Summary of Product Characteristics

1 NAME OF THE VETERINARY MEDICINAL PRODUCT

Apravet 100 g/kg premix for medicated feeding stuff for pigs

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each kg contains:

Active substance:
Apramycin sulfate 100 g (corresponds to apramycin 100,000,000 IU)

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Premix for medicated feeding stuff
Light brown granules

4 CLINICAL PARTICULARS

4.1 Target Species

Pigs.

4.2 Indications for use, specifying the target species

Treatment and metaphylaxis of bacterial enteritis caused by micro-organisms susceptible to apramycin such as *Escherichia coli*.

4.3 Contraindications

Do not use in the cases of hypersensitivity to apramycin or any of the excipients.
Do not use in animals suffering from kidney disorders.
Do not use in cats.

4.4 Special warnings for each target species

The uptake of medication by animals can be altered as a consequence of illness. In case of insufficient uptake of feed animals should be treated parenterally.
The use of the product should be combined with good management practices e.g. good hygiene, proper ventilation, no overstocking.

4.5 Special precautions for use

Special precautions for use in animals

Use of the veterinary medicinal 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 veterinary medicinal product is used.

Use of the veterinary medicinal product deviating from the instructions given in the Summary of Product Characteristics may increase the prevalence of bacteria resistant to the apramycin 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

People with known hypersensitivity to apramycin should administer the product with care.
During preparation and administration of the medicated feedingstuff, skin, eye and oral contact with the product, as well as inhalation of dust, should be avoided. Wear a protective suit, gloves and an appropriate dust mask (either a disposable half mask respirator conforming to European Standard EN149 or a non-disposable respirator conforming to European Standard EN140 with a filter to EN 143) when mixing and handling the product.
Wash any contaminated skin. Wash hands carefully with soap and water after handling of the product. In the event of accidental ingestion, seek medical assistance immediately and show the package label.

4.6 Adverse reactions (frequency and seriousness)

None known

4.7 Use during pregnancy, lactation or lay

Laboratory studies have not produced any evidence of teratogenic, foetotoxic or maternotoxic effects.
The use is not recommended in pregnant or lactating sows.

4.8 Interaction with other medicinal products and other forms of interactions

In certain conditions with a high degree of humidity there might be an apparent interaction with lectins.
Aminoglycosides may have a negative influence on the kidney function. The administration of these agents to animals suffering from renal impairment or in combination with agents that also affect renal function may therefore present a risk of intoxication.

Do not administer with other aminoglycosides due to their nephrotoxic potential.
Aminoglycosides may cause neuromuscular blockade. It is therefore recommended to take such an effect into account when anaesthetising treated animals.

4.9 Amounts to be administered and administration route

The dosage is 4,000-8,000 IU/kg of bodyweight per day (equivalent to 4-8 g of the product per 100kg of bodyweight per day).
Administer as the sole feeding stuff for at least 21 days. It is recommended to mix the required quantity of the product with a small amount of feed (20 – 50 kg) before mixing it in the total volume.

The consumption of the medicated feed may depend of the clinical condition of the animals. In order to guarantee a correct dosing, the concentration of the product in the feed should be adjusted accordingly.

To adjust dosing properly the following calculation can be used:

$$\frac{\text{… g product/kg b.w./day x average b.w. of pigs (kg)}}{\text{average daily intake of feed (kg/animal)}} = \text{… g of the product/kg of feed}$$

Medicated feed may be pelleted using a pre-conditioning step for 5 minutes at a temperature not exceeding 85°C.

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

A single 100 fold overdosing in 5 pigs did not result in any mortality.
A 25 to 50 fold overdosing during 28 days, did not provoke any toxic effect.

4.11 Withdrawal period(s)

Meat and offal: 1 day

5 PHARMACOLOGICAL or IMMUNOLOGICAL PROPERTIES

Pharmacotherapeutic group: intestinal antiinfectives, antibiotics.
ATCvet code: QA07AA92

5.1 Pharmacodynamic properties

As an aminoglycoside antibiotic apramycin binds to the 30S ribosomal subunit and interferes with the protein synthesis. Through mechanisms not yet completely elucidated, it acts on the cell wall and is bactericidal. The overall spectrum includes many aerobic or facultative anaerobic Gram-negative bacteria, including Enterobacteriaceae. It has no activity against anaerobic bacteria or under anaerobic conditions.
Susceptibility of the *E. coli* strains from pigs to apramycin can vary geographically and over time.
The most important mechanism of resistance against apramycin is the production of modifying enzymes that are usually encoded by resistance genes derived from plasmids. Depending on their spectrum, these enzymes may cause cross-resistance between aminoglycosides. Resistance may also be caused by a change of the ribosomal attachment sites, or the conveying system allowing the penetration of the cell.
Until harmonised international interpretative criteria relevant for susceptibility testing are available for apramycin, nationally approved and validated methods should be followed.

Resistance mechanisms: Different aminoglycoside 3-N acetyltransferase enzymes (AAC-3) have been related with resistance to apramycin. These enzymes confer different cross-resistance against other aminoglycosides. Apramycin resistance can be influenced by co-selection (resistance to apramycin has been described to be located in the same mobile genetic element that other resistant determinants in Enterobacteriaceae) and cross resistance (e. g. with gentamicin).

Resistance developed by chromosomal resistance is minimal for most of the aminoglycosides.

5.2 Pharmacokinetic particulars

The oral administration of apramycin is intended for antimicrobial activity within the gut; apramycin is poorly absorbed, but absorption may be increased in young animals and in animals with disrupted intestinal barrier.
Apramycin is excreted in its active form via the kidney.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Starch, pregelatinised
Wheat meal

6.2 Major incompatibilities

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

6.3 Shelf-life

Shelf-life of the veterinary medicinal product as packaged for sale: 3 years
Shelf-life after first opening the immediate packaging: 6 months
Shelf life after incorporation into meal feed: 3 months
Shelf life after incorporation into pelleted feed: 1 month

6.4 Special precautions for storage

Veterinary medicinal product as packaged for sale: Do not store above 25°C. Store in the original package. Protect from moisture.
Veterinary medicinal product after first opening of the immediate packaging: Do not store above 25°C.
Medicated feed (mashed and pelleted): Do not store above 25°C.

6.5 Nature and composition of immediate packaging

Polyethylene-lined multiple-layer paper bags of 1 kg, 5 kg and 20 kg.
Not all pack sizes may be marketed.

6.6 Special precautions for the disposal of unused veterinary medicinal products 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

Huvepharma NV
Uitbreidingstraat 80
2600 Antwerpen
Belgium

8 MARKETING AUTHORISATION NUMBER(S)

VPA10782/013/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 29th August 2013
Date of latest renewal: 27th July 2018

10 DATE OF REVISION OF THE TEXT

July 2018