1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Multishield DC Intramammary Suspension for Cattle [BE, DE, FR, HU, IE, IT, NL, PL, PT, RO, UK(NI)]
Multishield Secado [ES]
Cymastin DC [CZ, SK]

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 4.5 g syringe contains:

Active substances:

Neomycin	70 000 IU (equivalent to Neomycin Sulphate	100 mg)
Penethamate	77.2 mg (equivalent to Penethamate Hydriodide	100 mg)
Benzylpenicillin	227.2 mg (equivalent to Procaine Benzylpenicillin	400 mg)

Qualitative composition of excipients and other constituents
Liquid paraffin
Aluminium di/tristearate

A smooth off-white oily suspension.

3. CLINICAL INFORMATION

3.1 Target species

Cattle (cows at drying off).

3.2 Indications for use for each target species

Treatment of subclinical mastitis caused by bovine mastitis microorganisms susceptible to the combination of active substances, penicillin and neomycin, and as part of strategy for the prevention of new infections occurring during the dry period.

3.3 Contraindications

Do not use in lactating cows.
Do not use in cases of hypersensitivity to the active substances, β-lactam antibiotics, cephalosporin antibiotics, neomycin or other aminoglycoside antibiotics or to any of the excipients.
Do not use in cows with clinical mastitis.

3.4 Special warnings

None.

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 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.

The therapeutic efficacy of the veterinary medicinal product is only established against pathogens that are susceptible to the active substances.
Serious acute mastitis [potentially lethal] due to pathogens like *Pseudomonas aeruginosa*, can occur after drying off despite preventive treatment. Good aseptic practices should be thoroughly respected in order to reduce that risk; cows should be housed in a hygienic paddock far from the milking parlour and regularly checked several days after drying off.
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 lactam antimicrobials (penicillins and cephalosporins) due to the potential for cross-resistance.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:
Persons administering the veterinary medicinal product should avoid contact with this preparation as occasionally skin allergy may occur.
Penicillins and cephalosporins may cause sensitisation following injection, inhalation, ingestion or skin contact. Sensitivity to penicillins may lead to cross sensitivity to cephalosporins and vice versa. Allergic reactions to these substances may occasionally be serious.
People with known hypersensitivity to β-lactam antibiotics, cephalosporin antibiotics, neomycin or other aminoglycoside antibiotics should avoid contact with the veterinary medicinal product .
If you develop symptoms such as a skin rash following exposure, seek medical advice and show the package leaflet or the label to the physician. Swelling of the face, lips or eyes, or difficulty with breathing are more serious symptoms and require urgent medical attention.

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

3.6 Adverse events

Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Allergic reaction (allergic skin reaction, anaphylaxis)[1] Hypersensitivity[1]

[1]May occasionally be serious. If adverse reactions occur, the current treatment should be withdrawn and symptomatic treatment should be initiated.

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 and lactation:
The use is not recommended during lactation, except at the drying off stage.

3.8 Interaction with other medicinal products and other forms of interaction

No data available.

3.9 Administration routes and dosage

Intramammary use.

Dose: 100 mg of neomycin sulphate, 100 mg of Penethamate Hydriodide and 400 mg of Procaine Benzylpenicillin into each quarter. The contents of one syringe should be infused into each quarter via the teat canal immediately after the final milking of a lactation.
Before instillation, the udder should be milked out completely.
The teat and its orifice should be thoroughly cleaned and disinfected with a cleaning towel.
Care should be taken to avoid contamination of the injector nozzle.

Gently insert the content of one syringe into each quarter. Disperse the veterinary medicinal product by gentle massage of the teat and udder. The syringe must only be used once.

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

Overdosing may invalidate the stated milk and meat withdrawal times.

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: 28 days.
Milk: 96 hours post calving in cows with a dry period of more than 50 days.
50 days plus 96 hours after treatment from cows with a dry period of 50 days or less.

4. PHARMACOLOGICAL INFORMATION

4.1 ATCvet code: QJ51RC22

4.2 Pharmacodynamics

The veterinary medicinal product contains an aminoglycoside (neomycin sulphate) and two penicillin derivatives (procaine benzyl penicillin and penethamate hydriodide).

Aminoglycosides disturb the permeability of the bacterial cell membrane by an effect exerted during cell wall development. Once the aminoglycoside has entered the cell, it binds to the target site on the ribosome, inducing misreading of the genetic code. Neomycin in common with other aminoglycosides has activity predominantly against gram negative microorganisms.

Neomycin has been shown to have synergistic activity with β-lactam antibiotics against Gram positive bacteria.

Penicillins have a time-dependent, bacteriocidal effect by interfering with microbial cell wall synthesis. They inhibit the activity of transpeptidase enzymes which catalyse cross linkage of the glycopeptide polymer units that form the cell wall. Both Procaine benzylpenicillin and Penethamate hydroiodide are hydrolysed in the udder to release free penicillin.

Bovine mastitis microorganisms which can be treated with the product include susceptible isolates of *Staphylococcus aureus, Streptococcus agalactiae, Streptococcus uberis,* other susceptible *Streptococcus* spp, *Trueperella pyogenes* and susceptible isolates of *E.coli.*

The predominant mechanism of penicillin resistance in Gram-negative bacteria is the production of β-lactamase enzymes and this is also a well-recognised feature of some *Staphylococcus* spp isolates. Alteration of the penicillin binding proteins is a less prevalent resistance mechanism however this has been recorded in some bovine mastitis isolates of *Staphylococcus* spp. Reported penicillin resistance

levels vary considerably between geographical areas. The prevalence of resistance against neomycin remains low in those species.

Enzymatic modification is the most common type of aminoglycoside resistance. There are only limited reports of identification of the genes for enzymes active against neomycin in veterinary mastitis pathogens.

4.3 Pharmacokinetics

Penethamate hydriodide is an ester of benzylpenicillin which is rapidly hydrolysed at pH 7.3 to liberate free penicillin which quickly distributes throughout the udder tissue.
Procaine benzylpenicillin is a complex, sparingly soluble organic salt of benzylpenicillin and its use, in combination with a slow-release base, is intended to delay release of the active penicillin moiety at the site of administration and so give rise to a prolonged duration of action.

Neomycin is a poorly lipid soluble, basic aminoglycoside that shows a high degree of binding to udder tissue and has low systemic absorption thus it persists in the udder for a prolonged period after administration.

5. PHARMACEUTICAL PARTICULARS

5.1 Major incompatibilities

Not applicable.

5.2 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 2 years.

5.3 Special precautions for storage

Do not store above 25°C.
Do not refrigerate or freeze.

5.4 Nature and composition of immediate packaging

Low density polyethylene (LDPE) syringe.

Pack size:
Bucket containing 24 syringes.
Bucket containing 120 syringes.

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

Bimeda Animal Health Limited

7. MARKETING AUTHORISATION NUMBER(S)

8. DATE OF FIRST AUTHORISATION

Date of first authorisation: {DD month YYYY}.

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

{MM/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 OUTER PACKAGE

{BUCKET CONTAINING 24x SYRINGES}
{BUCKET CONTAINING 120x SYRINGES}

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Multishield DC Intramammary Suspension for Cattle [BE, DE, FR, HU, IE, IT, NL, PL, PT, RO, UK(NI)]
Multishield Secado [ES]
Cymastin DC [CZ, SK]

2. STATEMENT OF ACTIVE SUBSTANCES

Neomycin 70 000 IU (100 mg Neomycin Sulphate) per syringe
Penethamate 77.2 mg (100 mg Penethamate Hydriodide) per syringe
Benzylpenicillin 227.2 mg (400 mg Procaine Benzylpenicillin) per syringe

3. PACKAGE SIZE

24 syringes
120 syringes

4. TARGET SPECIES

Cattle (cows at drying off).

5. INDICATIONS

6. ROUTES OF ADMINISTRATION

Intramammary use.

7. WITHDRAWAL PERIODS

Withdrawal period:
Meat and offal: 28 days.
Milk: 96 hours post calving in cows with a dry period of more than 50 days.
50 days + 96 hours after treatment from cows with a dry period of 50 days or less.

8. EXPIRY DATE

Exp. {mm/yyyy}

9. SPECIAL STORAGE PRECAUTIONS

Do not store above 25°C.

Do not refrigerate or freeze.

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

Bimeda Animal Health Limited

14. MARKETING AUTHORISATION NUMBERS

15. BATCH NUMBER

Lot {number}

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

{SYRINGE LABEL}

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Multishield DC Intramammary Suspension for Cattle [BE, DE, FR, HU, IE, IT, NL, PL, PT, RO, UK(NI)]
Multishield Secado [ES]
Cymastin DC [CZ, SK]

2. QUANTITATIVE PARTICULARS OF THE ACTIVE SUBSTANCES

Neomcyin 70 000 IU (100 mg Neomycin Sulphate) per syringe
Penethamate 77.2 mg (100 mg Penethamate Hydriodide) per syringe
Benzylpenicillin 227.2 mg (400 mg Procaine Benzylpenicillin) per syringe

3. BATCH NUMBER

Lot {number}

4. EXPIRY DATE

Exp. {mm/yyyy}

B. PACKAGE LEAFLET

PACKAGE LEAFLET

1. Name of the veterinary medicinal product

Multishield DC Intramammary Suspension for Cattle [BE, DE, FR, HU, IE, IT, NL, PL, PT, RO, UK(NI)]
Multishield Secado [ES]
Cymastin DC [CZ, SK]

2. Composition

Each 4.5 g syringe contains:

Neomycin	70 000 IU	(equivalent to Neomycin Sulphate	100 mg)
Penethamate	77.2 mg	(equivalent to Penethamate Hydriodide	100 mg)
Benzylpenicillin	227.2 mg	(equivalent to Procaine Benzylpenicillin	400 mg)

A smooth off-white oily suspension.

3. Target species

Cattle (cows at drying off).

4. Indications for use

Treatment of subclinical mastitis caused by bovine mastitis microorganisms susceptible to the combination of active substances, penicillin and neomycin, and as part of strategy for the prevention of new infections occurring during the dry period.

5. Contraindications

Do not use in lactating cows.
Do not use in cases of hypersensitivity to the active substances, β-lactam antibiotics, cephalosporin antibiotics, neomycin or other aminoglycoside antibiotics or to any of the excipients.
Do not use in cows with clinical mastitis.

6. Special warnings

Special precautions for safe use in the target species:
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.

The therapeutic efficacy of the veterinary medicinal product is only established against pathogens that aresusceptible to the active substances.
Serious acute mastitis [potentially lethal] due to pathogens like *Pseudomonas aeruginosa*, can occur after drying off despite preventive treatment. Good aseptic practices should be thoroughly respected in

order to reduce that risk; cows should be housed in a hygienic paddock far from the milking parlour and regularly checked several days after drying off.
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 lactam antimicrobials (penicillins and cephalosporins) due to the potential for cross-resistance.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:
Persons administering the veterinary medicinal product should avoid contact with this preparation as occasionally skin allergy may occur.
Penicillins and cephalosporins may cause sensitisation following injection, inhalation, ingestion or skin contact. Sensitivity to penicillins may lead to cross sensitivity to cephalosporins and vice versa. Allergic reactions to these substances may occasionally be serious.
People with known hypersensitivity to β-lactam antibiotics, cephalosporin antibiotics, neomycin or other aminoglycoside antibiotics should avoid contact with the veterinary medicinal product.
If you develop symptoms such as a skin rash following exposure, seek medical advice and show this package leaflet or the label to the physician. Swelling of the face, lips or eyes, or difficulty with breathing are more serious symptoms and require urgent medical attention.

Pregnancy and lactation:
The use is not recommended during lactation, except at the drying off stage.

Interaction with other medicinal products and other forms of interaction:
No data available.

Overdose:
Overdosing may invalidate the stated milk and meat withdrawal times.

7. Adverse events

Very rare (<1 animal / 10,000 animals treated, including isolated reports):
Allergic reaction (allergic skin reaction, anaphylaxis)[1] Hypersensitivity[1]

[1]May occasionally be serious. If adverse reactions occur, the current treatment should be withdrawn and symptomatic treatment should be initiated.

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

Intramammary use.
Dose: 100 mg of neomycin sulphate, 100 mg of Penethamate Hydriodide and 400 mg of Procaine Benzylpenicillin into each quarter.

The contents of one syringe should be infused into each quarter via the teat canal immediately after the final milking of a lactation.

9. Advice on correct administration

Before instillation, the udder should be milked out completely. The teat and its orifice should be thoroughly cleaned and disinfected with a cleaning towel. Care should be taken to avoid contamination of the injector nozzle. Gently insert the content of one syringe into each quarter. Disperse the veterinary medicinal product by gentle massage of the teat and udder. The syringe must only be used once.

10. Withdrawal periods

Meat and offal: 28 days.
Milk: 96 hours post calving in cows with a dry period of more than 50 days.
50 days plus 96 hours after treatment from cows with a dry period of 50 days or less.

11. Special storage precautions

Keep out of the sight and reach of children.

Do not store above 25°C.
Do not refrigerate or freeze.
For single use only.
Do not use this veterinary medicinal product after the expiry date which is stated on the syringe label, and bucket 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

Marketing authorisation number:

Pack sizes:
Bucket containing 24 syringes.
Bucket containing 120 syringes.

Not all pack sizes may be marketed.

15. Date on which the package leaflet was last revised

{MM/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 manufacturer responsible for batch release:
Bimeda Animal Health Ltd.
2, 3 & 4 Airton Close
Tallaght, Dublin 24
Ireland

Local representatives and contact details to report suspected adverse reactions:

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

17. Other information