NIMTOL INJECTION

(Oxytetracycline, Flunixin)

SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE VETERINARY MEDICINAL PRODUCT

Nimtol Injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml Contains:
Oxytetracycline (as Hydrochloride)……..300mg
Flunixin (as Meglumine)…….……..…..20mg

3. PHARMACEUTICAL FORM

Solution for Injection

4. CLINICAL INFORMATION

4.1. Target species

Cattle, Sheep, Goat, Buffalo, Camel & Horse.

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 antipyretic 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. Do not 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

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. 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.

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

4.6. Adverse reactions (frequency and seriousness)

Very rare <1 animal / 10,000 animals treated, including isolated reports):	Hypersensitivity reaction [1] Injection site reaction [2] , Elevated temperature [3] Discoloured teeth[4]

[1] Can be fatal.
[2] Following intramuscular administration and may persist for up to 30 days (transient, usually mild). 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.
[3] Any increase is transient and will be unlikely to occur in animals already suffering from pyrexia.
[4]The use of tetracyclines during the period of tooth and bone development may lead to discolouration.

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 the national competent authority via the national reporting system. See package leaflet for respective contact details

4.7. Use during pregnancy and lactation or lay

Pregnancy and lactation:

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 is not recommended in pregnant and lactating animals.

4.8. Interaction with other veterinary medicinal products and other forms of interaction

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. Dosage 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:

Cattle, Buffalo & Camel:
Meat and offal: 28 days
Sheep & Goat: 21 days
Not authorised for use in lactating mares producing milk for human consumption

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Antibiotics with NSAID
ATCvet code: **QJ01AA56**

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 5-0H 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 ifthe 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 proaggregator 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 information

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. Ittends 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: Cmax:11.11 µg /ml; AUC 376.5 µg/ml/hour;
Tmax: 5.1 hour, T½ elimination 36.54 hour.
Flunixin: Cmax: 2.4 µg/ml; AUC 11.22 µg/ml/h; ; Tmax 1.0 hour, T½: elimination 4.51 hour.

Environmental Properties

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

6. PHARMACEUTICAL INFORMATION

6.1 Incompatibilities

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

6.2. Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 2 years.
Shelf life after first opening the container: use immediately in 28 days do not store.

6.3. Special precautions for storage

Store below 25^0C.
Protect from light.
Do not refrigerate or freeze
Keep out of reach of children.

6.4. Nature and composition of primary conditioning

This product will be supplied in 50 ml**,** amber glass vials, sealed with bromobutyl rubber stopper and aluminium flip off seal.

SPECIAL PRECAUTIONS FOR THE DISPOSAL OF WASTE MATERIALS
UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS

Any unused veterinary medicinal products or waste materials derived from such medicinal products should be disposed of in accordance with local requirements and placed in appropriate collection and disposal systems for unused or expired medicinal products.

7. MARKETING AUTHORISATION HOLDER

Nawan Laboratories (Pvt.) Ltd.
Plots No. 136-138, Sector-15,
Korangi Industrial Area, Karachi-74900, Pakistan.

8. MARKETING AUTHORISATION NUMBER

Reg. No.: 081321

9. DATE OF FIRST AUTHORISATION

Date of Reg.: 15-08-2016

10. DATE OF REVISION OF THE TEXT

20-01-2025

MANUFACTURED BY:

NAWAN LABORATORIES (PVT) LTD.

136, Sector 15, Korangi Industrial Area, Karachi-74900, Pakistan.