SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Parofor 175 mg/ml solution for injection for pigs.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

Active substance:

Paromomycin sulfate	250 mg, equivalent to paromomycin base 175 mg or 175 000 IU of paromomycin activity

Excipients:

Chlorocresol	1.0 mg
Sodium metabisulfite (E223)	3.0 mg

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection.
A clear yellow to amber solution.

4. CLINICAL PARTICULARS

4.1 Target species

Pigs (piglets).

4.2 Indications for use, specifying the target species

Paromomycin is indicated for the treatment of bacterial infections caused by pathogens which are susceptible to paromomycin, provided effective concentrations are achieved at the site of infection.

4.3 Contraindications

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

4.4 Special warnings for each target species

None.

4.5 Special precautions for use

Special precautions for use in animals

In the event of a suspected *Pseudomonas aeruginosa* infection, the susceptibility of this bacterial target pathogen must be determined before starting treatment.
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. Due to this risk of oto- and nephrotoxicity, the use of the product in neonates should be based on benefit-risk assessment by the responsible veterinarian.
Given the narrow margin of safety of aminoglycosides, the dosage should be reduced for overweight or dehydrated animals or animals suffering from renal insufficiency.

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 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. Official, national and regional antimicrobial policies should be taken into account when the product is used.
Aminoglycosides are considered as critical in human medicine. Consequently, they should not be used as a first intention treatment in veterinary medicine.

Use of the product deviating from the given instructions 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.

Special precautions to be taken by the person administering the veterinary medicinal product to animals

This product contains paromomycin, chlorocresol and sodium metabisulphite which can cause allergic reactions in some people. People with known hypersensitivity (allergy) to aminoglycosides, chlorocresol and/or sulphites should avoid contact with the product.
This product may cause skin and eye irritation and therefore contact with skin and eyes should be avoided. If the product has come into contact with skin or eyes, rinse immediately with plenty of water. Seek medical attention if irritation persists.
In case of accidental injection, seek medical attention immediately.
Do not eat, drink or smoke while handling this product and wash hands after use.

4.6 Adverse reactions (frequency and seriousness)

In rare occasions soft faeces has been observed.
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)

Aminoglycoside antibiotics such as paromomycin can cause oto- and nephrotoxicity.

4.7 Use during pregnancy, lactation or lay

Laboratory studies in rat and rabbit have not produced any evidence of teratogenic, foetoxic, maternotoxic effects. The safety of the product during pregnancy and lactation has not been established in target species. Therefore, the use of the veterinary medicinal product should be based on a risk/benefit assessment by the responsible veterinarian.

4.8 Interaction with other medicinal products and other forms of interaction

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

4.9 Amounts to be administered and administration route

For intramuscular use.
One injection per day for 3 to 5 days.

	Paromomycin sulfate/kg	*mL Parofor /weight*
Pigs Less than 50 kg	20 mg/kg (equivalent to 14000 IU)	0.4 mL/5 kg

Do not administer more than 3.8 ml per injection site.

To ensure a correct dosage and to prevent under-dosing, body weight must be determined as accurately as possible. Repeated injections should be done in distinct injection sites.

The closures should not be broached more than 30 times. In order to prevent excessive broaching of the stopper, a suitable multiple dosing device should be used.

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

None known.

4.11 Withdrawal period(s)

Meat and offal: 20 days

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: antibacterials for systemic use, aminoglycoside, paromomycin.
ATC vet code: QJ01GB92.

5.1 Pharmacodynamic properties

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.
Paromomycin acts in a concentration-dependent manner.
Paromomycin is active against the following pathogenic bacteria in particular: *Actinobacillus pleuropleumoniae*

Four mechanisms of resistance have been identified: changes of the ribosomes due to mutations, reduction of permeability of bacterial cell wall or active efflux, enzymatic modification of ribosomes and inactivation of aminoglycosides by enzymes. The first three resistance mechanisms arise from mutations of certain genes on bacterial chromosome. The fourth resistance mechanism only occurs following uptake of a transposon or plasmid coding for resistance. Paromomycin selects for resistance and cross-resistances at high frequency against a variety of other aminoglycosides among intestinal bacteria.

5.2 Pharmacokinetic properties

After single and repeated intramuscular injections, peak plasma concentrations are about 35.5 µg/ml (C_{max}) are observed between 15 and 30 minutes after dosing.
The mean elimination half-life is approximately 3.4 hours
No accumulation occurs following repeated intramuscular injections, once daily for 5 days of 14 mg/kg of paromomycin
Paromomycin is primarily eliminated via the gallbladder and urinary tract.

5.3 Environmental properties

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

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Chlorocresol
Disodium edetate (E386)
Sodium metabisulfite (E223)
Water for injections

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

Shelf-life of the veterinary medicinal product as packaged for sale: 2 years.
Shelf life after first opening of the package: 28 days.

6.4 Special precautions for storage

Product as packed for sale: Store the vials in the outer carton in order to protect from light.
After first opening: do not store above 25°C.

6.5 Nature and composition of immediate packaging

The product is packed in type I colourless glass vials of 100 ml closed with a bromobutyl stopper and sealed with aluminium cap. Each bottle is placed in a cardboard.

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. MARKETING AUTHORISATION HOLDER

Huvepharma N.V.
Uitbreidingstraat 80
2600 Antwerpen
Belgium

8. MARKETING AUTHORISATION NUMBER

Vm 30282/4039

9. DATE OF FIRST AUTHORISATION

18 October 2018

10. DATE OF REVISION OF THE TEXT

October 2018

Approved: 18 October 2018