SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

BOVIX MICROCLOX EDC, 600 mg Intramammary Suspension

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 3.6 g intramammary syringe contains:

Active substance:

Cloxacillin (as Cloxacillin Benzathine) 600 mg

Excipients:

Qualitative composition of excipients and other constituents
Stearic Acid
Aluminium Stearate
Liquid Paraffin

A white to off-white viscous suspension.

3. CLINICAL INFORMATION

3.1 Target species

Cattle (dairy cow at drying-off).

3.2 Indications for use for each target species

For the treatment of subclinical mastitis at drying off caused by *Streptococcus agalactiae, Streptococcus dysgalactiae, Streptococcus uberis, Staphylococcus aureus* and *Trueperella pyogenes.*

3.3 Contraindications

Do not use in cases of hypersensitivity to the active substance or to any of the excipients.

3.4 Special warnings

Cross-resistance has been shown between cloxacillin and different penicillins in methicillin-resistant *Staphylococcus aureus.* Use of cloxacillin should be carefully considered when susceptibility testing has shown resistance to other penicillins because its effectiveness may be reduced. The efficacy of the product has only been established for target organisms listed in section 3.2. Consequently, the occurrence of a severe mastitis after drying-off (sometimes fatal) due to other organisms, especially *Pseudomonas aeruginosa*, is possible. To reduce this risk it is important to observe strict aseptic technique for the administration of the product.
In some European regions, a high proportion of *Streptococcus uberis* isolates resistant to penicillinase-resistant penicillins have been detected from clinical cases in intramammary infections in bovine.

3.5 Special precautions for use

Special precautions for safe use in the target species:
Use of the product should be based on identification and 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 bacteria at farm level, or at local/regional level.
Use of the product should be in accordance with official, national and regional antimicrobial policies.
Use of the product deviating from the instructions given in the SPC may increase the prevalence of bacteria resistant to cloxacillin and may decrease the effectiveness of treatment with other beta-lactam antibiotics.Narrow spectrum antibiotic therapy with a lower risk of antimicrobial resistance selection should be used for first line treatment where susceptibility testing suggests the likely efficacy of this approach.
The product should not be used as part of herd health programmes. The veterinary medicinal product should only be used in individual animals. The feeding of waste milk containing residues of cloxacillin to calves should be avoided up to the end of the milk withdrawal period (except during the colostral phase), because it could select antimicrobial resistant bacteria within the intestinal microbiota of the calf and increase the faecal shedding of these bacteria.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:
Penicillins and cephalosporins may cause hypersensitivity (allergy) following injection, inhalation, ingestion or skin contact. Hypersensitivity to penicillins may lead to cross-reactions to cephalosporins and vice versa. Allergic reaction to these substances may occasionally be serious.
People with known hypersensitivity to penicillins and cephalosporins should avoid contact with the veterinary medicinal product. Handle this veterinary medicinal product with great care to avoid exposure. Personal protective equipment consisting of gloves should be worn when handling the veterinary medicinal product.
In case of accidental contact with the skin or eyes, wash immediately with water.
If you develop symptoms following exposure, such as skin rash, you should seek medical advice and show the doctor this warning. Swelling of the face, lips or eyes or difficulty with breathing are more serious symptoms and may require urgent medical attention. Wash hands after use.

Special precautions for the protection of the environment:
Not applicable.

3.6 Adverse events

Cattle: 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 or the national competent authority via the national reporting system. See the package leaflet for respective contact details.

3.7 Use during pregnancy, lactation or lay

Pregnancy:
Can be used during pregnancy.

3.8 Interaction with other medicinal products and other forms of interaction

Do not combine with bacteriostatic antibiotics.

No information is available on the safety and efficacy of this veterinary medicinal product when used with any other veterinary medicinal product.

3.9 Administration routes and dosage

For single intramammary use.

600 mg of cloxacillin i.e. the content of one syringe should be infused once into each quarter via the teat canal immediately after the last milking of the lactation.
Milk out thoroughly before starting administration. Before administering the veterinary medicinal product, the teat tips of the quarters to be treated should be thoroughly cleaned and disinfected, and care should be taken to avoid contamination of the syringe nozzle. Administer the full content of a syringe in the quarter. Massage after administration. After administration it is recommended to immerse the teat in an approved teat dip. Do not milk after treatment.

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

None known.

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

Meat and offal: zero days.
Milk:
- if calving occurs at least 42 days after treatment: 48 hours post calving.
- if calving occurs less than 42 days after treatment: 44 days after last treatment.

4. PHARMACOLOGICAL INFORMATION

4.1 ATCvet code: QJ51CF02

4.2. Pharmacodynamics

Cloxacillin is a semi-synthetic penicillin, belonging to the class of beta-lactamase-resistant penicillins. Cloxacillin is bactericidal in action and is not destroyed by staphylococcal beta-lactamase. It inhibits bacterial cell wall synthesis, leading to the death of susceptible bacteria. Its action is time-dependent.
The spectrum of activity of cloxacillin is primarily focused on Gram-positive bacteria like *Streptococcus agalactiae, Streptococcus dysgalactiae, Streptococcus uberis*, penicillin-resistant and sensitive staphylococci, and *Trueperella pyogenes*.
Resistance to beta-lactamase-resistant penicillins may arise via mutations of the penicillin-binding proteins of the bacterial cell wall. Being a penicillin, cloxacillin can exhibit cross-resistance to other antibiotics of the penicillin class. MIC distributions for cloxacillin are compiled from multiple sources, geographical regions, and time periods, using data from the EUCAST website and the VetPath programme:"

MIC data for Cloxacillin against target bacteria species

Target bacteria species	Isolate no	MIC_{50} (mg/L)	MIC_{90} (mg/L)	ECOFF (mg/L)	WT (mg/L) (wildtype organisms)
Streptococcus agalactiae	135	1 mg/L	2 mg/L	not established	not established

Streptococcus dysgalactiae	378	0.06 mg/L	0.125 mg/L	0.25 mg/L	≤ 0.25 mg/L
Streptococcus uberis	401	0.5 mg/L	2 mg/L	1 mg/L	≤ 1 mg/L
Staphylococcus aureus	1181	0.25 mg/L	0.5 mg/L	not established	not established
Trueperella pyogenes	94	0.25 mg/L	0.5 mg/L	not established	not established

4.3. Pharmacokinetics

Pharmacokinetic studies show that the intramammary use of cloxacillin benzathine leads to only minor systemic absorption of the active substance. The small part that enters the systemic circulation is excreted mainly through the urine and to a lesser extent through the bile.

5. PHARMACEUTICAL PARTICULARS

5.1 Major incompatibilities

Not applicable

5.2 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 24 months

5.3 Special precautions for storage

This veterinary medicinal product does not require any special storage conditions.

5.4 Nature and composition of immediate packaging

White low density polyethylene syringes containing 3.6 g (4.5 ml) of a sterile white hydrophobic suspension for intramammary infusion.The closure is a white low density polyethylene cap that secures the tightness of the syringe. It is fixed to the syringe barrel by push-fit. For single-use only.

Package size:
Cardboard box with 12 syringes x 3.6 g of veterinary medicinal product and wipes.
Cardboard box with 24 syringes x 3.6 g of veterinary medicinal product and wipes.
Cardboard box with 60 syringes x 3.6 g of veterinary medicinal product and wipes.
Cardboard box with 120 syringes x 3.6 g of veterinary medicinal product and wipes.

Not all pack sizes may be marketed.

5.5 Special precautions for the disposal of unused veterinary medicinal product 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

Kernfarm BV

7. MARKETING AUTHORISATION NUMBER(S)

8. DATE OF FIRST AUTHORISATION

Date of first authorisation: DD/MM/YYYY

9. DATE OF THE LAST REVISION OF THE SUMMARY OF THE PRODUCT CHARACTERISTICS

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).

LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

CARTON BOX

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

BOVIX MICROCLOX EDC, 600 mg Intramammary Suspension

2. STATEMENT OF ACTIVE SUBSTANCES

Each 3.6 g intramammary syringe contains 600 mg Cloxacillin (as Cloxacillin Benzathine)

3. PACKAGE SIZE

12 x 3.6 g
24 x 3.6 g
60 x 3.6 g
120 x 3.6 g

4. TARGET SPECIES

Cattle (dairy cow at drying-off)

5. INDICATIONS

6. ROUTES OF ADMINISTRATION

Intramammary use

7. WITHDRAWAL PERIOD

Withdrawal period:
Meat and offal: zero days.
Milk:
- if calving occurs at least 42 days after treatment: 48 hours post calving.
- if calving occurs less than 42 days after treatment: 44 days after last treatment.

8. EXPIRY DATE

Exp. {mm/yyyy}

9. SPECIAL STORAGE PRECAUTIONS

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 the sight and reach of children.

13. NAME OF THE MARKETING AUTHORISATION HOLDER

Kernfarm B.V.

14. MARKETING AUTHORISATION NUMBERS

To be completed nationally.

15. BATCH NUMBER

Lot {number}

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

Label for Syringe

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

BOVIX MICROCLOX EDC

2. QUALITATIVE PARTICULARS OF THE ACTIVE SUBSTANCES

Each 3.6 g intramammary syringe contains 600 mg Cloxacillin (as Cloxacillin Benzathine)

3. BATCH NUMBER

Lot {number}

4. EXPIRY DATE

Exp. {mm/yyyy}

PACKAGE LEAFLET

1. Name of the veterinary medicinal product

BOVIX MICROCLOX EDC, 600 mg Intramammary Suspension

2. Composition

Each 3.6 g intramammary syringe contains

Active substance:

Cloxacillin (as Cloxacillin Benzathine) 600 mg

A white to off-white viscous suspension.

3. Target species

Cattle (dairy cow at drying-off).

4. Indications for use

For the treatment of subclinical mastitis at drying off caused by *Streptococcus agalactiae, Streptococcus dysgalactiae, Streptococcus uberis, Staphylococcus aureus* and *Trueperella pyogenes.*

5. Contraindications

Do not use in cases of hypersensitivity to the active substance or to any of the excipients.

6. Special warnings

Special warnings:
Cross-resistance has been shown between cloxacillin and different penicillins in methicillin-resistant *Staphylococcus aureus.* Use of cloxacillin should be carefully considered when susceptibility testing has shown resistance to other penicillins because its effectiveness may be reduced.
The efficacy of the product has only been established for target organisms listed in section 3.2. Consequently, the occurrence of a severe mastitis after drying-off (sometimes fatal) due to other organisms, especially *Pseudomonas aeruginosa*, is possible. To reduce this risk it is important to observe strict aseptic technique for the administration of the product.
In some European regions, a high proportion of *Streptococcus uberis* isolates resistant to penicillinase-resistant penicillins have been detected from clinical cases in intramammary infections in bovine.

Special precautions for safe use in the target species:
Use of the product should be based on identification and 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 bacteria at farm level, or at local/regional level.
Use of the product should be in accordance with official, national and regional antimicrobial policies.
Use of the product deviating from the instructions given in the SPC may increase the prevalence of bacteria resistant to cloxacillin and may decrease the effectiveness of treatment with other beta-lactam

antibiotics.Narrow spectrum antibiotic therapy with a lower risk of antimicrobial resistance selection should be used for first line treatment where susceptibility testing suggests the likely efficacy of this approach.
The product should not be used as part of herd health programmes. . The veterinary medicinal product should only be used in individual animals. The feeding of waste milk containing residues of cloxacillin to calves should be avoided up to the end of the milk withdrawal period (except during the colostral phase), because it could select antimicrobial resistant bacteria within the intestinal microbiota of the calf and increase the faecal shedding of these bacteria.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:
Penicillins and cephalosporins may cause hypersensitivity (allergy) following injection, inhalation, ingestion or skin contact. Hypersensitivity to penicillins may lead to cross-reactions to cephalosporins and vice versa. Allergic reaction to these substances may occasionally be serious.
People with known hypersensitivity to penicillins and cephalosporins should avoid contact with the veterinary medicinal product. Handle this veterinary medicinal product with great care to avoid exposure. Personal protective equipment consisting of gloves should be worn when handling the veterinary medicinal product.
In case of accidental contact with the skin or eyes, wash immediately with water.
If you develop symptoms following exposure, such as skin rash, you should seek medical advice and show the doctor this warning. Swelling of the face, lips or eyes or difficulty with breathing are more serious symptoms and may require urgent medical attention. Wash hands after use.

Pregnancy:
Can be used during pregnancy.

Interactions with other medicinal products and other forms of interaction:
Do not combine with bacteriostatic antibiotics. No information is available on the safety and efficacy of this veterinary medicinal product when used with any other veterinary medicinal product.

Overdose:
None known.

7. Adverse events

Cattle: none known.

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 the local representative of the marketing authorisation holder using the contact details at the end of this leaflet, or via your national reporting system:

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

For single intramammary use,
600 mg of cloxacillin i.e. the content of one syringe should be infused once into each quarter via the teat canal immediately after the last milking of the lactation.

9. Advice on correct administration

Milk out thoroughly before starting administration. Before administering the veterinary medicinal product, the teat tips of the quarters to be treated should be thoroughly cleaned and disinfected, and care should be taken to avoid contamination of the syringe nozzle. Administer the full content of a syringe in the quarter. Massage after administration. After administration it is recommended to immerse the teat in an approved teat dip. Do not milk after treatment.

10. Withdrawal periods

Meat and offal: zero days.
Milk:
- if calving occurs at least 42 days after treatment: 48 hours post calving.
- if calving occurs less than 42 days after treatment: 44 days after last treatment.

11. Special storage precautions

Keep out of the sight and reach of children.

This veterinary medicinal product does not require any special storage conditions.

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.

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. 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

White low density polyethylene syringes containing 3.6 g (4.5 ml) of a sterile white hydrophobic suspension for intramammary infusion.The closure is a white low density polyethylene cap that secures the tightness of the syringe. It is fixed to the syringe barrel by push-fit. For single-use only.

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Cardboard box with 60 syringes x 3.6 g of veterinary medicinal product and wipes.
Cardboard box with 120 syringes x 3.6 g of veterinary medicinal product and wipes.

Not all pack sizes may be marketed

15. Date on which the package leaflet was last revised

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 reactions:
Kernfarm B.V.
De Corridor 14D
3621 ZB Breukelen
The Netherlands
Telephone: +31650638375

Manufacturer responsible for batch release:
CRIDA PHARM S.R.L.
Str. Stadionului, No. 1,
Oltenița, Călărași County,
915400, Romania

17. Other information