Summary of Product Characteristics

1 NAME OF THE VETERINARY MEDICINAL PRODUCT

Hexasol LA Solution for Injection

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:
Active substance:
Oxytetracycline
(as oxytetracycline dihydrate) 300 mg
Flunixin
(as flunixin meglumine) 20 mg
Excipients:
Sodium Formaldehyde Sulphoxylate 4.0 mg
For a full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Solution for injection.
A clear dark amber solution.

4 CLINICAL PARTICULARS

4.1 Target Species

Cattle.

4.2 Indications for use, specifying the target species

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

4.3 Contraindications

Use is contraindicated in animals suffering from cardiac, hepatic or renal disease, where there is a possibility of gastrointestinal ulceration or bleeding or where there is hypersensitivity to one of the ingredients of the product.

Avoid use in dehydrated, hypovolaemic or hypotensive animals as there is a potential risk of increased renal toxicity.

Do not use in cases of known resistance to tetracyclines.

Refer to section 4.11

4.4 Special warnings for each target species

None.

4.5 Special precautions for use

Special Precautions for use in animals:
Use in any animals less than 6 weeks of age or in aged animals may involve additional risk due to the anti-prostaglandin effects of flunixin on renal function. If such use cannot be avoided, animals may require careful clinical management.

Use of the 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.

Special Precautions to be taken by the person administering the veterinary medicinal product to animals:
In the case of accidental self injection, if an allergic reaction occurs, medical advice should be sought. In case of accidental contact with skin or eyes, rinse with copious amounts of water. If persistent irritation occurs, seek medical advice.

People with known hypersensitivity to tetracycline should avoid contact with this product.

4.6 Adverse reactions (frequency and seriousness)

In very rare cases hypersensitivity reactions may occur, which can be fatal.

A transient, usually mild reaction at the injection site may be observed following intramuscular administration and may persist for up to 30 days.

In certain cases a mild increase in body temperature may be noted following treatment. Any increase is transient and will be unlikely to occur in animals already suffering from pyrexia. Studies in cattle at the normal dose rate and twice the normal dose rate have shown transient and dose dependent reactions at the injection site leading to increased associated enzymatic activity.

The use of tetracyclines during the period of tooth and bone development may lead to discolouration.

The frequency of adverse reactions is defined using the following convention:

- very common (more than 1 in 10 animals displaying adverse reactions during the course of one treatment)
- common (more than 1 but less than 10 animals in 100 animals)
- uncommon (more than 1 but less than 10 animals in 1,000 animals)
- rare (more than 1 but less than 10 animals in 10,000 animals)
- very rare (less than 1 animal in 10,000 animals, including isolated reports).

4.7 Use during pregnancy, lactation or lay

Flunixin and oxytetracycline showed no evidence of embryotoxicity or teratogenicity in laboratory animals. The safety of the product was not assessed in pregnant and lactating animals. The use of the product is not recommended in pregnant and lactating animals.

4.8 Interaction with other medicinal products and other forms of interactions

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.

Concurrent use of potentially nephrotoxic drugs should be avoided.

Concurrent use of corticosteroids should be avoided.

4.9 Amounts to be administered and administration route

The product is indicated for deep intramuscular administration to cattle. The recommended dosage is 2 mg/kg flunixin and 30 mg/kg oxytetracycline (equivalent to 1 ml per 10 kg bodyweight).

This product is recommended for single administration only.

Maximum volume per injection site: 15 ml.

To ensure a correct dosage, bodyweight should be determined as accurately as possible.

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

The product administered to cattle at 4 mg/kg flunixin and 60 mg/kg oxytetracycline (twice the recommended dose) has been shown to be well tolerated. At twice the recommended dose, transient dysentery with or without apathy can occur. These symptoms resolve spontaneously without treatment within 48/72 hours. A transient

usually mild reaction at the injection site may be observed following intramuscular administration and may persist beyond the withdrawal period.

4.11 Withdrawal period(s)

Meat and offal: 28 days.
Not for use in cattle producing milk for human consumption.

5 PHARMACOLOGICAL or IMMUNOLOGICAL PROPERTIES

Pharmacotherapeutic group: Antibacterial, anti-inflammatory.
ATC vet code: QJ01A A56

5.1 Pharmacodynamic properties

Oxytetracycline and flunixin in the combined formulation provide anti-bacterial and anti-inflammatory activities respectively following a single administration.

Oxytetracycline is the 5-OH derivative of tetracycline. The tetracyclines are a family of broad-spectrum bacteriostatic antibiotics which inhibit protein synthesis in susceptible micro-organisms. The tetracyclines, including oxytetracycline are active against many gram-positive and gram-negative bacteria.

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 if 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.

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 central pyresis, pain perception and tissue inflammation, is 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.

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.

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.

After intramuscular administration of the recommended dose of the product to cattle (2 mg flunixin and 30 mg oxytetracycline per kg bodyweight) the following parameters were observed:

Oxytetracycline: C_{max} 11.11 µg/ml; AUC 376.5 µg/ml/hr; T_{max} 5.1 hrs, T½ elimination 36.54 hrs.
Flunixin: C_{max} 2.4 µg/ml; AUC 11.22 µg/ml/hr; T_{max} 1.0 hrs, T½ elimination 4.51 hrs.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Light Magnesium Oxide
Glycerol Formal
Polyethylene glycol
Sodium Formaldehyde Sulphoxylate
Monoethanolamine
Water for Injections

6.2 Major incompatibilities

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

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

Store below 25°C, protect from light.

6.5 Nature and composition of immediate packaging

Supplied in 50 ml, 100 ml, 250 ml and 500 ml Type I/II, amber glass vials, sealed with bromobutyl rubber bungs and aluminium caps.

Not all pack sizes may be marketed.

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

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

7 MARKETING AUTHORISATION HOLDER

Norbrook Laboratories (Ireland) Limited
Rossmore Industrial Estate
Monaghan
Ireland

8 MARKETING AUTHORISATION NUMBER(S)

VPA22664/049/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 05 February 1999
Date of last renewal: 28 July 2009

10 DATE OF REVISION OF THE TEXT

December 2018