SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

NIGLUMINE 50mg/ml solution for injection for cattle, horses and pigs

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains

Active substance :

Flunixin (meglumine) 50.0 mg (Equivalent to 82.9 mg flunixin meglumine)

Excipients: Phenol. ..... 5 mg

For the full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Solution for injection

Colourless to slightly yellowish clear solution

4. CLINICAL PARTICULARS

4.1 Target species

Cattle, horses and pigs.

4.2 Indications for use, specifying the target species

Cattle: For use in acute respiratory infection with appropriate antibiotic therapy to reduce clinical signs.

Horses: For the alleviation of inflammation and pain associated with musculoskeletal disorders, especially in acute to sub-acute stages and to relieve visceral pain associated with colic.

Pigs: For alleviation of Mastitis-Metritis-Agalactia Syndrome (MMA) with appropriate antibiotic treatment to reduce clinical signs**.**

4.3 Contraindications

Do not use in animals suffering from chronic musculoskeletal disorders.
Do not use in animals suffering from hepatic, renal, or cardiac disease.
Do not use in animals with lesions of the gastrointestinal tract (for example gastro-intestinal ulceration or bleeding).
Do not use when there is evidence of blood dyscrasia.
Do not use in animals with hypersensitivity to flunixin meglumine, to other NSAIDs than flunixin and to any other ingredient of the product.
Do not use in dehydrated, hypovolaemic or hypotensive animals.
Do not use in animals suffering from colic caused by ileus and which is associated with dehydration.

See sections 4.7, 4.8 and 4.11.

4.4 Special warnings for each target species

The cause of the underlying inflammatory condition or colic should be determined and treated with appropriate concomitant therapy.

4.5 Special precautions for use

Special precautions for use in animals

Use in any animal of less than 6 weeks of age (cattle and horses) 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 NSAIDs, which inhibit prostaglandin synthesis, are not administered to animals undergoing general anaesthesia until fully recovered.
In rare cases life threatening shock reactions after intravenous application can occurred due to the amount of propylenglycol. Therefore, Niglumine should be injected slowly and should be used at body temperature. At the first signs of incompatibility administration should be stopped and if necessary, a shock treatment should be initiated.
Locomotors activity during treatment with Niglumine should be restricted.
Sufficient water supply should be ensured.

Intraarterial injection to horses and cows should be avoided. Horses accidentally injected by intraarterial route may show adverse reactions. Signs can be ataxia, incoordination, hyperventilation, hysteria, and muscular weakness. All are transitory signs and disappear within a few minutes without antidote medication.

Pony breed may be more susceptible to side effects from NSAIDs. Use with caution.
In cattle, the cause of acute inflammatory condition should be determined, and treated with an appropriate concomitant therapy.
As flunixin may reduce clinical signs in cattle due to its anti-inflammatory activity, resistance towards the causal (i.e. antibiotic) therapy may be masked.
In horses the cause of colic must be determined and treated with concomitant therapy.
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 veterinary medicinal product to animals
People with known hypersensitivity to flunixin should avoid contact with the veterinary medicinal product. Reactions may be serious.
To avoid possible sensitisations reactions, avoid contact with skin. Personal protective equipment consisting of gloves should be worn when handling the veterinary medicinal product.
In case of spillage onto skin wash immediately with water.

Avoid introduction of contamination when handling the product.
Avoid self injection. In case of accidental self-injection it may cause acute pain and inflammation. Wash and disinfect the wound immediately. Seek medical advice and show the leaflet.

4.6 Adverse reactions (frequency and seriousness)

Adverse effects include the possibility of bleeding, gastrointestinal lesions (ulcer in gastric mucosa), vomits, papillary necrosis of kidney, ataxia and hyperventilation.
In pigs, the administration of the product may cause local irritation at the injection site. Discoloration at the injections site after withdrawal periods may occur and may not resolve in all animals by D28 post-injection.
Anaphylactic reactions were observed sometimes with lethal consequences.
Like other NSAIDs flunixin can induce kidney lesions in hypovolaemic and hypotensive animals during surgery.
Like with other NSAIDs, there is a risk of rare renal or idiosyncratic hepatic adverse effects.
If adverse reactions occur, the use of the product should be stopped and the advice of a veterinarian should be sought.

See section 4.8.

4.7 Use during pregnancy, lactation or lay

Studies in laboratory species have shown evidence of foetotoxic effects.
Safety of the product in pregnant sows and mares during pregnancy and lactation has not been tested. Consequently the product is contra-indicated at these stages in mares and sows.
The product can be used in cows during pregnancy.

4.8 Interaction with other medicinal products and other forms of interaction

Concurrent use or use within 24 hours with other non-steroidal anti-inflammatory drugs (NSAIDs) should be avoided for an increase in toxicity, specially gastrointestinal, even acetylsalicylic acid at low doses.

Concurrent administration with corticoids may increase the toxicity of both drugs, increasing the risk of gastrointestinal ulceration. Therefore, it should be avoided.

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

Flunixin may reduce the effect of some antihypertensive drugs for inhibiting prostaglandin synthesis, such as diuretics (ACE inhibitors), ARA (Angiotensin Receptor Antagonist) and ß-blockers.

Concurrent administration of potentially nephrotoxic drugs should be avoided, especially amynoglicosides
Flunixin may reduce renal elimination of some drugs increasing their toxicity, as occurs with aminoglycosides.

4.9 Amounts to be administered and administration route
Cattle and Horses: Intravenous
Pigs: Intramuscular

Cattle: 2.2 mg of Flunixin/kg body weight and day (Equivalent to 2 ml of NIGLUMINE/45 kg body weight) injected intravenously and repeated as necessary at 24 hour intervals for up to 3 consecutive days.

Horses:
1.1 mg flunixin /kg body weight and day (equivalent to 1 ml of Niglumine 45 kg body weight) injected intravenously at 24 hour intervals for up to 5 consecutive days according to response.

Pigs:
2.2 mg of flunixin /kg body weight and day (equivalent to 2 ml of Niglumine/45 kg body weight) injected intramuscular at 12 hour interval for up to two times according to response with a concurrent antimicrobial therapy. In order to reduce local irritation at the injection site, injection volume should be limited to 5ml/ site.

4.10 Overdose (symptoms, emergency procedures, antidotes), if necessary
Flunixin meglumine is a non-steroidal anti-inflammatory drug. Overdose is associated with gastrointestinal toxicity. Symptoms of ataxia and incoordination may also appear.
In horses, from 3 times (3.3 mg/kg body weight) the recommended dose intravenously administered, a transient increase of the blood pressure can occur.

No adverse reactions have been reported in cattle after intravenous administration of 3 times (6.6 mg/Kg body weight) the recommended dose.

4.11 Withdrawal period(s)

Cattle: Meat and offal: 4 days
Milk: 24 hours
Horses: Meat and offal: 28 days
Pigs: Meat and offal: 28 days

Not permitted for use in lactating horses producing milk for human consumption.

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: non-steroidal anti-inflammatory drug (NSAID) with analgesic and anti-pyretic properties.
ATCvet code: QM01AG90

5.1 Pharmacodynamic properties

Flunixin meglumine acts as a reversible non-selective inhibitor of cyclo-oxygenase (COX), an enzyme that converts arachidonic acid to unstable cyclic endoperoxides, which are transformed into prostaglandins, prostacyclines and thromboxanes. Some of these prostanoids, like prostaglandins, are involved in physiopathological mechanisms of inflammation, pain and fever, therefore their inhibition would be responsible of their therapeutic effects. As prostaglandins are involved in other physiological processes, COX inhibition would be also responsible of several adverse reactions like gastrointestinal or renal lesions.

Prostaglandins take part in the complex processes involved in the development of endotoxic shock.

5.2 Pharmacokinetic particulars

Cattle

Flunixin meglumine administered by intravenous route to cattle, as a single dose of 2.2 mg/Kg, leads to an elimination half-life of 4 hours.

Horses

Flunixin meglumine administered by intravenous route to horses, as a single dose of 1.1 mg/Kg, leads to an elimination half-life of 2 hours.

Pigs

The administration of an IM injection of C14 labelled Flunixin Meglumine to pigs (1.1 mg/kg) gave a recuperation of 57% of radioactivity in urine and 21% in faeces in the 96-hours after treatment. Maximum plasmatic levels were reached at 5 to 30 minutes after treatment.

In the study of plasmatic levels of Flunixin (Meglumine) 5% in sows after the intramuscular administration of 2.2 mg of Flunixin (Meglumine) / kg body weight, a Cmax of 3360.33 ng/ml, a half-life of 4.7 h and Tmax of 0.72 were obtained.

Environmental properties

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

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Phenol

Sodium formaldehyde sulfoxylate

Disodium edetate

Sodium hydroxide

Propylene glycol (E1520)

Hydrochloric acid

Water for injection

6.2 Major incompatibilities

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

6.3 Shelflife

Shelf-life of the veterinary medicinal product as packaged for sale: 5 years

Shelf-life after first opening of immediate packaging: 28 days

6.4 Special precautions for storage

This veterinary medicinal product does not require any special storage conditions.

6.5 Nature and composition of immediate packaging:

Clear glass vials, quality type II (European Pharmacopoeia), of 50 and 100 ml, provided with grey rubber stoppers of bromobutyl, formulation PH 4001/45, and metallic aluminium capsules with blue FLIP-OFF opening ring.

Clear glass vials, quality type II (European Pharmacopoeia), of 250 ml, provided with pink rubber stoppers of bromobutyl and silicate, and gold coloured seal capsule.

Package size:

Cardboard box with 1 vial of 50 ml

Cardboard box with 1 vial of 100 ml

Cardboard box with 1 vial of 250 ml

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 materials derived from such veterinary medicinal products should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

LABORATORIOS CALIER, S.A.

C/ Barcelonès, 26 (Pla del Ramassà)

LES FRANQUESES DEL VALLÈS, (Barcelona)

SPAIN

8. MARKETING AUTHORISATION NUMBER (S)

Spain: 1727-ESP

Austria: Z.Nr 8-00754

Belgium: 8505 IE 4 F 12

Bulgaria: 963 / 20.06.2008

Germany: 401141.00.00

Hungary:

Vial 50 ml 2436/1/08 MgSzH ÁTI

Vial 100 ml 2436/2/08 MgSzH ÁTI

Vial 250 ml 2436/3/08 MgSzH ÁTI

Italy:

Vial 50 ml AIC n 104047/016

Vial 100 ml AIC n 104047/028

Vial 250 ml AIC n 104047/030

Portugal: 081/01/RFVPT

Romania: 080097/6.11.2008.

The Netherlands: NL 101828

9. DATE OF THE FIRST AUTHORISATION /RENEWAL OF THE AUTHORISATION

Date of first authorisation: 27 February 2007

10. DATE OF REVISION OF THE TEXT

January 2019

PROHIBITION OF SALE, SUPPLY AND/OR USE

Under veterinary prescription

Administration only by a veterinary surgeon in case of intravenous administration.