SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Parofor 70 000 IU/g powder for use in drinking water/ milk for cattle (pre-ruminant) and pigs.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each gram contains:

Active substance:

70 000 IU of paromomycin activity as paromomycin sulfate

Excipients:

Qualitative composition of excipients and other constituents
Silica (E551), colloidal anhydrous
Glucose monohydrate

A white to almost white powder.

3. CLINICAL INFORMATION

3.1 Target species

Cattle (pre-ruminant), pigs.

3.2 Indications for use for each target species

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

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.
Do not use in turkeys due to the risk of selection for antimicrobial resistance in intestinal bacteria.

3.4 Special warnings

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

Paromomycin selects for resistance and cross-resistances at high frequency against a variety of other aminoglycosides among intestinal bacteria.

3.5 Special precautions for use

Special precautions for safe use in the target species:

Use of the veterinary medicinal 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 of susceptibility of the target pathogen at farm level or at local/regional level. Use of the veterinary medicinal product should be in accordance with official, national and regional antimicrobial policies.

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 veterinary medicinal product following the advice of the veterinarian.
The use of the veterinary medicinal product should be combined with good management practices e.g. good hygiene, proper ventilation, no overstocking.
Since the veterinary medicinal product is potentially ototoxic and nephrotoxic, it is recommended to assess kidney function.
Special care should be taken when considering administration of the veterinary medicinal 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 veterinary medicinal product in neonates should be based on benefit-risk assessment by the responsible veterinarian. Prolonged or repeated use of the veterinary medicinal product should be avoided by improving management practices and through cleansing and disinfection.
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 crossresistance.
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 veterinary medicinal product contains paromomycin, which can cause allergic reactions in some people. People with known hypersensitivity to paromomycin or to any aminoglycosides should avoid contact with the veterinary medicinal product. 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. Wash hands after use. In case of accidental ingestion, seek medical advice immediately and show the package leaflet or the label to the physician.
When handling this veterinary medicinal product, inhalation of the dust must be avoided by wearing a disposable half-mask respirator conforming to European Standard EN 149 or a non-disposable respirator to European Standard EN 140 with a filter to EN 143.
Use in a well-ventilated area. Avoid inhaling the powder while preparing the medicated water or milk replacer. Avoid contact with the skin and eyes. In case of accidental contact with the skin or eyes, rinse with plenty of water and seek medical attention if irritation persists.

Special precautions for the protection of the environment:

Not applicable.

3.6 Adverse events

Cattle (pre-ruminant), pigs:

Rare	Loose stool

(1 to 10 animals / 10,000 animals treated):	
Undetermined frequency (cannot be estimated from available data)	Nephropathy[1] Internal ear disorder[1]

[1]Aminoglycoside antibiotics such as paromomycin can cause nephro- and ototoxicity.

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

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

3.8 Interaction with other medicinal products and other forms of interaction

General anaesthetics and muscle relaxants increase the neuro-blocking effect of aminoglycosides, which can lead to acute paralysis and apnoea.
Do not use concurrently with loop diuretics and potentially oto- or nephrotoxic substances.

3.9 Administration routes and dosage

In drinking water/milk use
Cattle (pre-ruminant):
For administration in milk/milk replacer
17500 – 35000 IU of paromomycin per kg BW/day (equivalent to 2.5-5 g of veterinary medicinal product/10 kg BW/day)
Duration of treatment: 3-5 days

Pigs:
For administration in drinking water.
17500 – 28000 IU of paromomycin per kg BW/day (equivalent to 2.5-4 g of veterinary medicinal product/10 kg BW/day)
Duration of treatment: 3-5 days

To ensure a correct dosage, body weight should be determined as accurately as possible.
The use of suitably calibrated measuring equipment is recommended.

Based on the recommended dose and the number and weight of animals to be treated, the exact daily concentration of the veterinary medicinal product should be calculated according to the following formula:

$$\frac{\text{mg veterinary medicinal product/ kg body weight / day} \times \text{mean body weight (kg) of animals to be treated}}{\text{Mean daily water/milk/milk replacer consumption (l/animal)}} = \ldots \text{ mg veterinary medicinal product per litre drinking water/milk/milk replacer}$$

The intake 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 may need to be adjusted accordingly.
Medicated drinking water/milk/milk replacer and any stock solutions should be freshly prepared. Any remaining quantities of medicated fluids should be removed after 6 hours (in milk/milk replacer) or after 24 hours (in water).

For the administration of the veterinary medicinal product commercially available dosing pumps can be used. The solubility of the veterinary medicinal product has been tested at the maximum concentration of 95 g/L.

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

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

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

Cattle (pre-ruminant)
Meat and offal: 20 days
Pigs
Meat and offal: 3 days

4. PHARMACOLOGICAL INFORMATION

4.1 ATCvet code:

QA07AA06.

4.2 Pharmacodynamics

Paromomycin belongs to the group of aminoglycoside antibiotics. Paromomycin changes the reading of messenger-RNA, which disrupts protein synthesis. The bactericidal activity of paromomycin is mainly attributed to its irreversible binding to ribosomes. Paromomycin has broad spectrum activity against numerous Gram-positive and Gram-negative bacteria, including *E. coli*.
Paromomycin acts in a concentration-dependant manner. Five mechanisms of resistance have been identified: changes of the ribosome due to mutations, reduction of permeability of bacterial cell wall or active efflux, inactivation of aminoglycosides by enzymes and enzymatic substitution of the molecular target. The first three resistance mechanisms arise from mutations of certain genes on chromosomes. The fourth and fifth resistance mechanisms only occurs following intake of a transposon or plasmid coding for resistance.

4.3 Pharmacokinetics

Following oral administration of paromomycin, hardly any absorption takes place and the molecule is eliminated unchanged via the faeces.

Environmental properties

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

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: 6 months.
Shelf life after reconstitution in drinking water: 24 hours
Shelf life after reconstitution in milk/milk replacer: 6 hours

5.3 Special precautions for storage

Do not store above 25°C. Keep the sachet tightly closed.

5.4 Nature and composition of immediate packaging

Block-bottom polyethylene/aluminium/polyethylene terephthalate sachet of 1000 g – 500 g – 250 g
Sachet of polyethylene foil/aluminium/polypropylene foil of 25 g, placed into a cardboard box, 40 sachets per box.
Not all pack sizes may be marketed.

5.5 Special precautions for the disposal of unused veterinary medicinal product 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(S)

8. DATE OF FIRST AUTHORISATION

<Date of first authorisation:> <{DD/MM/YYYY}> <{DD month YYYY}.>

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

<{MM/YYYY}>
<{DD/MM/YYYY}>
<{DD month YYYY}>

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).

LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

Carton box 40 x 25 g

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Parofor 70 000 IU/g powder for use in drinking water/ milk

2. STATEMENT OF ACTIVE SUBSTANCES

Each gram contains:

70 000 IU of paromomycin activity as paromomycin sulfate

3. PACKAGE SIZE

40 x 25g

4. TARGET SPECIES

Cattle (pre-ruminant), pigs.

5. INDICATIONS

6. ROUTES OF ADMINISTRATION

In drinking water/milk use

7. WITHDRAWAL PERIODS

Withdrawal periods:
Cattle (pre-ruminant)
Meat and offal: 20 days
Pigs
Meat and offal: 3 days

8. EXPIRY DATE

Exp {mm/yyyy}
Once opened use within 6 months. Once opened use by….
Medicated drinking water should be refreshed or replaced every 24 hours.
Shelf life after reconstitution in milk/milk replacer: 6 hours.

9. SPECIAL STORAGE PRECAUTIONS

Do not store above 25°C. Keep the sachet tightly closed.

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

Huvepharma NV

14. MARKETING AUTHORISATION NUMBERS

To be completed nationally

15. BATCH NUMBER

Lot:

PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGE

Sachet of 25 g

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Parofor 70 000 IU/g powder for use in drinking water/ milk

2. STATEMENT OF ACTIVE SUBSTANCES

Each gram contains:

70 000 IU of paromomycin activity as paromomycin sulfate

3. TARGET SPECIES

Cattle (pre-ruminant), pigs.

4. ROUTES OF ADMINISTRATION

Read the package leaflet before use.

In drinking water/milk use

5. WITHDRAWAL PERIODS

Withdrawal periods:
Cattle (pre-ruminant)
Meat and offal: 20 days
Pigs
Meat and offal: 3 days

6. EXPIRY DATE

Exp {mm/yyyy}
Once opened use within 6 months. Once opened use by….
Medicated drinking water should be refreshed or replaced every 24 hours.
Shelf life after reconstitution in milk/milk replacer: 6 hours.

7. SPECIAL STORAGE PRECAUTIONS

Do not store above 25°C. Keep the sachet tightly closed.

8. NAME OF THE MARKETING AUTHORISATION HOLDER

Huvepharma NV

9. BATCH NUMBER

Lot

PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGE

Sachet of 1000 g, 500g or 250 g

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Parofor 70 000 IU/g powder for use in drinking water/ milk

2. STATEMENT OF ACTIVE SUBSTANCES

Each gram contains:

70 000 IU of paromomycin activity as paromomycin sulfate

3. PACKAGE SIZE

250 g
500 g
1000 g

4. TARGET SPECIES

Cattle (pre-ruminant), pigs.

5. INDICATIONS

6. ROUTES OF ADMINISTRATION

In drinking water/milk use
Read the package leaflet before use.

7. WITHDRAWAL PERIODS

Withdrawal periods:
Cattle (pre-ruminant):
Meat and offal: 20 days
Pigs:
Meat and offal: 3 days

8. EXPIRY DATE

Exp {mm/yyyy}
Once opened use within 6 months. Once opened use by….
Medicated drinking water should be refreshed or replaced every 24 hours.
Shelf life after reconstitution in milk/milk replacer: 6 hours.

9. SPECIAL STORAGE PRECAUTIONS

Do not store above 25°C. Keep the sachet tightly closed.

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

Huvepharma NV

14. MARKETING AUTHORISATION NUMBERS

To be completed nationally

15. BATCH NUMBER

Lot:

PACKAGE LEAFLET

1. Name of the veterinary medicinal product

Parofor 70 000 IU/g powder for use in drinking water/ milk for cattle (pre-ruminant) and pigs.

2. Composition

Each gram contains:

Active substance:

70 000 IU of paromomycin activity as paromomycin sulfate

A white to almost white powder.

3. Target species

Cattle (pre-ruminant), pigs.

4. Indications for use

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

5. 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.
Do not use in turkeys due to the risk of selection for antimicrobial resistance in intestinal bacteria.

6. Special warnings

Special warnings

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

Paromomycin selects for resistance and cross-resistances at high frequency against a variety of other aminoglycosides among intestinal bacteria.

Special precautions for safe use in the target species:

Use of the veterinary medicinal 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 of susceptibility of the target pathogen at farm level or at local/regional level. Use of the veterinary medicinal product should be in accordance with official, national and regional antimicrobial policies.

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 veterinary

medicinal product following the advice of the veterinarian.
The use of the veterinary medicinal product should be combined with good management practices e.g. good hygiene, proper ventilation, no overstocking.
Since the veterinary medicinal product is potentially ototoxic and nephrotoxic, it is recommended to assess kidney function.
Special care should be taken when considering administration of the veterinary medicinal 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 veterinary medicinal product in neonates should be based on benefit-risk assessment by the responsible veterinarian. Prolonged or repeated use of the veterinary medicinal product should be avoided by improving management practices and through cleansing and disinfection.
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 crossresistance.
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 veterinary medicinal product contains paromomycin, which can cause allergic reactions in some people. People with known hypersensitivity to paromomycin or to any aminoglycosides should avoid contact with the veterinary medicinal product. 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. Wash hands after use. In case of accidental ingestion, seek medical advice immediately and show the package leaflet or the label to the physician.
When handling this veterinary medicinal product, inhalation of the dust must be avoided by wearing a disposable half-mask respirator conforming to European Standard EN 149 or a non-disposable respirator to European Standard EN 140 with a filter to EN 143.
Use in a well-ventilated area. Avoid inhaling the powder while preparing the medicated water or milk replacer. Avoid contact with the skin and eyes. In the event of accidental contact with the skin or eyes, rinse with plenty of water and seek medical attention if irritation persists.

Pregnancy:

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

Interaction with other medicinal products and other forms of interaction:

General anaesthetics and muscle relaxants increase the neuro-blocking effect of aminoglycosides, which can lead to acute paralysis and apnoea. Do not use concurrently with loop diuretics and potentially oto- or nephrotoxic substances.

Overdose:

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

Major incompatibilities**:**

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

7. Adverse events

Rare (1 to 10 animals / 10,000 animals treated):	Loose stool (diarrhea)
Undetermined frequency (cannot be estimated from available data)	Nephropathy[1] Internal ear disorder[1]

[1]Aminoglycoside antibiotics such as paromomycin can cause nephro- and ototoxicity.

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 or the local representative of the marketing authorisation holder using the contact details at the end of this leaflet, or via your national reporting system: {national system details}

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

In drinking water/milk use
Cattle (pre-ruminant):
For administration in milk/milk replacer
17500 – 35000 IU of paromomycin per kg BW/day (equivalent to 2.5-5 g of veterinary medicinal product/10 kg BW/day)
Duration of treatment: 3-5 days

Pigs:
For administration in drinking water.
17500 – 28000 IU of paromomycin per kg BW/day (equivalent to 2.5-4 g of veterinary medicinal product/10 kg BW/day)
Duration of treatment: 3-5 days)

To ensure a correct dosage body weight should be determined as accurately as possible.
The use of suitably calibrated measuring equipment is recommended.

Based on the recommended dose and the number and weight of animals to be treated, the exact daily concentration of the veterinary medicinal product should be calculated according to the following formula::

$$\frac{\text{mg veterinary medicinal product/ kg body weight / day} \times \text{mean body weight (kg) of animals to be treated}}{\text{Mean daily water/milk/milk replacer consumption (l/animal)}} = \ldots \text{ mg veterinary medicinal product per litre drinking water/milk/milk replacer}$$

The intake 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 may need to be adjusted accordingly.

9. Advice on correct administration

Medicated drinking water/milk/milk replacer and any stock solutions should be freshly prepared. Any remaining quantities of medicated fluids should be removed after 6 hours (in milk/milk replacer) or after 24 hours (in water).

To assure administration of the exact daily amount of veterinary medicinal product suitably calibrated weighing equipment should be used. For the administration of the veterinary medicinal product commercially available dosing pumps can be used. The solubility of the veterinary medicinal product has been tested at the maximum concentration of 95 g/L.

10. Withdrawal periods

Cattle (pre-ruminant)
Meat and offal: 20 days
Pigs
Meat and offal: 3 days

11. Special storage precautions

Keep out of the sight and reach of children.

Do not store above 25°C.
Keep the sachet tightly closed.

Do not use this veterinary medicinal product after the expiry date which is stated on the sachet after "Exp". The expiry date refers to the last day of that month.

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

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 applicable national collection system. These measures should help to protect the environment.
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

To be completed nationally for the marketing authorisation numbers

Pack size: sachet of 1000 g – 500 g – 250 g
Cardboard box containing 40 sachets of 25 grams.
Not all pack sizes may be marketed.

15. Date on which the package leaflet was last revised

{MM/YYYY}
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>:

Huvepharma NV
Uitbreidingstraat 80
2600 Antwerpen
Belgium
+32 3 288 18 49
pharmacovigilance@huvepharma.com

Manufacturer responsible for batch release
Biovet JSC
39 Petar Rakov Str
4550 Peshtera
Bulgaria

Local representatives and contact details to report suspected adverse reactions
To be completed nationally

17. Other Information

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