[Version 9.1,06/2024]

ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Apravet 100 000 IU/g premix for medicated feeding stuff for pigs and rabbits (PT, BE, FR, HU, ES, UK)

Apravet SC 100 000 IU/g premix for medicated feeding stuff for pigs and rabbits (IT)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Active substance:

Each g contains:

Active Substance:
Apramycin 100 000 IU – international units.
(as apramycin sulphate).

Excipients:

Qualitative composition of excipients and other constituents
Starch, pregelatinised
Wheat flour

Light brown granules.

3. CLINICAL INFORMATION

3.1 Target species

Pigs and rabbits.

3.2 Indications for use for each target species

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

Rabbits:
Reduction in mortality and clinical signs related to epizootic enterocolitis due to *Escherichia coli.*

The presence of the disease in the group must be established before the veterinary medicinal product is used.

3.3 Contraindications

Do not use in the cases of hypersensitivity to the active substance, to other aminoglycosides or to any of the excipients.
Do not use in cats.

3.4 Special warnings

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 veterinary medicinal product should be combined with good management practices e.g.

good hygiene, proper ventilation, no overstocking.

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 susceptibility testing of the target pathogen(s). If this is not possible, therapy should be based on epidemiological information and knowledge of susceptibility of the target pathogens at farm level, or at local/regional level.
Use of the veterinary medicinal product deviating from the instructions given in the SPC 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 or any other aminoglycoside should avoid contact with the veterinary medicinal product.
This veterinary medicinal product may cause irritation after skin or eye contact or inhalation. During preparation and administration of the medicated feedingstuff, skin, eye and oral contact with the veterinary medicinal 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 veterinary medicinal product.
In the event of eye contact, rinse the affected area with plenty of water. In the event of skin contact, wash thoroughly with soap and water. If irritation persists, seek medical advice. Wash hands after use.
In the event of accidental ingestion, seek medical assistance immediately and show the package label to the physician. In case of onset of symptoms after exposure such as skin rash, seek medical advice immediately and show the package label to the physician. Swelling of the lips, face and eyes or difficulty breathing are more serious symptoms and require urgent medical assistance.

Special precautions for the protection of the environment:

Not applicable.

3.6 Adverse events

None known.

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 See the package leaflet for respective contact details.

3.7 Use during pregnancy, lactation or lay

Pregnancy and lactation:
Laboratory studies in the rat and rabbit have not produced any evidence of teratogenic effects.
The use is not recommended during the whole part of the pregnancy and in lactating animals..

3.8 Interaction with other medicinal products and other forms of interaction

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.

In certain conditions with a high degree of humidity there might be an apparent interaction with lectins.

3.9 Administration routes and dosage

In-feed use.

Pigs:
The dosage is 4 000-8 000 IU/kg of bodyweight per day (equivalent to 4-8 g of the veterinary medicinal product per 100kg of bodyweight per day).
Administer as the sole feeding stuff for at least 21 days.

Rabbits:
The dosage is 12 000 IU/kg of bodyweight per day (equivalent to 12 g of the veterinary medicinal product per 100kg of bodyweight per day) for a period up to 21 days.

To ensure a correct dosage, bodyweight should be determined as accurately as possible.
For all species, 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 veterinary medicinal product in the feed should be adjusted accordingly.

To adjust dosing properly following calculation can be used:

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

Mixing Instructions:
It is recommended to initially mix the veterinary medicinal product with a small amount of the feeding stuff (20-50 kg) before incorporating it in the full amount of feeding stuff.
Medicated feed may be pelleted using a pre-conditioning step for 5 minutes at a temperature not exceeding 85°C.

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

No adverse effects were observed in pigs that were given up to nine times the recommended dose.

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

Pigs: meat and offal - 21 days.
Rabbits: meat and offal - 1 day.

4. <PHARMACOLOGICAL> <IMMUNOLOGICAL> INFORMATION

4.1 ATC vet code:

QA07AA92

4.2 Pharmacodynamics

Aminoglycosides are concentration-dependent antibiotics. As an aminoglycoside antibiotic, apramycin binds to the 30S ribosomal subunit and interferes with protein synthesis of the bacteria. Through mechanisms not yet completely elucidated, it increases the permeability of the bacterial cell membrane and subsequently has a bactericidal action.
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.
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 system allowing the penetration of the cell.
Susceptibility of the *E. coli* strains from pigs to apramycin can vary geographically and over time. Until harmonised international interpretative criteria relevant for susceptibility testing are available for apramycin, nationally approved and validated methods should be followed.

4.3 Pharmacokinetics

Apramycin is very poorly absorbed orally. The oral administration of apramycin is intended for antimicrobial activity within the gut. Tissue distribution is limited.
Very little metabolism of apramycin takes place in the animal.
Apramycin is excreted in its active form via the kidney.

Environmental properties
Apramycin is persistent in soils.

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: 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.

5.3 Special precautions for storage

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

5.4 Nature and composition of immediate packaging

Polyethylene bag in a three-ply paper bag.

Pack Sizes:
Bags of 1 kg, 5 kg or 20 kg.

Not all pack sizes may be marketed.

5.5 Special precautions for the disposal of unused veterinary medicinal products 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 systems 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).

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGE

{PAPER BAG - NO SEPARATE OUTER PACKAGING, LABEL AND PACKAGE LEAFLET ARE ATTACHED TO THE BAG}

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Apravet 100 000 IU/g premix for medicated feeding stuff (PT, BE, FR, HU, ES, UK)

Apravet SC 100 000 IU/g premix for medicated feeding stuff (IT)

Apramycin

2. STATEMENT OF ACTIVE SUBSTANCES

Each g contains:

Active substance:
Apramycin 100 000 IU.
(as apramycin sulphate).

3. PACKAGE SIZE

1 kg, 5 kg or 20 kg.

4. TARGET SPECIES

Pigs and rabbits.

5. INDICATIONS

Read the package leaflet before use.

6. ROUTES OF ADMINISTRATION

In-feed.

7. WITHDRAWAL PERIODS

Withdrawal period:
Pigs: meat and offal - 21 days.
Rabbits: meat and offal - 1 day.

8. EXPIRY DATE

Exp. {mm/yyyy}
Once opened, use by…

9. SPECIAL STORAGE PRECAUTIONS

Veterinary medicinal product as packaged for sale: Do not store above 25°C. Store in the original bag. Protect from moisture.
Veterinary medicinal product after first opening of the bag: Do not store above 25°C. Store in the original bag.

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 sight and reach of children.

13. NAME OF THE MARKETING AUTHORISATION HOLDER

Huvepharma NV

14. MARKETING AUTHORISATIN NUMBERS

EU/0/00/000/000

15. BATCH NUMBER

Lot {number}

B. PACKAGE LEAFLET

PACKAGE LEAFLET

1. Name of the veterinary medicinal product

Apravet 100 000 IU/g premix for medicated feeding stuff for pigs and rabbits (PT, BE, FR, HU, ES, UK)

Apravet SC 100 000 IU/g premix for medicated feeding stuff for pigs and rabbits (IT)

Apramycin

2. Composition

Each g contains:

Active substance:
Apramycin 100 000 IU.
(as apramycin sulphate).

Excipients:
Starch, pregelatinised
Wheat flour

light brown granules.

3. Target species

Pigs and rabbits.

4. Indications for use

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

Rabbits:
Reduction in mortality and clinical signs related to epizootic enterocolitis due to *Escherichia coli.*

The presence of the disease in the group must be established before the veterinary medicinal product is used.

5. Contraindications

Do not use in the cases of hypersensitivity to the active substance, to other aminoglycosides or to any of the excipients.
Do not use in cats.

6. Special warnings

Special warnings for safe use in the target species:

The uptake of medication by animals can be altered as a consequence of illness. In case of insufficient uptake of feed animals alternative treatment should be considered, for example, by injection.
The use of the veterinary medicinal product should be combined with good management practices e.g. good hygiene, proper ventilation, no overstocking.

Special precautions for use in animals:

Use of the veterinary medicinal product should be based on susceptibility testing of the target pathogen(s). If this is not possible, therapy should be based on epidemiological information and knowledge of susceptibility of the target pathogens at farm level, or at local/regional level.
Use of the veterinary medicinal product deviating from the instructions given in the SPC 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 or any other aminoglycoside should avoid contact with the veterinary medicinal product.
This veterinary medicinal product may cause irritation after skin or eye contact or inhalation. 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 veterinary medicinal product.
In the event of eye contact, rinse the affected area with plenty of water. In the event of skin contact, wash thoroughly with soap and water. If irritation persists, seek medical advice. Wash hands after use.
In the event of accidental ingestion, seek medical assistance immediately and show the package label to the physician. In case of onset of symptoms after exposure such as skin rash, seek medical advice immediately and show the package label to the physician. Swelling of the lips, face and eyes or difficulty breathing are more serious symptoms and require urgent medical assistance.

Pregnancy and lactation:

Laboratory studies in the rat and rabbit have not produced evidence of adverse effects in pregnant animals. The use is not recommended during the whole part of the pregnancy and in lactating animals.

Interaction with other medicinal products and other forms of interaction:

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.

In certain conditions with a high degree of humidity there might be an apparent interaction with lectins.

Overdose (symptoms, emergency procedures, antidotes):

No adverse effects were observed in pigs that were given up to nine times their recommended use level.

Major incompatibilities:

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

Environmental properties

Apramycin is very persistent in soils

7. Adverse events

None known.
If you notice any serious effects or other effects not mentioned in this leaflet, please inform your veterinary surgeon.

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 its local representative> using the contact details at the end of this leaflet.

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

In-feed use.

Pigs:
The dosage is of 4 000-8 000 IU/kg of bodyweight per day (equivalent to 4-8 g of the veterinary medicinal product per 100 kg of bodyweight per day).
Administer as the sole feeding stuff for at least 21 days.

Rabbits:
The dosage is of 12 000 IU/kg of bodyweight per day (equivalent to 12 g of the veterinary medicinal product per 100kg of bodyweight) for a period up to 21 days.

9. Advice on correct administration

For all species, 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 veterinary medicinal product in the feed should be adjusted accordingly.

To ensure a correct dosage, bodyweight should be determined as accurately as possible.

To adjust dosing properly following calculation can be used:

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

Mixing Instructions:
It is recommended to initially mix the veterinary medicinal product with a small amount of the feeding stuff (20-50 kg) before incorporating it in the full amount of feeding stuff.
Medicated feed may be pelleted using a pre-conditioning step for 5 minutes at a temperature not exceeding 85°C.

10. Withdrawal periods

Pigs: meat and offal - 21 days.
Rabbits: meat and offal - 1 day.

11. Special storage precautions

Keep out of the sight and reach of children.

Veterinary medicinal product as packaged for sale: Do not store above 25°C. Store in the original bag. Protect from moisture.

Veterinary medicinal product after first opening of the immediate bag: Do not store above 25°C. Store in the original bag. Keep the bag tightly closed in order to protect from light and moisture.
Medicated feed (mashed and pelleted): Do not store above 25°C.

Do not use this veterinary medicinal product after the expiry date which is stated on the label 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 incorporation into meal feed: 3 months.
Shelf life after incorporation into pelleted feed: 1 month.

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 systems. These measures should help to protect the environment.

Keep out of the sight and reach of children.

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

Polyethylene bag in a three-ply paper bag

Pack sizes:
Bag of 1 kg.
Bag of 5 kg.
Bag of 20 kg.

Not all pack sizes may be marketed.

Consideration should be given to official guidance on the incorporation of medicated premixes in final feeds.

15. Date on which the package leaflet was last revised

<{MM/YYYY}>
<{DD/MM/YYYY}>
<{DD month 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 events:
Huvepharma NV
Uitbreidingstraat 80
2600 Berchem

Belgium
+32 3 288 18 49

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