[Version 8.2,01/2021]

ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Revozyn RTU 400 mg/ml suspension for injection for cattle

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

1 ml suspension contains:
Active substance:
Penethamate hydriodide 400 mg

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Suspension for injection.
A white to yellowish white oily suspension.

4. CLINICAL PARTICULARS

4.1 Target species

Cattle (lactating cows).

4.2 Indications for use, specifying the target species

Treatment of clinical and subclinical mastitis in lactating cows caused by staphylococci and streptococci, sensitive to penicillin.

4.3 Contraindications

Do not use in cases of known hypersensitivity to the active substance, or to any of the excipients.
Do not administer by intravenous injection.

4.4 Special warnings for each target species

None.

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 and local 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 SPC may increase the prevalence of bacteria resistant to benzylpenicillin and may decrease the effectiveness of treatment with other beta-lactams due to the potential for cross-resistance.

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

This veterinary medicinal product can cause sensitisation and contact dermatitis.
Hypersensitivity to penicillins may lead to cross reactions to cephalosporins, and *vice versa*.
Allergic reactions to these substances may occasionally be serious.
Direct skin contact or self-injection should be avoided . Gloves should be worn when handling the veterinary medicinal product.
Do not handle this veterinary medicinal product if you know you are sensitised, or if you have been advised not to work with such preparations.
Wash hands after use.
When the veterinary medicinal product comes into contact with the skin, wash immediately with plenty of water. If symptoms following exposure such as skin rash develop, or in the event of self-injection, you should seek medical advice and show the physician the package leaflet. Swelling of the face, lips or eyes, or difficulty with breathing are more serious symptoms and require urgent medical attention.

4.6 Adverse reactions (frequency and seriousness)

The symptoms of adverse reactions range from mild skin reactions such as urticaria and dermatitis to severe reactions such as anaphylactic shock (very rarely, less than 1 animal in 10,000 animals treated) which very rarely may be fatal. In addition sensitisation against penicillins may occur.

4.7 Use during pregnancy, lactation or lay

Can be used during pregnancy or lactation.

4.8 Interaction with other medicinal products and other forms of interaction

Penicillins should not be administered concurrently with bacteriostatic antibiotics.

4.9 Amounts to be administered and administration route

Shake well before use.
Only for intramuscular administration, preferably in the neck.
Administer alternately on the left and the right side.

10,000-15,000 IU (10-15 mg penethamate hydriodide) per kg body weight per day, during 3 days, corresponding to 2.5-3.75 ml per 100 kg body weight per day, during 3 days.

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

In case of overdose, no adverse effects other than those mentioned in section 4.6 are to be expected.

4.11 Withdrawal period(s)

Milk: 4 days.
Meat and offal: 10 days.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Beta-lactamase sensitive penicillins.
ATCvet code: QJ01CE90.

5.1 Pharmacodynamic properties

In aqueous environment penethamate is hydrolysed to form benzylpenicillin and diethylaminoethanol. The mode of action of benzylpenicillin is by prevention of cell wall synthesis during bacterial cell growth and its activity is primarily bactericidal and time-dependent. The antimicrobial spectrum of the active substance corresponds to that of benzylpenicillin which is effective against beta-lactamase negative *Streptococcus agalactiae, Streptococcus dysgalactiae, Streptococcus uberis* and *Staphylococcus aureus*. In 2012 the MIC_{90} values for penicillin in Sweden were 0.12 µg/ml for *S. aureus*, 0.12 µg/ml for *S. dysgalactiae* and 0.12 µg/ml for *S. uberis*. In 2012 the MIC_{90} values for penicillin in Germany were 0.031 µg/ml for *S. agalactiae*, 0.015 µg/ml for *S. dysgalactiae* and 0.125 µg/ml for *S. uberis*. In 2013 the MIC_{90} values for penicillin in Switzerland were 1.0 µg/ml for *S. aureus*, ≤0.12 µg/ml for *S. dysgalactiae* and ≤0.12 µg/ml for *S. uberis*. EUCAST reports an Epidemiological Cut OFF value (ECOFF) of 0.125 µg/ml for *S. aureus* and an ECOFF of 0.125 µg/ml for *S. agalactiae*. For *S. dysgalactiae* and *S. uberis* no ECOFF values are determined.

The most frequent mechanism of resistance is producing beta-lactamases (more specifically penicillinase especially in *S. aureus*), which break the beta-lactam ring of penicillins making them inactive.

5.2 Pharmacokinetic particulars

Penethamate hydriodide is the diethylaminoethyl ester of penicillin, which contains an acidic carboxylic acid grouping. The ester is non-ionised and has high lipid solubility. The major pharmacokinetic properties of penethamate hydriodide are its rapid absorption with high bioavailability and rapid metabolism *in vivo* to penicillin, the therapeutically active molecule. In circulation it is rapidly hydrolysed to diethylaminoethanol and penicillin, with approximately 90% existing as penicillin. The parent compound readily penetrates into milk, as a consequence of its high lipid solubility. In milk, it is hydrolysed to penicillin and this maintains the plasma/milk concentration gradient for the parent compound. This is a mechanism of passive diffusion from a fluid of pH 7.4 to a more acid pH in milk. With a pKa value of 2.7, penicillin is highly ionised in both plasma and milk. The pH gradient between plasma (pH 7.4) and milk (pH 6.6-6.8) is reduced in mastitis but nevertheless is not abolished.
C_{max} is 682 ng/mL, AUC_{last} is 7770 h*ng/mL and elimination half-life is 6.84 hours.
Apart from excretion in the milk, benzylpenicillin is also excreted via the kidneys.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Ethyl oleate
Lecithin

6.2 Major incompatibilities

Do not mix with any other veterinary medicinal product.

6.3 Shelf life

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

6.4. Special precautions for storage

Store below 30 °C.
Keep upright.

6.5 Nature and composition of immediate packaging

Multidose 50 ml uncoloured glass (type II, Ph. Eur.) vials, closed with fluoropolymer coated rubber type I (Ph. Eur.) stoppers secured with aluminium caps.
1 Vial in a cardboard box.

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

Eurovet Animal Health BV
Handelsweg 25
5531 AE Bladel
The Netherlands

8. MARKETING AUTHORISATION NUMBER(S)

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9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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10 DATE OF REVISION OF THE TEXT

PROHIBITION OF SALE, SUPPLY AND/OR USE

Not applicable.

ANNEX II

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

{ Carton 50 ml }

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Revozyn RTU 400 mg/ml suspension for injection for cattle
Penethamate hydriodide

2. STATEMENT OF ACTIVE SUBSTANCES

1 ml suspension contains:
Active substance:
Penethamate hydriodide 400 mg

3. PHARMACEUTICAL FORM

Suspension for injection

4. PACKAGE SIZE

50 ml

5. TARGET SPECIES

Cattle (lactating cows)

6. INDICATION(S)

7. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.

8. WITHDRAWAL PERIOD(S)

Withdrawal period(s):
Milk: 4 days.
Meat and offal: 10 days.

9. SPECIAL WARNING(S), IF NECESSARY

Read the package leaflet before use.
Penicillins and cephalosporins may occasionally cause severe allergic reactions.
See package leaflet for user warnings.

10. EXPIRY DATE

EXP {month/year}
Shelf life after first opening the immediate packaging: 28 days.
Once broached, use by: _____/_____/_____

11. SPECIAL STORAGE CONDITIONS

Store below 30 °C.
Keep upright.

12. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCTS OR WASTE MATERIALS, IF ANY

Disposal: read package leaflet.

13. THE WORDS "FOR ANIMAL TREATMENT ONLY" AND CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE, IF APPLICABLE

For animal treatment only. To be supplied only on veterinary prescription.

14. THE WORDS "KEEP OUT OF THE SIGHT AND REACH OF CHILDREN"

Keep out of the sight and reach of children.

15. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Eurovet Animal Health BV
Handelsweg 25
5531 AE Bladel
The Netherlands

16. MARKETING AUTHORISATION NUMBER(S)

17. MANUFACTURER'S BATCH NUMBER

Lot: {number}

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

Vial 50 ml

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Revozyn RTU 400 mg/ml suspension for injection for cattle (lactating cows)
Penethamate hydriodide

2. QUANTITY OF THE ACTIVE SUBSTANCE(S)

1 ml suspension contains:
Active substance:
Penethamate hydriodide 400 mg

3. CONTENTS BY WEIGHT, BY VOLUME OR BY NUMBER OF DOSES

50 ml

4. ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.

5. WITHDRAWAL PERIOD(S)

Withdrawal period(s):
Milk: 4 days.
Meat and offal: 10 days.

6. BATCH NUMBER

Lot:{number}

7. EXPIRY DATE

EXP: {month/year}
Once broached, use by: _____/_____/_____

8. THE WORDS "FOR ANIMAL TREATMENT ONLY"

For animal treatment only.

B. PACKAGE LEAFLET

PACKAGE LEAFLET:
Revozyn RTU 400 mg/ml
Suspension for injection for cattle

1. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER AND OF THE MANUFACTURING AUTHORISATION HOLDER RESPONSIBLE FOR BATCH RELEASE, IF DIFFERENT

Marketing authorisation holder:
Eurovet Animal Health BV
Handelsweg 25, 5531 AE Bladel
The Netherlands

Manufacturer responsible for batch release:
Eurovet Animal Health BV
Handelsweg 25,
5531 AE Bladel
The Netherlands

Produlab Pharma B.V.
Forellenweg 16,
4941 SJ Raamsdonksveer,
The Netherlands

Only the site testing and releasing the batches will be mentioned on the printed leaflet.

2. NAME OF THE VETERINARY MEDICINAL PRODUCT

Revozyn RTU 400 mg/ml suspension for injection for cattle
Penethamate hydriodide

3. STATEMENT OF THE ACTIVE SUBSTANCE(S) AND OTHER INGREDIENT(S)

1 ml suspension contains:
Active substance:
Penethamate hydriodide 400 mg

A white to yellowish white oily suspension.

4. INDICATION(S)

Treatment of clinical and subclinical mastitis in lactating cows caused by staphylococci and streptococci, sensitive to penicillin.

5. CONTRAINDICATIONS

Do not use in cases of known hypersensitivity to the active substance, or to any of the excipients.
Do not administer by intravenous injection.

6. ADVERSE REACTIONS

The symptoms of adverse reactions range from mild skin reactions such as urticaria and dermatitis to severe reactions such as anaphylactic shock (very rarely, less than 1 animal in 10,000 animals treated) which very rarely may be fatal. In addition sensitisation against penicillins may occur.

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 inform your veterinary surgeon.

Alternatively you can report via your national reporting system {national system details}.

7. TARGET SPECIES

Cattle (lactating cows).

8. DOSAGE FOR EACH SPECIES, ROUTE(S) AND METHOD OF ADMINISTRATION

Shake well before use.
Only for intramuscular administration, preferably in the neck.
Administer alternately on the left and the right side.

10,000-15,000 IU (10-15 mg penethamate hydriodide) per kg body weight per day, during 3 days, corresponding to 2.5-3.75 ml per 100 kg body weight per day, during 3 days.

9. ADVICE ON CORRECT ADMINISTRATION

None.

10. WITHDRAWAL PERIOD(S)

Milk: 4 days.
Meat and offal: 10 days.

11. SPECIAL STORAGE PRECAUTIONS

Keep out of the sight and reach of children.

Store below 30 °C.
Keep upright.
Do not use this veterinary medicinal product after the expiry date which is stated on the label and carton after EXP. The expiry date refers to the last day of that month.
Shelf life after first opening the immediate packaging: 28 days.

12. SPECIAL WARNING(S)

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 and local 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 this leaflet may increase the prevalence of bacteria resistant to benzylpenicillin and may decrease the effectiveness of treatment with other beta-lactams due to the potential for cross-resistance.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:
This veterinary medicinal product can cause sensitisation and contact dermatitis.
Hypersensitivity to penicillins may lead to cross reactions to cephalosporins, and *vice versa*. Allergic reactions to these substances may occasionally be serious.
Direct skin contact or self-injection should be avoided. Gloves should be worn when handling the veterinary medicinal product.
Do not handle this veterinary medicinal product if you know you are sensitised, or if you have been advised not to work with such preparations.
Wash hands after use.
When the veterinary medicinal product comes into contact with the skin, wash immediately with plenty of water. If symptoms following exposure such as skin rash develop, or in the event of self-injection, you should seek medical advice and show the physician the package leaflet. Swelling of the face, lips or eyes or difficulty with breathing are more serious symptoms and require urgent medical attention.

Pregnancy and lactation:
Can be used during pregnancy or lactation.

Interaction with other medicinal products and other forms of interaction:
Penicillins should not be administered concurrently with bacteriostatic antibiotics.

Overdose (symptoms, emergency procedures, antidotes):
In case of overdose, no adverse effects other than those mentioned in the 'Adverse reactions' section are to be expected.

Incompatibilities:
Do not mix with any other veterinary medicinal product.

13. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCT OR WASTE MATERIALS, IF ANY

Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal products should be disposed of in accordance with local requirements.

14. DATE ON WHICH THE PACKAGE LEAFLET WAS LAST APPROVED

15. OTHER INFORMATION

For any information about this veterinary medicinal product, please contact the local representative of the marketing authorisation holder.

Pack size: 50 ml.