SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Parofor 140 000 IU/ml Veterinary
Oral solution for pre-ruminant cattle

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

Active substance:

140 000 IU of paromomycin activity

Excipients:

Methyl parahydroxybenzoate (E218)	1.0 mg
Propyl parahydroxybenzoate	0.1 mg
Sodium metabisulfite (E223)	4.0 mg

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Oral solution.
A clear yellow to amber solution.

4. CLINICAL PARTICULARS

4.1 Target species

Cattle (pre-ruminant calves).

4.2 Indications for use, specifying the target species

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

4.3 Contraindications

Do not use in animals with known hypersensitivity to paromomycin, other aminoglycosides or any of the excipients listed in section 6.1.
Do not use in cases with impaired function of the kidneys or liver.
Do not use in ruminating animals.

4.4 Special warnings for each target species

In field studies investigating the effect of the 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.

4.5 Special precautions for use

Special precautions for use in animals
The use of the product should be combined with good management practices e.g. good hygiene, proper ventilation and no overstocking. Repeated use of the 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 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 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 product contains paromomycin, which can cause allergic reactions in some people.
People with known hypersensitivity (allergy) to paromomycin or any other aminoglycosides should avoid contact with the product.
Avoid contact with the skin and eyes.
Personal protective equipment consisting of protective clothing and impervious gloves should be worn when handling the veterinary medicinal product.
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 physician this warning. Swelling of the face, lips and eyes or difficulty in breathing are more serious symptoms and require urgent medical attention.
Do not eat, drink and smoke when handling the product.
Do not ingest. In case of accidental ingestion, seek medical advice immediately and show the label to the physician.
Wash hands after use.

4.6 Adverse reactions (frequency and seriousness)

Aminoglycoside antibiotics such as paromomycin can cause oto- and nephrotoxicity.
Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorization of the medical product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Any suspected adverse events should be reported to the Ministry of Health according to the National Regulation by using an online form
https://sideeffects.health.gov.il/

4.7 Use during pregnancy, lactation or lay

Not applicable.

4.8 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.

4.9 Amounts to be administered and administration route

For oral use.

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

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

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

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

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.

4.11 Withdrawal period(s)

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

5. PHARMACOLOGICAL IMMUNOLOGICAL PROPERTIES

Pharmacotherapeutic group: intestinal anti-infectives; antibiotics.
ATCvet code: QA 07 AA 06.

5.1 Pharmacodynamic properties

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.

5.2 Pharmacokinetic particulars

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.

5.3 Environmental properties

The active ingredient paromomycin is very persistent in soil.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Methyl parahydroxybenzoate (E218)
Propyl parahydroxybenzoate
Sodium metabisulfite (E223)
Purified water

6.2 Major Incompatibilities

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

6.3 Shelf life

The expiry date of the product is indicated on the packaging materials.
Shelf life after first opening the immediate packaging: 3 months.

6.4 Special precautions for storage

Do not store above 25°C.

6.5 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.

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 materials derived from such veterinary medicinal products should be disposed of in accordance with local requirements.

7. Registration holder

M.P Vet
POB 7004
Petach-Tiqva 49170

8. Registration number

169-06-35197-00

Approved on: 01/2022