ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGE

Bottle of 125 ml, 250 ml, 500 ml or 1 L

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Parofor 140 mg/ml solution for use in drinking water, milk or milk replacer for pre-ruminant cattle and pigs.
Paromomycin (as sulfate).

2. STATEMENT OF ACTIVE SUBSTANCES

Per ml:

Paromomycin sulfate	200 mg equivalent to paromomycin base 140 mg or 140.000 IU of paromomycin activity

3. PHARMACEUTICAL FORM

Solution for use in drinking water, milk or milk replacer.

4. PACKAGE SIZE

125 ml, 250 ml, 500 ml, 1 L

5. TARGET SPECIES

Cattle (pre-ruminant calves), pigs.

6. INDICATION(S)

7. METHOD AND ROUTE(S) OF ADMINISTRATION

Oral use.
Read the package leaflet before use.

8. WITHDRAWAL PERIOD

Withdrawal periods:
Pre-ruminant cattle
Meat and offal: 20 days
Pigs
Meat and offal: 3 days

9. SPECIAL WARNING(S), IF NECESSARY

Read the package leaflet before use.

10. EXPIRY DATE

EXP
Shelf life after first opening: 3 months. Once opened use by….
Medicated drinking water, milk or milk replacer should be refreshed or replaced every 6 hours (in milk/milk replacer) or every 24 hours (in water).

11. SPECIAL STORAGE CONDITIONS

Product as packed for sale: do not store above 25°C.
After first opening: do not store above 25°C.

12. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCTS OR WASTE MATERIALS, IF ANY

Disposal: read the package leaflet.

13. THE WORDS "FOR ANIMAL TREATMENT ONLY" AND CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE, IF APPLICABLE

For animal treatment only. To be supplied only on veterinary prescription.

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

Keep out of the sight and reach of children.

15. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Huvepharma NV
Uitbreidingstraat 80
2600 Antwerpen
Belgium

16. MARKETING AUTHORISATION NUMBER(S)

Vm 30282/4033

17. MANUFACTURER'S BATCH NUMBER

Lot:

B. PACKAGE LEAFLET

PACKAGE LEAFLET

Parofor 140 mg/ml solution for use in drinking water, milk or milk replacer for pre-ruminant cattle and pigs.

1. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER AND OF THE MANUFACTURING AUTHORISATION HOLDER RESPONSIBLE FOR BATCH RELEASE, IF DIFFERENT

Marketing authorisation holder:

Huvepharma NV
Uitbreidingstraat 80
2600 Antwerpen
Belgium

Manufacturer responsible for batch release:

Biovet JSC
39 Petar Rakov Str
4550 Peshtera
Bulgaria

2. NAME OF THE VETERINARY MEDICINAL PRODUCT

Parofor 140 mg/ml solution for use in drinking water, milk or milk replacer for pre-ruminant cattle and pigs.
Paromomycin (as sulfate).

3. STATEMENT OF THE ACTIVE SUBSTANCE(S) AND OTHER INGREDIENT(S)

Per 1 ml:
Active substance:

Paromomycin sulfate	200 mg equivalent to paromomycin base 140 mg or 140.000 IU of paromomycin activity

Excipients:

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

A clear yellow to amber solution for use in drinking water, milk or milk replacer.

4. INDICATION(S)

Treatment of gastro-intestinal infections caused by *Escherichia coli*.

5. CONTRAINDICATIONS

Do not use in animals with hypersensitivity to paromomycin, other aminoglycosides or any of the excipients.

Do not use in cases with impaired function of the kidneys or liver.
Do not use in ruminating animals. Do not use in turkeys due to the risk of selection for antimicrobial resistance in intestinal bacteria.

6. ADVERSE REACTIONS

On rare occasions soft faeces have been observed.
Aminoglycoside antibiotics such as paromomycin can cause oto- and nephrotoxicity.
The frequency of adverse reactions is defined using the following convention:
- very common (more than 1 in 10 animals treated displaying adverse reaction(s))
- common (more than 1 but less than 10 animals in 100 animals treated)
- uncommon (more than 1 but less than 10 animals in 1,000 animals treated)
- rare (more than 1 but less than 10 animals in 10,000 animals treated)
- very rare (less than 1 animal in 10,000 animals treated, including isolated reports).

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 inform your veterinary surgeon.

7. TARGET SPECIES

Cattle (pre-ruminant calves), pigs.

8. DOSAGE FOR EACH SPECIES, ROUTE(S) AND METHOD OF ADMINISTRATION

Oral use
Pre-ruminant cattle:
For administration in milk/milk replacer.
25-50 mg paromomycin sulfate per kg BW/day (equivalent to 0.125 – 0.25 ml of product/kg BW/day).
Duration of treatment: 3-5 days.

Pigs:
For administration in drinking water.
25-40 mg paromomycin sulfate per kg BW/day (equivalent to 0.125 – 0.2 ml of product/kg BW/day).
Duration of treatment: 3-5 days.

To ensure accurate measurement of the required volume of product, suitably calibrated measuring equipment should be used.

For administration via drinking water, milk or milk replacer, the exact daily amount of product should be calculated, based on the recommended dose, and the number and weight of the animals to be treated, according to the following formula:

$$\frac{\text{ml product / kg body weight / day} \times \text{Mean body weight (kg) of animals to be treated}}{\text{Mean daily water/milk/milk replacer consumption (litre) per animal}} = \text{.... ml product per liter drinking water /milk/milk replacer}$$

To ensure a correct dosage body weight should be determined as accurately as possible.
The uptake of medicated water/milk /milk replacer depends on several factors including clinical conditions of the animals and the local conditions such as ambient temperature and humidity. In order to obtain the correct dosage, drinking water/milk/milk replacer uptake has to be monitored and the concentration of paromomycin has to be adjusted accordingly.

9. ADVICE ON CORRECT ADMINISTRATION

Medicated drinking water/milk/milk replacer and any stock solutions should be freshly prepared by carefully mixing the product in the requisite quantity of fresh potable water /milk/milk replacer every 6 hours (in milk/milk replacer) or every 24 hours (in water).

10. WITHDRAWAL PERIODS

Pre-ruminant cattle
Meat and offal: 20 days
Pigs
Meat and offal: 3 days

11. SPECIAL STORAGE PRECAUTIONS

Keep out of the sight and reach of children.

Product as packed for sale: do not store above 25°C.
After first opening: do not store above 25°C.
After reconstitution: there are no special restrictions on storage conditions.
Do not use this veterinary medicinal product after the expiry date which is stated on the bottle after “EXP”. The expiry date refers to the last day of that month.

Shelf life after first opening of the immediate packaging: 3 months
Shelf life after reconstitution in drinking water: 24 hours
Shelf life after reconstitution in milk/milk replacer: 6 hours

12. SPECIAL WARNING(S)

Special warnings for each target species

Cross-resistance has been shown between paromomycin and some antimicrobials in the aminoglycosides class in Enterobacterales. Use of the product should be carefully considered when susceptibility testing has shown resistance to aminoglycosides because its effectiveness may be reduced.

Special precautions for use in animals

The uptake of medication by animals can be altered as a consequence of illness. In case of insufficient uptake of water/milk animals should be treated parenterally using a suitable injectable product following the advice of the veterinarian.
The use of the product should be combined with good management practices e.g. good hygiene, proper ventilation, no overstocking.

Since the product is potentially ototoxic and nephrotoxic, it is recommended to assess kidney function.
Special care should be taken when considering administration of the product to newborn animals due to the known higher gastrointestinal absorption of paromomycin in neonates. This higher absorption could lead to an increased risk of oto- and nephrotoxicity. The use of the product in neonates should be based on a benefit/risk assessment by the responsible veterinarian.
Prolonged or repeated use of the product should be avoided by improving management practices and through cleansing and disinfection.
Use of the product should be based on identification and susceptibility testing of the target pathogen(s)isolated from the animal. If this is not possible, therapy should be based on epidemiological information and knowledge ofsusceptibility of the target pathogen at farm level or at local/regional level.
Use of the product should be in accordance with official, national and regional antimicrobial policies.
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 crossresistance. Paromomycin selects for resistance and cross-resistances at high frequency against a variety of other aminoglycosides among intestinal bacteria.
Aminoglycosides are considered as critical in human medicine. Consequently, they should not be used as a first line treatment in veterinary medicine.

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 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.

Pregnancy

Laboratory studies in the rat and rabbit have not produced any evidence of teratogenic, foetotoxic or maternotoxic effects. The use is not recommended during pregnancy.

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.

Overdose

Paromomycin when administered orally is hardly resorbed. Harmful effects due to accidental overdosing are highly unlikely.

Incompatibilities

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

Environmental properties

The active ingredient paromomycin sulfate is very persistent in the environment.

13. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCT OR WASTE MATERIALS, IF ANY

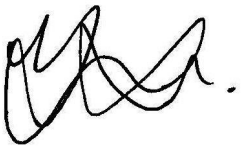
Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal products should be disposed of in accordance with local requirements.

14. DATE ON WHICH THE PACKAGE LEAFLET WAS LAST APPROVED

May 2022

15. OTHER INFORMATION

Pack size: bottles of 125 ml, 250 ml, 500 ml and 1 L.
Not all pack sizes may be marketed.



Approved: 04 August 2022