# PART I.B.2. PROPOSAL FOR PACKAGING, LABELLING AND PACKAGE INSERT

# PACKAGE LEAFLET

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

### 1. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER AND OF THE MANUFACTURING AUTHORISATION HOLDER RESPONSIBLE FOR BATCH RELEASE, IF DIFFERENT

Marketing authorisation holder and manufacturer responsible for batch release
Laboratorios Calier, S.A.
Barcelonès, 26 (Pla del Ramassà)
Les Franqueses del Vallès (Barcelona)
SPAIN

### 2. NAME OF THE VETERINARY MEDICINAL PRODUCT

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

### 3. STATEMENT OF THE ACTIVE SUBSTANCE(S) AND OTHER INGREDIENT(S)

Each ml contains:
**Active substance:**
Flunixin (meglumine)..... 50.0 mg
(Equivalent to 82.9 mg flunixin meglumine)
**Excipients:**
Phenol..... 5 mg
Other excipients .....q.s.

Colourless to slightly yellowish clear solution

### 4. INDICATION(S)

**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.

### 5. 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.

## 6. ADVERSE REACTIONS

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.
If you notice any serious effects or other effects not mentioned in this leaflet, please inform your veterinary surgeon.
Alternatively, you can report via your national reporting system {national system details.

## 7. TARGET SPECIES

Cattle, horses and pigs

## 8. DOSAGE FOR EACH SPECIES, ROUTE(S) AND METHOD OF ADMINISTRATION

Routes of administration:
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 of 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.

## 9. ADVICE ON CORRECT ADMINISTRATION

None

## 10. 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.

## 11. SPECIAL STORAGE PRECAUTIONS

Keep out of the sight and reach of children
This veterinary medicinal product does not require any special storage conditions
Do not use this veterinary medicinal product after the expiry date which is stated on the label and carton after EXP
Shelf-life after first opening the container: 28 days

## 12. SPECIAL WARNING(S)

Special warnings for each target species:
The cause of the underlying inflammatory condition or colic should be determined and treated with appropriate concomitant therapy.

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.

Pregnancy and lactation:
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.

Interaction with other medicinal products and other forms of interaction:
Concurrent use or use within 24 hours with other nonsteroidal 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.
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

Overdose (symptoms, emergency procedures, antidotes): 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.
After intramuscular administration of 5 times the recommended dose, irritation signs could occur (sudation, cough, movement of head).
No adverse reactions have been reported in cattle after intravenous administration of 3 times (6.6 mg/kg body weight) the recommended dose.

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

## 13. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCT OR WASTE MATERIALS, IF ANY

Medicines should not be disposed of via wastewater or household waste.
Ask your veterinary surgeon how to dispose of medicines no longer required. These measures should help to protect the environment.

## 14. DATE ON WHICH THE PACKAGE LEAFLET WAS LAST APPROVED

## 15. OTHER INFORMATION

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 size may be marketed.
To be supplied only on veterinary prescription.
Administration only by a veterinary surgeon in case of intravenous administration.

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