1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Gabbrovet 140 mg/ml solution for use in drinking water, milk or milk replacer for pre-ruminant cattle and pigs [FR AT BE BG HR CY CZ DK EE DE EL HU IE LV LT LU NL PL PT RO SK SI ES IS UK]
AMMINOFARMA BS 140 mg/ml solution for use in drinking water, milk or milk replacer for pre-ruminant cattle and pigs [IT]

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

Active substance:
Paromomycin (as sulfate) 140 mg
(equivalent to 140 000 IU of paromomycin activity)
(equivalent to approximately 200 mg of paromomycin sulfate)

Excipients:

Benzyl alcohol	(E1519)	7.5 mg
Sodium metabisulfite	(E223)	3.0 mg

For the full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Solution for use in drinking water, milk or milk replacer
Pale yellow to yellow solution

4. CLINICAL PARTICULARS

4.1 Target species

Cattle (pre-ruminant cattle), pigs

4.2 Indications for use, specifying the target species

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

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 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.

4.4 Special warnings for each target species

None.

4.5 Special precautions for use

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 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 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.
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.
Aminoglycosides are considered as critical in human medicine. Consequently, they should not be used as a first intention 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 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.

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

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

Oral use.
Pre-ruminant cattle: administration in milk/milk replacer.
Pigs: administration in drinking water.
Duration of treatment: 3-5 days.

Pre-ruminant cattle 1.25 – 2.5 ml of product/10 kg BW/day, equivalent to 17500 - 35000 IU of paromomycin per kg BW/day (i.e. approximately 25-50 mg paromomycin sulfate per kg BW/day).

Pigs: 1.25 – 2 ml of product/10 kg BW/day, equivalent to 17500 - 28000 IU of paromomycin per kg BW/day (i.e. approximately 25-40 mg paromomycin sulfate per kg BW/day).

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

$$\frac{\text{ml product/ kg BW/day} \times \text{Mean bodyweight (kg) of animals to be treated}}{\text{Mean daily water consumption (litre) per animal}} = \text{ml product per litre drinking water/day/ animal/}$$

To ensure a correct dosage bodyweight should be determined as accurately as possible.
The uptake of medicated water 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, uptake of drinking water has to be monitored and the concentration of paromomycin has to be adjusted accordingly.

Medicated drinking water/milk/milk replacer and any stock solutions should be freshly prepared every 6 hours (in milk/milk replacer) or every 24 hours (in water).

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

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

4.11 Withdrawal period(s)

Cattle:
Meat and offal: 20 days

Pigs:
Meat and offal: 3 days

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: intestinal antiinfectives; antibiotics; paromomycin.
ATC vet code: QA07AA06.

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, including *E. coli*.
Paromomycin acts in a concentration-dependant manner. Five 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 and fifth resistance mechanism only occurs following uptake of mobile genetic elements 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 particulars

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

5.3. Environmental properties

The active ingredient paromomycin sulfate is persistent in the environment

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Benzyl alcohol (E1519)
Sodium metabisulfite (E223)
Disodium edetate
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

Shelf-life of the veterinary medicinal product as packaged for sale in 125 ml bottles: 1 year
Shelf-life of the veterinary medicinal product as packaged for sale in 250 ml bottles: 18 months
Shelf-life of the veterinary medicinal product as packaged for sale in 500 ml bottles: 2 years
Shelf-life of the veterinary medicinal product as packaged for sale in 1,000 ml bottles: 30 months
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 or milk replacer: 6 hours

6.4. Special precautions for storage

125 ml and 250 ml bottles:
Do not store above 25°C

500 ml and 1000 ml bottles:
No special storage conditions required

All Presentations:
After first opening, keep the bottle tightly closed.

6.5 Nature and composition of immediate packaging

Nature of container
- White high density polyethylene bottles
- Polypropylene screw stopper equipped with a polyethylene seal
- Polypropylene dosing device of 30 ml graduated every 5 ml

Pack sizes:
Box containing 1 plastic bottle of 125 ml,
Box containing 1 plastic bottle of 250 ml
Box containing 1 plastic bottle of 500 ml
Box containing 1 plastic bottle of 1,000 ml
Plastic bottle of 125 ml
Plastic bottle of 250 ml
Plastic bottle of 500 ml
Plastic bottle of 1,000 ml

For each listed pack size, a dosing device is joined.

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 product should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

8. MARKETING AUTHORISATION NUMBER(S)

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

10 DATE OF REVISION OF THE TEXT