PART IB - 1

SUMMARY OF PRODUCT CHARACTERISTICS

CYCLOSOL LA

UK/V/0177/001/R/001

EUROVET ANIMAL HEALTH B.V.
The Netherlands

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Cyclosol LA, 200 mg/ml
Solution for injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each millilitre contains:

Active substance	
Oxytetracycline (as dihydrate)	200.0 mg
(Equivalent to 216 mg Oxytetracycline dihydrate)	
Excipients:	
Sodium formaldehyde sulphoxylate dihydrate (preservative)	5.0 mg
Povidone (complexing agent)	50.0 mg

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Solution for Injection
A clear yellow to reddish-brown aqueous solution."

4. CLINICAL PARTICULARS

4.1 Target species

Cattle and pigs

4.2 Indication for use

Cattle: For the treatment of respiratory infections caused by oxytetracycline susceptible organisms such as *Arcanobacterium (Actinomyces) pyogenes* and *Haemophilus somnus.*
Pigs: For the treatment of respiratory infections caused by oxytetracycline susceptible organisms such as *Pasteurella multocida.*

4.3 Contraindications

Hypersensitivity to tetracyclines. The use of oxytetracycline in animals with an impaired liver and/or kidney function should be avoided.

4.4 Special warnings for each target species

None

4.5 Special precautions for use

Special precautions for use in animals
It is strongly recommended to divide the intramuscular dosages over two or more injection sites

(see posology).
For the 250 mL pack, the use of a multidose syringe is recommended. To refill the syringe, the use of a draw off needle is recommended to avoid excessive broaching of the stopper.
It is recommended to use Cyclosol LA in the early stages of disease and to evaluate the response to treatment within 72 hours.
Resistance against oxytetracycline may vary. Use of the product should be based on susceptibility testing and taking into account official and local antimicrobial policies.
Inappropriate use of the product may increase the prevalence of bacteria resistant to oxytetracycline and may decrease the effectiveness of treatment with tetracyclines due to the potential for cross resistan**ce.**
Because oxytetracycline can retard skeletal development and may cause discoloration and enamel hypoplasia of fetal teeth, the product should be used cautiously in the last half of pregnancy
Special precautions to be taken by the person administering the veterinary medicinal product to animals
Persons with a known hypersensitivity to tetracyclines should not handle this product. The direct or indirect contact of the user via skin or mucosa should be avoided because of the risk of sensitisation. Wash hands after use. In case of contact with eyes or skin, wash immediately with water as irritation may occur.

4.6 Undesirable effects (frequency and seriousness)

Hypersensitivity reactions (cattle), hepatotoxicity and haematologic effects have been reported, but are rare. In case of a serious anaphylactic reaction in cattle the administration of epinephrine, antihistamines and corticosteroids should be considered
Treated animals, particularly those with poor skin pigmentation, may develop photodermatitis when exposed to intensive sunlight. Following intramuscular administration a transient swelling and/or yellow staining (and local necrosis) will occur at the site of the injection. Swelling will be visible for several days after injection. Following injection a small drop in milk production may be observed in lactating animals for up to 3 days.

4.7 Use during pregnancy and lactation

The placenta is readily passed by oxytetracycline and concentration in the foetal blood may reach those of the maternal circulation, although concentration is usually somewhat lower. The product is not recommended in the last 2-3 weeks of pregnancy
Tetracyclines are deposited in deciduous and permanent teeth causing discoloration, enamel hypoplasia, and reduced mineralisation. Tetracyclines can retard fetal skeletal development.
Oxytetracycline is excreted in the milk; concentrations are generally low.

4.8 Interaction with other medicaments and other forms of interactions

Oxytetracycline should not be administered simultaneously with penicillins or cephalosporins.

4.9 Amounts to be administered and administration route

The product is indicated for (deep) intramuscular injection. It is strongly recommended to divide the intramuscular dosages over two or more injection sites - maximum 15 ml per injection site in cattle over 150 kg body weight and 7 ml in pigs and calves. Injection sites should be alternated.

- Pigs
  20 mg oxytetracycline per kg bodyweight, if necessary repeat after 72 hours
- Cattle **not** producing milk for human consumption
  20 mg oxytetracycline per kg bodyweight, if necessary repeat after 72 hours
- Cattle producing milk for human consumption
  20 mg oxytetracycline per kg bodyweight as a single injection only

4.10 Overdose (symptoms, emergency procedures, antidotes)

After intramuscular administration of the antibiotic in lethal dosages, central nervous system symptoms as excitation and convulsions, followed by depression, generalized muscular paralysis and respiratory arrest, preceding death were observed (death usually occurs through respiratory failure). Long-term treatment may result in gastrointestinal disturbances and changes of gut flora (supra-infections). High dosages or chronic administration of oxytetracycline may delay bone growth and healing in young animals. Chronic overdose may lead to drug accumulation and nephrotoxicity. There are no known antidotes to oxytetracycline toxicity.

4.11 Withdrawal periods

Cattle	: meat and offal	: 35 days
	milk	: 8 days
Pigs	: meat and offal	: 28 days

5. PHARMACOLOGICAL PROPERTIES

ATCvet code: QJ01A A06
Pharmacotherapeutic group: Tetracycline antimicrobial

5.1 Pharmacodynamic properties

Oxytetracycline is a bacteriostatic antibiotic. It exerts its action by inhibiting the protein synthesis of the bacterial cell. Inhibition of bacterial protein synthesis results in disturbance of all functions necessary for the life of bacteria, especially cell-division, and the formation of the cell wall are impaired.
Resistance is usually plasmid-mediated. Micro-organisms that have become resistant to one tetracycline frequently exhibit resistance to the others

5.2 Pharmacokinetic properties

Absorption of oxytetracycline following intramuscular injection of CYCLOSOL LA is fast. In pigs the C_{max} is measured within 2 to 3 hours; the C_{max} is approximately 4 µg/ml. In cattle absorption is somewhat slower; the C_{max} is measured after 3 to 5 hours; the C_{max} is approximately 3 to 6 µg/ml.
A plasma concentration of 0.5 µg/ml or more is maintained for 72 hours in cattle and pigs. Concentrations of 0.1 µg/ml are maintained for 5 days. Bioavailability of CYCLOSOL LA is approximately 100%.
High concentrations of oxytetracycline are detectable in kidney, liver, and urine, but oxytetracycline is widely distributed in the body, including lungs and muscle. The placenta is readily passed by oxytetracycline and concentration in the foetal blood may reach that of the maternal circulation.
Oxytetracycline apparently is not metabolized *in vivo* and is eliminated primarily unchanged, via glomerular filtration. It is also excreted into the GI tract via both biliary and nonbiliary routes and may become inactive after chelation with faecal material.

6. PHARMACEUTICALS PARTICULARS

6.1 List of excipients

Magnesium oxide light
Ethanolamine (for pH adjustment)
Povidone K 17 (complexing agent)
Sodium formaldehyde sulphoxylate dihydrate
N-Methyl-2-pyrrolidone
Water for Injections (in bulk)

6.2 Incompatibilities

In the absence of compatibility studies this veterinary medicinal product must not be mixed with other veterinary medicinal products in the same syringe.

6.3 Shelf life

Shelf-life of the veterinary medicinal product as packaged for sale: 30 months
Shelf-life after first opening the container: 14 days

6.4 Special precautions for storage

Do not freeze. Keep container in the outer carton

6.5 Nature and composition of immediated packaging

Amber coloured, glass type II vials containing 50/100/250 ml solution for injection. Not all pack sizes may be marketed.

6.6 Special precautions for the disposal of unused medicinal product or waste materials derived from the use of such products

Any unused product or waste material should be disposed of in accordance with national requirements

7. MARKETING AUTHORIZATION HOLDER

Name : Eurovet Animal Health B.V.
Address : Handelsweg 25, PO Box 179, 5530 AD Bladel
Country : The Netherlands

8. MARKETING AUTHORIZATION NUMBER

UK: 16849/4000
NL: REG NL 10105
EL: 63408/1-12/2003
AT: 8-00577

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Common renewal date: 02 July 2008

10. DATE OF REVISION OF THE TEXT

23 July 2008