SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Cyclofin 300 mg/ml + 20 mg/ml solution for injection for cattle

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains
Active substances:
Oxytetracycline (as oxytetracycline dihydrate) 300 mg
Flunixin (as flunixin meglumine) 20 mg

Excipient:
Sodium Formaldehyde Sulphoxylate 2.0 mg

For a full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Solution for injection.
A orange to reddish-brown solution, practically free from visible particles.

4. CLINICAL PARTICULARS

4.1 Target species

Cattle

4.2 Indications for use, specifying the target species

For the treatment of bovine respiratory disease caused by *Mannheimia (Pasteurella) haemolytica* where an anti-inflammatory and anti-pyretic effect is required.

4.3 Contraindications

Do not use in in animals suffering from cardiac, hepatic, or renal disease, where there is a possibility of gastrointestinal ulceration or bleeding.

Do no use in dehydrated, hypovolaemic or hypotensive animals as there is a potential risk of increased renal toxicity.

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

Do not use the veterinary medicinal product where there are signs of blood dyscrasias or haemostasis alteration.

4.4 Special warnings for each target species

Cross-resistance has been shown between oxytetracycline and other antimicrobials belonging to the tetracyclines class in *Mannheimia (Pasteurella) haemolytica*. When susceptibility testing has shown resistance to other tetracycline antimicrobials the use of oxytetracycline should be carefully considered because its effectiveness may be reduced.

4.5 Special precautions for use

i) Special precautions for use in animals

Use in any animals less than 6 weeks of age or in aged animals may involve additional risk. If such use cannot be avoided, animals may require a reduced dosage and careful clinical management.
It is preferable that prostaglandin inhibiting drugs are not administered to animals undergoing general anaesthesia until fully recovered.

Use of the veterinary medicinal product should be based on identification and susceptibility testing of the target pathogens. If this is not possible, therapy should be based on epidemiological information and knowledge of susceptibility of the target pathogens at farm level, or at local/regional level.
Use of the veterinary medicinal product should be in accordance with official, national, and regional antimicrobial policies.

Flunixin is toxic to avian scavengers. Do not administer to animals susceptible to enter wild fauna food chain. In case of death or sacrifice of treated animals, ensure that they are not made available to wild fauna.

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

This veterinary medicinal product may be harmful after accidental self-injection. In case of accidental self-injection seek medical advice immediately and show the package leaflet or the label to the physician.

This veterinary medicinal product may be irritating to the skin and/or eye. Avoid skin and/or eye contact. Latex or nitrile gloves should be worn during application. In case of accidental contact with skin or eyes, rinse with copious amounts of water. If irritation persists, seek medical advice.

This veterinary medicinal product may cause hypersensitivity reactions due to the presence of oxytetracycline, flunixin, polyethylene glycol or ethanolamine. People with known hypersensitivity to tetracyclines, NSAIDs or one of the excipients should avoid contact with the veterinary medicinal product. If allergic symptoms develop, such as a skin rash, swelling of the face, lips or eyes or difficulty in breathing, you should seek medical attention immediately and show the package leaflet or label to the doctor.

Daily exposure of laboratory animals (rats) to glycerol formal results in teratogenic and foetotoxic effects. Pregnant women and women of child-bearing age should take particular caution to avoid exposure when administering the veterinary medicinal product.

iii) Other precautions

4.6 Adverse reactions (frequency and seriousness)

Cattle:

Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Hypersensitivity reactions[a]
Undetermined frequency (cannot be estimated from the available data)	Injection site reaction[b], Mild increase in body temperature[c], Dental discoloration[d], Bone discoloration[d]

[a] May occur, which can be fatal.
[b] A usually mild reaction at the injection site may be observed following intramuscular administration and may persist for up to 30 days. Studies in cattle at the normal dose rate have shown transient and dose dependent reactions at the injection site.
[c] Any increase is transient and will be unlikely to occur in animals already suffering from pyrexia.
[d] The use of tetracyclines during the period of tooth and bone development may lead to discoloration.

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 national competent authority via the national reporting system or the marketing authorisation holder (or their local representative). See the package leaflet for contact details.

4.7 Use during pregnancy, lactation or lay

The safety of the veterinary medicinal product has not been established during pregnancy and lactation.

Studies in laboratory animals have shown evidence of foetotoxicity after oral (rabbit and rat) and intramuscular (rat) administration of flunixin at maternotoxic doses, and a lengthening of the duration of gestation (rat).

Use is not recommended during pregnancy and lactation.

4.8 Interaction with other medicinal products and other forms of interaction

Concurrent use of potentially nephrotoxic drugs should be avoided (e.g. aminoglycosides). Flunixin may reduce the renal excretion of certain veterinary medicinal products and increase their toxicity, such as for aminoglycosides.

Some NSAIDs may be highly bound to plasma proteins and compete with other highly bound drugs which can lead to toxic effects.

Do not administer other NSAIDs concurrently or within 24 hours of each other. Additional therapy with a NSAID may be administered after 24 hours if required.

Concurrent use of corticosteroids should be avoided.

Flunixin may reduce the effect of some anti-hypertensive medicinal products, such as diuretics and beta blockers, by inhibition of prostaglandin synthesis.

4.9 Amount to be administered and administration route

Indicated for deep intramuscular administration to cattle.
The recommended dosage is 1 ml per 10 kg bodyweight (equivalent to 2 mg/kg flunixin and 30 mg/kg oxytetracycline).
To ensure a correct dosage, bodyweight should be determined as accurately as possible. The veterinary medicinal product is recommended for administration on a single occasion only. Maximum volume per injection site: 15ml.

If concurrent treatment is administered use a separate injection site.

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

Following administration at twice the recommended treatment dose (4 mg/kg flunixin and 60 mg/kg oxytetracycline) the veterinary medicinal product is expected to be well tolerated. At this 2x dose level transient dysentery with or without apathy may occur; symptoms resolving without treatment within 48-72 hours. Studies in cattle at twice the normal dose rate have shown transient and dose dependent reactions at the injection site.
At higher dose levels, above 3x the recommended treatment dose, there is an increased risk of renal toxicity. This may manifest as elevated plasma urea and creatinine levels and pathological changes to the kidneys (cortical tubular necrosis).

Management of overdose should be symptomatic, ensuring adequate hydration is maintained.

4.11 Withdrawal period

Meat and offal: 35 days

Not authorised for use in cattle producing milk for human consumption

5. PHARMACOLOGICALPROPERTIES

Pharmacotherapeutic group: Antibacterials for systemic use - oxytetracycline, combinations

ATC Vet Code: QJ01AA56

5.1 Pharmacodynamic properties

The veterinary medicinal product provides initial anti-inflammatory activity for 24-36 hours and sustained anti-bacterial activity for 5-6 days following a single intramuscular injection.

The tetracyclines are a family of broad-spectrum bacteriostatic antibiotics which inhibit protein synthesis in susceptible microorganisms. Oxytetracycline is active against *Mannheimia (Pasteurella) haemolytica* associated with acute respiratory disease in cattle.

After oxytetracycline diffuses through the outer bacterial cell membrane, an active carrier mediated process transports the drugs through the inner cytoplasmic membrane. Inside the cell, oxytetracycline binds irreversibly to receptors on the 30S sub-unit of the bacterial ribosome where it interferes with the binding of the aminoacyl-transfer RNA to the acceptor site on the messenger RNA ribosome complex. This effectively prevents the addition of amino acids to the elongating peptide chain, inhibiting protein synthesis. Acquired resistance to oxytetracycline has been noted. Such resistance is usually plasmid mediated. Cross-resistance to other tetracyclines occurs. Continuous treatment with low doses of oxytetracycline can also result in increased resistance to other antibiotics.

Flunixin meglumine is a relatively potent non-narcotic, non-steroidal analgesic with anti-inflammatory, anti-endotoxic and anti-pyretic properties.

Flunixin meglumine acts as a reversible inhibitor of cyclo-oxygenase, an important enzyme in the arachidonic acid cascade pathway which is responsible for converting arachidonic acid to cyclic endoperoxides. Consequently, synthesis of eicosanoids, important mediators of the inflammatory process involved in pyrexia, pain perception and tissue inflammation, are inhibited. Through its effects on the arachidonic acid cascade, flunixin also inhibits the production of thromboxane, a potent platelet pro-aggregator and vasoconstrictor which is released during blood clotting. Flunixin exerts its antipyretic effect by inhibiting prostaglandin E2 synthesis in the hypothalamus. By inhibiting the arachidonic acid cascade pathway, flunixin also produces an anti-endotoxic effect by suppressing eicosanoid formation and therefore preventing their involvement in endotoxin associated disease states.

5.2 Pharmacokinetic particulars

Once absorbed, tetracyclines are well distributed throughout the body, with highest concentrations found in liver, spleen, kidney and lung. Tetracyclines are slowly excreted in urine, explaining their long persistence in blood.

Flunixin is characterised by a very high degree of plasma protein binding and hence volumes of distribution are generally low. The unbound fraction is distributed throughout the body fluid, including the CNS. It tends to accumulate in inflamed tissue. Renal excretion contributes extensively to the elimination of flunixin from the body.

5.3 Environmental properties

Flunixin is toxic to avian scavengers although foreseen low exposure leads to low risk.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium Formaldehyde Sulphoxylate
Magnesium Oxide, Light
Glycerol Formal
Polyethylene Glycol 200
Ethanolamine
Water for Injections

6.2 Major Incompatibilities

In the absence of compatibility studies, this veterinary medicinal product must not be mixed with any other veterinary medicinal product.

6.3 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 2 years
Shelf life after first opening the immediate packaging: 28 days.

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.
Following withdrawal of the first dose, the product should be used within 28 days. Discard unused material.

6.5 Nature and composition of immediate packaging

Supplied in 100 ml type II, clear glass vials, with a stopper, 20 mm, bromobutyl, and aluminium cap, 20 mm.
One glass vial is packaged in a cardboard box.

6.6 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.
Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal products should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

Dechra Regulatory B.V.
Handelsweg 25
5531 AE Bladel
The Netherlands

8. MARKETING AUTHORISATION NUMBER

Vm 50406/5046

9. DATE OF FIRST AUTHORISATION

05 September 2023

10. DATE OF REVISION OF THE TEXT

July 2025

11. CLASSIFICATION OF VETERINARY MEDICINAL PRODUCTS

Veterinary medicinal product subject to prescription.

Gavin Hall

Approved: 01 July 2025