ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Pirsue 5 mg/ml intramammary solution for cattle

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Active substance:

Pirlimycin (as Pirlimycin hydrochloride) 50 mg/10 ml

For the full list of excipients see Section 6.1

3. PHARMACEUTICAL FORM

Intramammary solution.

4. CLINICAL PARTICULARS

4.1 Target species

Cattle (lactating dairy cows).

4.2 Indications for use, specifying the target species

For the treatment of subclinical mastitis in lactating cows due to Gram-positive cocci susceptible to pirlimycin including staphylococcal organisms such as *Staphylococcus aureus*, both penicillinase-positive and penicillinase-negative, and coagulase-negative staphylococci; streptococcal organisms including *Streptococcus agalactiae*, *Streptococcus dysgalactiae* and *Streptococcus uberis.*

4.3 Contraindications

Resistance against pirlimycin.
Treatment of infections due to Gram-negative bacteria such as *E. coli*.
Do not treat cows with palpable udder changes due to chronic subclinical mastitis.

4.4 Special warnings for each target species

None.

4.5 Special precautions for use

Special precautions for use in animals

Susceptibility testing of the target bacteria should be carried out prior to treatment.

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

Avoid contact with the solution. Wash hands and any exposed skin with soap and water and remove contaminated clothing immediately after use. Flush eyes with water for 15 minutes immediately after exposure. Hold eyelids open to ensure complete contact with water.

4.6 Adverse reactions (frequency and seriousness)

None known.

4.7 Use during pregnancy, lactation or lay

The product is indicated for use in lactating dairy cows and can be used during pregnancy.

4.8 Interaction with other medicinal products and other forms of interaction

Cross-resistance may occur between pirlimycin and other lincosamides or macrolides.

4.9 Amounts to be administered and administration route

Administration: by intramammary infusion only.

Infuse one syringe (50 mg pirlimycin) into each infected quarter.
Treatment consists of eight infusions of one syringe every 24 hours.

Care must be taken not to introduce pathogens into the teat in order to reduce the risk of *E. coli* infections. Ensure adequate cleansing of the teat (and udder - if needed) before infusion. The following instructions should therefore be followed carefully.
Clean hands before handling the cow's udder. Wash the udder if it is dirty.
Where necessary, wash teats thoroughly with warm water containing a suitable dairy cleansing agent and dry them thoroughly. Disinfect teat end using a suitable cleansing agent. The teat end should be cleaned until no more dirt appears on the swab. Use a separate disinfectant towelette for each teat. Do not touch cleaned teat ends before administering the infusion substance.

Insertion: Remove the white end cap by pulling straight up. Gently insert the cannula into the teat canal; carefully infuse the product.
Push plunger with continuous pressure gently and slowly to dispense entire contents into the gland and massage the quarter to distribute the product into the milk cistern. Following infusion, dip all teats with a disinfectant teat dip.

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

No data on overdosing are available.

4.11 Withdrawal period(s)

Meat and offal: 23 days.
Milk: 5 days.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Antibacterial for intramammary use.
ATCvet code: QJ51FF90.

5.1 Pharmacodynamic properties

Pirlimycin hydrochloride is a semi-synthetic lincosamide antibiotic. The lincosamides (clindamycin, lincomycin, and pirlimycin) inhibit protein synthesis in Gram-positive and in anaerobic bacteria as well as in *Mycoplasma* spp. They work by binding to the 50S ribosomal subunit, therefore hindering the aminoacyl-tRNA binding and inhibiting the peptidyltransferase reaction, which interferes with protein synthesis within the bacteria.

Gram-positive isolates with an MIC > 2 µg/ml are to be considered resistant. Enteric bacteria such as *E. coli* are intrinsically resistant to pirlimycin.

Pirlimycin has a basic pKa (8.5). This means it will be more active in an acid environment and tends to concentrate, relative to plasma, in areas with lower pH, such as abscesses. Pirlimycin has been shown to accumulate in polymorphonuclear cells, however, intracellular killing of *Staphylococcus aureus* was not demonstrated.

5.2 Pharmacokinetic particulars

After intramammary infusion, mean parent concentrations in milk were 10.3 µg/ml at 12 hours and 0.77 µg/ml at 24 hours. Similar concentrations were reached at 12 and 24 hours after a second infusion at a 24 hour interval. Of the dose infused, 10-13% is excreted in the urine, and 24-30% via the faeces; the remainder is excreted in the milk.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Anhydrous citric acid
Sodium citrate
Water for injection

6.2 Major incompatibilities

None known.

6.3 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 3 years.

6.4 Special precautions for storage

Do not store above 25 °C. Keep the syringes in the original container.

6.5 Nature and composition of immediate packaging

Polyethylene intramammary syringes (containing 10 ml sterile aqueous solution), packaged in cardboard boxes containing 8 or 24 syringes. Also packaged as 120 syringes in a plastic bucket.

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 medical product or waste materials derived from such veterinary medicinal product should be disposed of in accordance with the local requirements.

7. MARKETING AUTHORISATION HOLDER

Zoetis Belgium SA
Rue Laid Burniat 1
1348 Louvain-la-Neuve
BELGIUM

8. MARKETING AUTHORISATION NUMBER(S)

EU/2/00/027/001-003

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 29/01/2001.
Date of last renewal: 08/02/2006.

10. DATE OF REVISION OF THE TEXT

Detailed information on this veterinary medicinal product is available on the website of the European Medicines Agency (http://www.ema.europa.eu/).

PROHIBITION OF SALE, SUPPLY AND/OR USE

Not applicable.

ANNEX II

A. MANUFACTURERS RESPONSIBLE FOR BATCH RELEASE

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

C. STATEMENT OF THE MRLs

A. MANUFACTURERS RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturers responsible for batch release

Norbrook Laboratories Limited
Station Works, Camlough Road,
Newry, County Down,
BT35 6JP
UNITED KINGDOM

or

Zoetis Belgium SA
Rue Laid Burniat 1
1348 Louvain-la-Neuve
BELGIUM

The printed package leaflet of the medicinal product must state the name and address of the manufacturer responsible for the release of the concerned batch.

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Veterinary medicinal product subject to prescription.

C. STATEMENT OF THE MRLs

The active substance in Pirsue 5 mg/ml intramammary solution for cattle is an allowed substance as described in table 1 of the annex to Commission Regulation (EU) No 37/2010:

Pharmaco-logically active substance	Marker residue	Animal species	MRLs	Target tissues	Other provisions	Therapeutic classification
Pirlimycin	Pirlimycin	Bovine	100 µg/kg 100 µg/kg 1000 µg/kg 400 µg/kg 100 µg/kg	Muscle Fat Liver Kidney Milk	NO ENTRY	Anti-infectious agents/ Antibiotics

The excipients listed in section 6.1 of the SPC are considered as not falling within the scope of Regulation (EC) No 470/2009 when used as in this veterinary medicinal product.

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

8 syringes x10 ml in an outer carton box
24 syringes x10 ml in an outer carton box, including 3 package inserts
120 syringes x10 ml in a plastic bucket, including 15 package inserts

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Pirsue 5 mg/ml intramammary solution for cattle

2. STATEMENT OF ACTIVE SUBSTANCES

Pirlimycin (as Pirlimycin hydrochloride) 50 mg/10 ml.

3. PHARMACEUTICAL FORM

Intramammary solution

4. PACKAGE SIZE

8 intramammary syringes x10 ml
24 intramammary syringes x10 ml
120 intramammary syringes x10 ml

5. TARGET SPECIES

Cattle (lactating dairy cows).

6. INDICATION(S)

For the treatment of subclinical mastitis in lactating cows due to Gram-positive cocci susceptible to pirlimycin including staphylococcal organisms such as *Staphylococcus aureus*, both penicillinase-positive and penicillinase-negative, and coagulase-negative staphylococci; streptococcal organisms including *Streptococcus agalactiae*, *Streptococcus dysgalactiae* and *Streptococcus uberis.*

7. METHOD AND ROUTE(S) OF ADMINISTRATION

Intramammary use.

Read the package leaflet before use.

Infuse one syringe (50 mg pirlimycin) into each infected quarter.
Treatment consists of eight infusions of one syringe every 24 hours.
Care must be taken not to introduce pathogens into the teat in order to reduce the risk of *E. coli* infections. Ensure adequate cleansing of the teat (and udder - if needed) before infusion.

Insertion: Remove the white end cap by pulling straight up. Gently insert the cannula into the teat canal; carefully infuse the product.

Push plunger with continuous pressure gently and slowly to dispense entire contents into the gland and massage the quarter to distribute the product into the milk cistern. Following infusion, dip all teats with a disinfectant teat dip.

8. WITHDRAWAL PERIOD(S)

Withdrawal period(s):
Meat and offal: 23 days.
Milk: 5 days.

9. SPECIAL WARNING(S), IF NECESSARY

Avoid contact with the solution. Wash hands and any exposed skin with soap and water and remove contaminated clothing immediately after use. Flush eyes with water for 15 minutes immediately after exposure. Hold eyelids open to ensure complete contact with water.
Cross-resistance may occur between pirlimycin and other lincosamides or macrolides.

10. EXPIRY DATE

EXP {month/year}

11. SPECIAL STORAGE CONDITIONS

Do not store above 25 °C. Keep the syringes in the outer carton.

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

Zoetis Belgium SA
Rue Laid Burniat 1
1348 Louvain-la-Neuve
BELGIUM

16. MARKETING AUTHORISATION NUMBER(S)

EU/2/00/027/001
EU/2/00/027/002
EU/2/00/027/003

17. MANUFACTURER'S BATCH NUMBER

Lot{number}

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

{label on the syringe}

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Pirsue 5 mg/ml

2. QUANTITY OF THE ACTIVE SUBSTANCE(S)

50 mg Pirlimycin

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

10 ml

4. ROUTE(S) OF ADMINISTRATION

Intramammary use.

5. WITHDRAWAL PERIOD(S)

Withdrawal period(s):
Meat and offal: 23 days.
Milk: 5 days.

6. BATCH NUMBER

Lot{number}

7. EXPIRY DATE

EXP {month/year}

8. THE WORDS “FOR ANIMAL TREATMENT ONLY”

For animal treatment only.

B. PACKAGE LEAFLET

PACKAGE LEAFLET:
Pirsue 5 mg/ml intramammary solution 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:

Zoetis Belgium SA
Rue Laid Burniat 1
1348 Louvain-la-Neuve
BELGIUM

Manufacturer responsible for batch release:

Norbrook Laboratories Limited
Station Works, Camlough Road,
Newry, County Down,
BT35 6JP
UNITED KINGDOM

or

Zoetis Belgium SA
Rue Laid Burniat 1
1348 Louvain-la-Neuve
BELGIUM

2. NAME OF THE VETERINARY MEDICINAL PRODUCT

Pirsue 5 mg/ml intramammary solution for cattle

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

Pirlimycin (as Pirlimycin hydrochloride) 50 mg/10 ml

4. INDICATION(S)

For the treatment of subclinical mastitis in lactating cows due to Gram-positive cocci susceptible to pirlimycin including staphylococcal organisms such as *Staphylococcus aureus*, both penicillinase-positive and penicillinase-negative, and coagulase-negative staphylococci; streptococcal organisms including *Streptococcus agalactiae*, *Streptococcus dysgalactiae*, and *Streptococcus uberis.*

5. CONTRAINDICATIONS

Resistance against pirlimycin.
Treatment of infections due to Gram-negative bacteria such as *E. coli*.
Do not treat cows with palpable udder changes due to chronic subclinical mastitis.

6. ADVERSE REACTIONS

None known.

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

Cattle (lactating dairy cows).

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

Intramammary use.

Infuse one syringe (50 mg pirlimycin) into each infected quarter.
The treatment consists of eight infusions of one syringe every 24 hours.

9. ADVICE ON CORRECT ADMINISTRATION

Care must be taken not to introduce pathogens into the teat in order to reduce the risk of *E. coli* infections. Ensure adequate cleansing of the teat (and udder - if needed) before infusion. The following instructions should therefore be followed carefully.
Clean hands before handling the cow's udder. Wash the udder if it is dirty. Where necessary, wash the teats thoroughly with warm water containing a suitable dairy cleansing agent and dry them thoroughly. Disinfect teat end using a suitable cleansing agent. The teat end should be cleaned until no more dirt appears on the swab. Use a separate disinfectant towelette for each teat. Do not touch cleaned teat ends before administering the infusion substance.

Insertion: Remove the white end cap by pulling straight up. Gently insert the cannula into the teat canal; carefully infuse the product.
Push plunger with continuous pressure gently and slowly to dispense entire contents into the gland and massage the quarter to distribute the product into the milk cistern. Following infusion, dip all teats with a disinfectant teat dip.

Susceptibility testing of the target bacteria should be carried out prior to treatment.

10. WITHDRAWAL PERIOD(S)

Meat and offal: 23 days.
Milk: 5 days.

11. SPECIAL STORAGE PRECAUTIONS

Keep out of the sight and reach of children.
Do not store above 25 °C. Keep the syringes in the original container.
Do not use this veterinary medicinal product after the expiry date which is stated on the label and the container.

12. SPECIAL WARNING(S)

Avoid contact with the solution. Wash hands and any exposed skin with soap and water and remove contaminated clothing immediately after use. Flush eyes with water for 15 minutes immediately after exposure. Hold eyelids open to ensure complete contact with water.
Cross-resistance may occur between pirlimycin and other lincosamides or macrolides.

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.

14. DATE ON WHICH THE PACKAGE LEAFLET WAS LAST APPROVED

Detailed information on this veterinary medicinal product is available on the website of the European Medicines Agency (http://www.ema.europa.eu/).

15. OTHER INFORMATION

Not all pack sizes may be marketed.