephrotoxicity) [1] Internal ear disorder (ototoxicity)[1]

[1]can be caused by aminoglycoside antibiotics such as paromomycin

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 its local representative 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

Not applicable.

3.8 Interaction with other medicinal products and other forms of interaction

General anaesthetics and muscle relaxing products increase the neuro-blocking effect of aminoglycosides. This may cause paralysis and apnoea.
Do not use concurrently with strong diuretics and potentially oto- or nephrotoxic substances.

3.9 Administration routes and dosage

For oral use.

Dose rate: 35 000 IU of paromomycin/kg BW/day for 7 consecutive days, i.e. 2.5 ml of veterinary medicinal product / 10 kg BW/day for 7 consecutive days.

To ensure a correct dosage, the use of either a syringe or an appropriate device for oral administration is necessary and the veterinary medicinal product should be administered directly in the mouth of the animal.

To ensure a correct dosage, bodyweight should be determined as accurately as possible.

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

Do not administer for more than 7 days since clinical signs associated with gastrointestinal lesions were observed after prolonged treatment duration. In 2 to 5 week old calves, overdoses in excess of 35 000 IU paromomycin/kg bodyweight may induce gastrointestinal lesions (ulceration, pustules, chronic hyperplastic inflammation) mostly in the rumen and reticulum. Bruxism and poor appetite have been reported. Repeated overdose may be associated with death.

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

Due to accumulation of paromomycin in the liver and kidneys, any repeated course of treatment during the withdrawal period must be avoided.
Meat and offal: 62 days

4. PHARMACOLOGICAL INFORMATION

4.1 ATCvet code:

QA07AA06.

4.2 Pharmacodynamics

Paromomycin has antiprotozoal activity, although its mechanism of action is unclear. In *in vitro* studies using HCT-8 and Caco-2 cell lines inhibitory activity against *C. parvum* was observed.
Resistance of cryptosporidia to paromomycin has not been described to date. Nevertheless, the use of aminoglycosides is associated with the occurrence of bacterial resistance. Paromomycin may select for cross-resistance to other aminoglycosides.

4.3 Pharmacokinetics

The bioavailability of paromomycin when administered as a single oral dose of 35 000 IU paromomycin/kg bodyweight to 2 - 6 week old calves was 2.75%.
With regard to the absorbed fraction, the mean peak plasma concentration (C_{max}) was 1.48 mg/l, the mean time to attain the peak plasma concentration (T_{max}) was 4.5 hours and the mean terminal half-life ($t_{1/2, el}$) was 11.2 hours. The main part of the dose is eliminated unchanged in the faeces while the absorbed fraction is excreted almost exclusively in urine as unchanged paromomycin.
Paromomycin displays age-related pharmacokinetics, with the greatest systemic exposure occurring in newborn animals.

Environmental properties

The active ingredient paromomycin is very persistent in soil.

5. PHARMACEUTICAL PARTICULARS

5.1 Major incompatibilities

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

5.2 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 2 years.
Shelf life after first opening the immediate packaging: 3 months.

5.3. Special precautions for storage

Do not store above 25°C.

5.4 Nature and composition of immediate packaging

White high density polyethylene bottle with tamper-evident screw polypropylene closure.
Bottle sizes are:
125 ml

250 ml
500 ml
1 L.
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 system applicable to the veterinary medicinal product concerned.

6. NAME OF THE MARKETING AUTHORISATION HOLDER

Huvepharma NV

7. MARKETING AUTHORISATION NUMBER

Vm 30282/3014

8. DATE OF FIRST AUTHORISATION

19 July 2018

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

December 2023

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).

Approved: 28 April 2024