[Version 8.2,01/2021]

ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

OCUREV Lyophilisate and solvent for suspension

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each dose (1 drop – approx. 35 µl) of the reconstituted vaccine contains:

Active substance:
Live attenuated *Brucella melitensis*, strain Rev-1 (smooth phase) …… 1 – 2 x10^9 cfu*

* cfu: colony forming units

Excipient(s):
Patent Blue V (E-131) …… 0.1 mg/ml

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Lyophilisate and solvent for suspension.

4. CLINICAL PARTICULARS

4.1 Target species

Sheep and goats (replacement).

4.2 Indications for use, specifying the target species

For active immunisation of sheep and goats to reduce infection and clinical signs caused by *Brucella melitensis.*

4.3 Contraindications

Do not vaccinate females in the pregnancy/lactation period (see item 4.7).

4.4 Special warnings for each target species

The vaccine is only used in replacement flocks.
Vaccinate healthy animals only.

4.5 Special precautions for use

Special precautions for use in animals

Application should be done under strict veterinary control and comply with the established requirements of the legislation in force. The measures to be adopted for the vaccinated animals and their waste materials, in accordance with the legislation in force, as well as other safety measures that official authorities determine should be taken into account.

The risk of vaccinated animals transmitting the vaccine strain to other stock living with them is practically negligible. Therefore, if non vaccinated animals (including cattle) have contact with the

vaccine strain from animals vaccinated with this speciality, they could give positive results in the serological tests. To prevent this possibility, it is advisable that vaccination is done, ideally, in an area different from the one used to house the bulk of the herd and that the vaccinated animals are kept segregated during two weeks from vaccination, as during this period the excretion of the vaccine strain can be produced through the body fluids (nasal cavities and conjunctiva).

Special warning: The microorganism is detectable at 15 days after vaccination in some organs. Taking into account that there could be a potential persistence in cranial lymph nodes for longer time, vaccinated animals should not be slaughtered in the period of 3 months after vaccination. Just in case they should be slaughtered, they will be subjected to the procedures applicable to the animals considered positive to Brucellosis, and the official veterinary documents that legislation in force requires will be necessary.

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

The vaccine can be pathogenic for humans. Since this vaccine has been prepared with a live, attenuated microorganism, appropriate measures must be taken to prevent contamination of the handler and other people that collaborate in the process. If accidental contamination during handling of the vaccine were to occur, seek medical advice immediately and show the package insert to the doctor.

It should not be administered by pregnant women.

During the administration of the product, the person or people who carry it out should be protected with glasses, gloves and mask, hold tightly the head of the animal to avoid sudden movements, and perform it in a safe-guard place in order to protect themselves from gusts of wind. The contact of the glove with the mucouses and/or open wounds during and after administration should be avoided.

It should be also taken into account that the period of excretion of the vaccine strain through the body fluids of the vaccinated animals can last until 2 weeks after administration.

Do not smoke, drink nor eat during the administration.

4.6 Adverse reactions (frequency and seriousness)

Hypersensitivity reactions may occur. This event is very rare. Should this be the case, an appropriate antihistaminic therapy must be administered.

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).

4.7 Use during pregnancy, lactation or lay

Do not use during the whole pregnancy and lactation.

4.8 Interaction with other medicinal products and other forms of interaction

No information is available on the safety and efficacy of this vaccine when used with any other veterinary medicinal product. A decision to use this vaccine before or after any other veterinary medicinal product therefore needs to be made on a case by case basis.

4.9 Amounts to be administered and administration route

Dose: 1 drop (approx. 35 µl) per ocular use to sheep and goats from 3 to 6 months of age.

Maintain usual aseptic conditions.

Reconstitute the vaccine with the coloured solvent, wait some minutes and shake gently to prevent foaming. Carefully remove seal and stopper and place the dropper on the vial mouth. Dispense only 1 drop in the eye of the animal. If there is no warranty that the drop has been deposited correctly, the procedure can be repeated in the other eye.

The vaccine should be administered within 6 hours after reconstitution.

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

With a ten fold dose it was observed a slight hyperthermia at 4 hours.

4.11 Withdrawal period(s)

30 days (see 4.5).

5. IMMUNOLOGICAL PROPERTIES

Pharmacotherapeutic group: Live bacterial vaccines for sheep and goats.
ATC vet code: QI04AE/QI03AE.

Rev-1 is an attenuated, smooth strain of *B. melitensis*, streptomycin non-dependent, isolated from streptomycin dependent cells, which was obtained from the virulent strain 6056.

The vaccine organism is streptomycin resistant.

The Rev-1 strain has the following characteristics:

- It stimulates active immunity and induces cell immune response against *Brucella* infections.
- Conjunctival administration induces a weak and short-lasting serological response that avoids the interference with the conventional brucellosis serological tests 4 months after vaccination.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lyophilisate
Tryptone
Sucrose
Thiourea
Ascorbic acid
Sodium glutamate
Highly purified water

Solvent
Sodium chloride
Patent Blue V (E-131)
Highly 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:
2 years for 10 and 50 doses vials.
1 year for 25 doses vials.

Shelf-life after reconstitution according to directions: 6 hours.

6.4. Special precautions for storage

Store and transport refrigerated (2 °C – 8 °C).
Protect from light.
Do not freeze.
May be transported and stored up to a maximum of 37ºC for a period not longer than 7 days.

6.5 Nature and composition of immediate packaging

The material of the container is as follows:

Lyophilisate
- 11 cc, Type I neutral glass vial (pack sizes of 10, 25 and 50 doses).
- Type I vacuum closing, butyl rubber stopper.
- Aluminium seal.

Solvent
- 3 cc, Type I neutral glass vial containing 0.5 ml (10 doses), 1 ml (25 doses) or 2 ml (50 doses).
- Type I insulin butyl rubber stopper.
- Type insulin aluminium seal.

- Sterile PVC dropper adjustable to the vial.

Pack sizes:

1 cardboard box with 1 vial of 10 doses, 1 vial of 0.5 ml of solvent and one dropper.
1 cardboard box with 1 vial of 25 doses, 1 vial of 1 ml of solvent and one dropper.
1 cardboard box with 1 vial of 50 doses, 1 vial of 2 ml of solvent and one dropper.

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

CZ Vaccines S.A.U.
A Relva s/n – Torneiros
36410 O Porriño
Pontevedra

Spain

8. MARKETING AUTHORISATION NUMBER(S)

Spain: 1481 ESP
Portugal: R744DGV
France: FR/V/1723018 6/2017

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorization: 20/11/2002
Date of last renewal:

10 DATE OF REVISION OF THE TEXT

PROHIBITION OF SALE, SUPPLY AND/OR USE>
Not applicable.

Veterinary medicinal product subject to prescription.
Veterinary use.
Administration under control or supervision of a veterinary surgeon.

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

{NATURE/TYPE}

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

OCUREV Lyophilisate and solvent for suspension

2. STATEMENT OF ACTIVE SUBSTANCES

Each dose (1 drop-approx. 35 µl) of the reconstituted vaccine contains:

Live attenuated *Brucella melitensis*, strain Rev-1 (smooth phase) …… $1 – 2 \times 10^9$ cfu
Patent Blue V (E-131) …… 0.1 mg/ml

3. PHARMACEUTICAL FORM

Lyophilisate and solvent for suspension

4. PACKAGE SIZE

10 doses
25 doses
50 doses

5. TARGET SPECIES

Sheep and goats (replacement)

6. INDICATION(S)

For active immunisation of sheep and goats to reduce infection and clinical signs caused by *Brucella melitensis*

7. METHOD AND ROUTE(S) OF ADMINISTRATION

Ocular use. Administer 1 drop (1 dose) in the eye of the animal
Read the package leaflet before use

8. WITHDRAWAL PERIOD(S)

Withdrawal period: 30 days

9. SPECIAL WARNING(S), IF NECESSARY

Do not administer to females in the pregnancy/lactation period

Accidental administration or contact with the mucosa is dangerous – see package leaflet before use

10. EXPIRY DATE

EXP {month/year}
Once reconstituted, the vaccine should be used within 6 hours

11. SPECIAL STORAGE CONDITIONS

Store and transport at 2-8ºC
Protect from light
Do not freeze
May be transported and stored up to a maximum of 37ºC for a period not longer than 7 days

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

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

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

CZ Vaccines S.A.U.
36410 O Porriño – Spain

16. MARKETING AUTHORISATION NUMBER(S)

Spain: 1481 ESP
Portugal: R744DGV
France: FR/V/1723018 6/2017

17. MANUFACTURER'S BATCH NUMBER

Batch {number}

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

FREEZE-DRIED

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

OCUREV Lyophilisate and solvent for suspension

2. QUANTITY OF THE ACTIVE SUBSTANCE(S)

Live attenuated *Brucella melitensis*, Rev-1 (smooth phase) …… 1-2 x 10^9 cfu

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

10 doses
25 doses
50 doses

4. ROUTE(S) OF ADMINISTRATION

Ocular use

5. WITHDRAWAL PERIOD(S)

30 days

6. BATCH NUMBER

Batch {number}

7. EXPIRY DATE

EXP {month/year}
Once reconstituted, the vaccine should be used within 6 hours

8. THE WORDS "FOR ANIMAL TREATMENT ONLY"

For animal treatment only.

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

SOLVENT

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

DILUENT FOR OCUREV Lyophilisate and solvent for suspension

2. QUANTITY OF THE ACTIVE SUBSTANCE(S)

Patent Blue V (E-131) …… 0.1 mg/ml

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

0.5 ml
1 ml
2 ml

4. ROUTE(S) OF ADMINISTRATION

Ocular use

5. WITHDRAWAL PERIOD(S)

Not applicable

6. BATCH NUMBER

Batch {number}

7. EXPIRY DATE

EXP {month/year}

8. THE WORDS "FOR ANIMAL TREATMENT ONLY"

For animal treatment only.

B. PACKAGE LEAFLET

PACKAGE LEAFLET:
OCUREV
Lyophilisate and solvent for suspension

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

CZ Vaccines S.A.U.
A Relva s/n – Torneiros
36410 O Porriño
Pontevedra
Spain

2. NAME OF THE VETERINARY MEDICINAL PRODUCT

OCUREV Lyophilisate and solvent for suspension

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

Each dose (1 drop-approx. 35 µl) of the reconstituted vaccine contains:

Active substance:
Live attenuated *Brucella melitensis*, strain Rev-1 (smooth phase) …… 1 – 2 x10^9 cfu*

* cfu: colony forming units

Excipient(s):
Patent Blue V (E-131) …… 0.1 mg/ml

4. INDICATION(S)

For active immunisation of sheep and goats to reduce infection and clinical signs caused by *Brucella melitensis.*

5. CONTRAINDICATIONS

Do not vaccinate females in the pregnancy/lactation period.

6. ADVERSE REACTIONS

Hypersensitivity reactions may occur. This event is very rare. Should this be the case, an appropriate antihistaminic therapy must be administered.

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).

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.

7. TARGET SPECIES

Sheep and goats (replacement).

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

Dose: 1 drop (approx. 35 µl) per ocular use to sheep and goats from 3 to 6 months of age.

Maintain usual aseptic conditions.

Reconstitute the vaccine with the coloured solvent, wait some minutes and shake gently to prevent foaming. Carefully remove seal and stopper and place the dropper on the vial mouth. Dispense only 1 drop in the eye of the animal. If there is no warranty that the drop has been deposited correctly, the procedure can be repeated in the other eye.

The vaccine should be administered within 6 hours after reconstitution.

9. ADVICE ON CORRECT ADMINISTRATION

Application should be done under strict veterinary control and comply with the established requirements of the legislation in force. The measures to be adopted for the vaccinated animals and their waste materials, in accordance with the legislation in force, as well as other safety measures that official authorities determine should be taken into account.

10. WITHDRAWAL PERIOD(S)

30 days.

11. SPECIAL STORAGE PRECAUTIONS

Keep out of the reach and sight of children.

Store and transport refrigerated (2 °C – 8 °C).
Protect from light.
Do not freeze.

Do not use after the expiry date which is stated on the label.
Shelf-life after dilution or reconstitution according to directions: 6 hours.
May be transported and stored up to a maximum of 37ºC for a period not longer than 7 days.

12. SPECIAL WARNING(S)

Special warnings for each target species:
The vaccine is only used in replacement flocks.
Vaccinate healthy animals only.

Special precautions for use in animals:

The risk of vaccinated animals transmitting the vaccine strain to other stock living with them is practically negligible. Therefore, if non vaccinated animals (including cattle) have contact with the vaccine strain from animals vaccinated with this speciality, they could give positive results in the serological tests. To prevent this possibility, it is advisable that vaccination is done, ideally, in an area different from the one used to house the bulk of the herd and that the vaccinated animals are kept segregated during two weeks from vaccination, as during this period the excretion of the vaccine strain can be produced through the body fluids (nasal cavities and conjunctiva).

Special warning: The microorganism is detectable at 15 days after vaccination in some organs. Taking into account that there could be a potential persistence in cranial lymph nodes for longer time, vaccinated animals should not be slaughtered in the period of 3 months after vaccination. Just in case they should be slaughtered, they will be subjected to the procedures applicable to the animals considered positive to Brucellosis, and the official veterinary documents that legislation in force requires will be necessary.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:
The vaccine can be pathogenic for humans. Since this vaccine has been prepared with a live, attenuated microorganism, appropriate measures must be taken to prevent contamination of the handler and other people that collaborate in the process. If accidental contamination during handling of the vaccine were to occur, seek medical advice immediately and show the package insert to the doctor.

It should not be administered by pregnant women.

During the administration of the product, the person or people who carry it out should be protected with glasses, gloves and mask, hold tightly the head of the animal to avoid sudden movements, and perform it in a safe-guard place in order to protect themselves from gusts of wind. The contact of the glove with the mucouses and/or open wounds during and after administration should be avoided.

It should be also taken into account that the period of excretion of the vaccine strain through the body fluids of the vaccinated animals can last until 2 weeks after administration.

Do not smoke, drink nor eat during the administration.

Use during pregnancy, lactation or lay:
Do not use during the whole pregnancy and lactation.

Interaction with other medicinal products and other forms of interaction:
No information is available on the safety and efficacy of this vaccine when used with any other veterinary medicinal product. A decision to use this vaccine before or after any other veterinary medicinal product therefore needs to be made on a case by case basis.

Overdose:
With a ten fold dose it was observed a slight hyperthermia at 4 hours.

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

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

Medicines should not be disposed of via wastewater or household waste.
Ask your veterinary surgeon or pharmacist how to dispose of medicines no longer required.

These measures should help to protect the environment.
Any unused product or waste materials should be disposed of in accordance with local requirements.

14. DATE ON WHICH THE PACKAGE LEAFLET WAS LAST APPROVED

15. OTHER INFORMATION

Pharmacotherapeutic group: Live bacterial vaccines for sheep and goats.
ATC vet code: QI04AE/QI03AE.

Rev-1 is an attenuated, smooth strain of *B. melitensis*, streptomycin non-dependent, isolated from streptomycin dependent cells, which was obtained from the virulent strain 6056.

The vaccine organism is streptomycin resistant.

The Rev-1 strain has the following characteristics:

- It stimulates active immunity and induces cell immune response, the principal defence mechanism against *Brucella* infections.
- Conjunctival administration induces a weak and short-lasting serological response that avoids the interference with the conventional brucellosis serological tests 4 months after vaccination.

Pack sizes:

Outer box with 1 vial of 10 doses and 1 vial of 0.5 ml of solvent and one sterile dropper.
Outer box with 1 vial of 25 doses and 1 vial of 1 ml of solvent and one sterile dropper.
Outer box with 1 vial of 50 doses and 1 vial of 2 ml of solvent and one sterile dropper.

Not all pack sizes may be marketed.

Veterinary medicinal product subject to prescription.
Veterinary use.
Administration under control or supervision of a veterinary surgeon.