[Version 9.1,11/2024]

ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Norflunix 50 mg/ml solution for injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

Active substances:
Flunixin 50.0 mg
(equivalent to flunixin meglumine 83.0 mg)

Excipients:

Qualitative composition of excipients and other constituents	**Quantitative composition if that information is essential for proper administration of the veterinary medicinal product**
Phenol	5.0 mg
Sodium formaldehyde sulfoxylate	2.5 mg
Disodium edetate	
Propylene glycol	
Sodium hydroxide	
Hydrochloric acid	
Water for injections	

A clear colourless solution.

3. CLINICAL INFORMATION

3.1 Target species

Pigs.

3.2 Indications for use for each target species

Adjunctive therapy in the treatment of swine respiratory disease.
Adjunctive treatment of postpartum dysgalactia (Mastitis-Metritis-Agalactia) syndrome in sows.
Alleviation of acute inflammation and pain associated with musculoskeletal disorders.
Reduction of post-operative pain following castration and tail docking in sucking piglets.

3.3 Contraindications

Do not use in animals suffering from cardiac, hepatic, or renal disease or where there is the possibility of gastro-intestinal ulceration or bleeding.
Do not use in cases of hypersensitivity to the active substance or to any of the excipients.
Do not use if haematopoiesis or haemostasis is impaired.
Do not use in case of colic caused by ileus and associated with dehydration.

3.4 Special warnings

None.

3.5 Special precautions for use

Special precautions for safe use in the target species:

Inject slowly as life threating symptoms of shock can occur due to the content of propylene glycol.
NSAIDs are known to have the potential to delay parturition through a tocolytic effect by inhibiting prostaglandins that are important in signalling the initiation of parturition. Use of the veterinary medicinal product in the immediate postpartum period may interfere with uterine involution in the expulsion of the fetal membranes resulting in retention of the placenta.
The veterinary medicinal product should have a temperature close to body temperature. Stop injection immediately after first symptoms of shock and start shock treatment if necessary.
Use of NSAID's in hypovolemic animals or animals with shock should be subject to a benefit-risk evaluation performed by the responsible veterinarian due to the risk of renal toxicity.
Use in very young as well as in old animals may involve additional risks. If such treatment cannot be avoided, careful clinical observation is indicated. The underlying cause of pain or inflammation should be determined and, when appropriate, antibiotic or re-hydration therapy should be given concurrently.
NSAIDs can cause phagocytosis inhibition and, therefore, in the treatment of inflammatory states associated with bacterial infections, appropriate concurrent antimicrobial therapy should be established.

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

This veterinary medicinal product may cause hypersensitivity (allergy) reactions. People with known hypersensitivity to non-steroidal anti-inflammatory drugs such as flunixin and/or propylene glycol should avoid contact with the veterinary medicinal product. In case of hypersensitivity reactions seek medical advice and show the package leaflet or the label to the physician.

This veterinary medicinal product may cause skin and eye irritation. Avoid contact with skin or eyes. Wash hands after use In case of accidental skin contact, wash affected area immediately with plenty of water.

In case of accidental eye contact, rinse eyes immediately with plenty of water. If skin and /or eye irritation persists, seek medical advice immediately and show the package leaflet or the label to the physician.
Accidental self-injection may cause pain and inflammation. In case of accidental self-injection, seek medical advice immediately and show the package leaflet or the label to the physician.
Laboratory studies in rats with flunixin have shown evidence of foetotoxic effects. Pregnant women should use the veterinary medicinal product with serious caution to avoid accidental self-injection.

Special precautions for the protection of the environment:

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.

3.6 Adverse events

Pigs

Uncommon (1 to 10 animals / 1,000 animals treated):	Injection site reaction (such as injection site skin discolouration, pain, irritation and swelling) [1].
Rare (1 to 10 animals / 10,000 animals treated):	Liver disorder; Renal disorder (Nephropathy, Papillary necrosis)[2].
Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Anaphylaxis (e.g. Anaphylactic shock, Hyperventilation, Convulsion, Collapse, Death)[3]; Ataxia[3]; Blood and lymphatic system disorder[4], Haemorrhage; Digestive tract disorder (gastrointestinal irritation, gastrointestinal ulceration, digestive tract haemorrhage, vomiting, nausea, blood in faeces, diarrhoea)[2]; Delay of parturition[5], stillbirth[5], retained placenta[6]; Appetite loss.

[1] Resolves spontaneously within 14 days.
[2] Occurs primarily in hypovolaemic and hypotensive animals.
[3] After intravenous administration. Stop the infusion immediately at the first sign of symptoms, and begin anti-shock treatment if needed.[4] Blood count abnormalities.
[5] Due to a tocolytic effect induced by inhibition of the synthesis of prostaglandins, responsible for the initiation of parturition.
[6] If the product is used during the postpartum period.

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 its local representative or the national competent authority via the national reporting system. See the package leaflet for respective contact details.

3.7 Use during pregnancy, lactation or lay

Pregnancy:
The safety of the veterinary medicinal product has been established in pregnant sows. Do not use the veterinary medicinal product within 48 hours before expected parturition in sows.
Laboratory studies in rats have revealed fetotoxicity of flunixin after intramuscular administration at maternotoxic doses as well as an extension of the gestation period.
The veterinary medicinal product should be administered within the first 36 hours postpartum only following a benefit/risk assessment performed by the responsible veterinarian and treated animals should be monitored for retained placenta.

Fertility:
The safety of the veterinary medicinal product has not been established in boars intended for breeding. Do not use in breeding boars.

3.8 Interaction with other medicinal products and other forms of interaction

Do not administer other non-steroidal anti-inflammatory drugs (NSAIDs) concurrently or within 24 hours of each other. Do not administer corticosteroids concurrently. Concurrent use of other NSAIDs or corticosteroids may increase the risk of gastro-intestinal ulceration. Some NSAIDs may be highly bound to plasma proteins and compete with other highly bound drugs which can lead to toxic effects. Flunixin may decrease the effect of some antihypertensive drugs by inhibiting prostaglandin synthesis, such as diuretics, ACE inhibitors (angiotensin converting enzyme inhibitors) and β-blockers. Concomitant administration of potentially nephrotoxic drugs (e.g., aminoglycoside antibiotics) should be avoided.

3.9 Administration routes and dosage

Intramuscular use.
Adjunctive therapy in the treatment of swine respiratory disease, adjunctive treatment of postpartum dysgalactia (Mastitis-Metritis-Agalactia) syndrome in sows, alleviation of acute inflammation and pain associated with musculoskeletal disorders
2.2 mg flunixin/kg bodyweight (2 ml per 45 kg) once daily for up to 3 consecutive days. The injection volume should be limited to a maximum of 4 ml per injection site.

Reduction of post-operative pain following castration and tail docking in sucking piglets
A single administration of 2.2 mg of flunixin per kg bodyweight (0.2 mL per 4.5 kg), 15-30 minutes before the procedure.
Particular care should be taken with regard to the accuracy of dosing including the use of an appropriate dosing device and careful estimation of body weight.

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

3.10 Symptoms of overdose (and where applicable, emergency procedures and antidotes)

Overdose is associated with gastrointestinal toxicity. Ataxia and incoordination may also occur.
In case of overdose, symptomatic treatment should be administered.

Pigs treated with 11 or 22 mg flunixin/kg bodyweight (i.e., 5X or 10X the recommended clinical dose) had increased spleen weight. Discoloration at the injection sites that resolved over the time was observed with higher incidence or severity in pigs treated with higher doses.
In pigs, at 2 mg/kg twice daily, a painful reaction at the injection site and an increase in leukocyte counts were observed.

3.11 Special restrictions for use and special conditions for use, including restrictions on the use of antimicrobial and antiparasitic veterinary medicinal products in order to limit the risk of development of resistance

Not applicable.

3.12 Withdrawal periods

Meat and offal: 24 days.

4. PHARMACOLOGICAL INFORMATION

4.1 ATCvet code :
QM01AG90

4.2 Pharmacodynamics
Flunixin meglumine is a non-steroidal anti-inflammatory drug with analgesic and anti-pyretic activity.

Flunixin meglumine acts as a reversible non-selective inhibitor of cyclo-oxygenase (both COX 1 and COX 2 forms), 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 E_2 synthesis in the hypothalamus. Although flunixin does not have a direct effect on endotoxins once they have been produced, it reduces the production of prostaglandins and therefore reduces the majority of its effects. Prostaglandins belong to the complex processes involved in endotoxic shock development.

Due to the involvement of prostaglandins in other physiological processes, COX inhibition would also be responsible for different adverse reactions, such as gastrointestinal or renal damage.

4.3 Pharmacokinetics

In pigs, after intramuscular administration of 2.2 mg of flunixin meglumine/kg, a maximum plasma concentration of around 3 µg/ml was detected approximately 20 minutes after injection. The bioavailability, expressed as a fraction of the dose absorbed, was found to be 93%. The volume of distribution was 2 l/kg, while the elimination half-life was 3.6 hours. Excretion (mostly as unchanged drug) occurred primarily in the urine, but was also detected in the faeces.

Environmental properties

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

5. PHARMACEUTICAL PARTICULARS

5.1 Major incompatibilities

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

5.2 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

5.3 Special precautions for storage

Store below 25ºC.
Keep the vial in the outer carton in order to protect from light.

5.4 Nature and composition of immediate packaging

Type I clear colourless glass vials, with bromobutyl bungs and aluminium caps.

Package sizes:
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.

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

Medicines should not be disposed of via wastewater or household waste.

Use take-back schemes for the disposal of any unused veterinary medicinal product or waste materials derived thereof in accordance with local requirements and with any national collection systems applicable to the veterinary medicinal product concerned.

6. NAME OF THE MARKETING AUTHORISATION HOLDER

Norbrook Laboratories (Ireland) Limited

7. MARKETING AUTHORISATION NUMBER(S)

8. DATE OF FIRST AUTHORISATION

Date of first authorisation: 15 de abril 2003

9. DATE OF THE LAST REVISION OF THE SUMMARY OF THE PRODUCT CHARACTERISTICS

10. CLASSIFICATION OF VETERINARY MEDICINAL PRODUCTS

Veterinary medicinal product subject to prescription.

Detailed information on this veterinary medicinal product is available in the Union Product Database (https://medicines.health.europa.eu/veterinary).