SUMMARY OF PRODUCT CHARACTERISTICS

1. Name of the Veterinary Medicinal Product

Pyroflam 50 mg/ml Solution for Injection for Cattle, Horses and Pigs

2. Qualitative and Quantitative Composition

Active Substance

Flunixin (as flunixin meglumine)	50 mg/ml

Excipients

Phenol	5 mg/ml
Sodium Formaldehyde Sulphoxylate Dihydrate	2.5 mg/ml
Excipients	to 1 ml

For the full list of excipients, see section 6.1

3. Pharmaceutical Form

Solution for injection.
A clear colourless solution

4. Clinical Particulars

4.1 *Target species*:

Cattle
Horses
Pigs

4.2 *Indications for use, specifying the target species:*

In horses:
- alleviation of inflammation and pain associated with musculo-skeletal disorders.
- alleviation of visceral pain associated with colic.
- adjunctive therapy in the treatment of endotoxaemia and septic shock..

In cattle:
- reduction of acute inflammation associated with respiratory disease.
- adjunctive therapy in the treatment of acute mastitis.

In pigs:
Adjunctive therapy in the treatment of swine respiratory diseases.

4.3 ***Contraindications:***

Use is contraindicated in animals suffering from cardiac, hepatic or renal disease, where there is the possibility of gastrointestinal ulceration or bleeding, where there is evidence of a blood dyscrasia.

Do not use in case of hypersensitivity to flunixin meglumine, other NSAIDs or any of the excipients.

Do not use in case of haemorrhagic disorders.

Do not use in animals suffering from chronic musculo-skeletal disorders.

Do not administer to pregnant sows, gilts at mating and in breeding boars.

Do not use the product within 48 hours before expected parturition in cows.

4.4 ***Special Warnings for Each Target Species:***

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

4.5 ***Special Precautions for Use:***

(i) Special precautions for use in animals:

Avoid intra-arterial injection.
Use in any animal less than 6 weeks of age or in aged animals may involve additional risk. If such use cannot be avoided animals may require a reduced dosage and careful clinical management.
Avoid use in any dehydrated, hypovolaemic or hypotensive animal except in the case of endotoxaemia or septic shock.
It is preferable that NSAIDs, which inhibit prostaglandin synthesis are not administered to animals undergoing general anaesthesia until fully recovered.
Do not use in piglets weighting less than 6 kg.
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. The use of the product in the immediate post-partum period may interfere with uterine involution and expulsion of foetal membranes resulting in retained placentae.

(ii) Special precautions to be taken by the person administering the product to the animals:

- The product may cause reactions in sensitive individuals. If you have known hypersensitivity for non-steroidal anti-inflammatory products and/or to polyethylene glycol do not handle the product. Reactions may be serious.

- To avoid possible sensitisation reactions, avoid contact with the skin. Gloves should be worn during application.
- In case of skin contact, wash exposed area with plenty of water and soap. If symptoms persist seek medical advice.
- Avoid eye contact. In the case of accidental contact with eyes, rinse immediately with plenty of water and seek medical advice.
- Avoid accidental self-injection. In case of accidental self-injection, seek medical advice immediately and show the package leaflet or the label to the physician.
- Wash hands after use.

(iii) Other precautions:
None.

4.6 ***Adverse reactions (frequency and seriousness):***

Flunixin meglumine is a non steroidal anti-inflammatory drug (NSAID). Untoward effects include gastrointestinal irritation, ulceration, hepatic idiosyncratic reactions, and, especially in dehydrated or hypovolaemic animals, potential for renal damage.

In pigs, transient irritation may occur at the injection site, this resolves spontaneously within 14 days.

4.7 ***Use during pregnancy, lactation or lay:***

May be used in pregnant and lactating cattle.

For pregnant mares, use only according to the benefit/risk assessment by the Responsible Veterinarian.

Do not administer to pregnant sows, gilts at mating and in breeding boars.

The product should only be administered within the first 36 hours post-partum following a benefit/risk assessment performed by the responsible veterinarian and treated animals should be monitored for retained placentae.

4.8 ***Interactions with other medicinal products and other forms of interaction:***

Monitor drug compatibility closely where adjunctive therapy is required.

Do not administer other non-steroidal anti-inflammatory drugs (NSAIDs) concurrently or within 24 hours of each other, as it may increase the toxicity, mainly gastro-intestinal, even with low doses of acetylsalicylic acid. Some NSAIDs may be highly bound to plasma proteins and compete with other highly bound drugs which can lead to toxic effects.

The concurrent administration of corticoids may increase toxicity of the two products and increase the risk of gastro-intestinal ulceration. It should

therefore be avoided.

Flunixin may reduce the effect of some anti-hypertensive medicinal product by inhibition of the prostaglandins synthesis, such as diuretics, Angiotensin Conversion Enzyme (ACE) inhibitors and beta blockers.
Concurrent administration of potentially nephrotoxic drugs, particularly aminoglycosides, should be avoided.
Flunixin may reduce renal elimination of some drugs and increase their toxicity (for example, aminoglycosides).

4.9 ***Amount to be administered and administration route:***

For intravenous administration to cattle and horses.

HORSES: For use in equine colic, the recommended dose rate is 1.1 mg flunixin/kg bodyweight equivalent to 1 ml per 45 kg bodyweight. Treatment may be repeated once or twice if colic recurs.

For use in musculo-skeletal disorders, the recommended dose rate is 1.1 mg flunixin/kg bodyweight equivalent to 1 ml per 45 kg bodyweight, once daily for up to 5 days according to clinical response.

For the treatment of endotoxaemia or septic shock associated with gastric torsion and with other conditions in which the circulation of blood to the gastrointestinal tract is compromised: 0.25 mg/kg (1 ml per 200 kg) every 6-8 hours.

CATTLE The recommended dose rate is 2.2 mg flunixin/kg bodyweight equivalent to 2 ml per 45 kg bodyweight. Repeat as necessary at 24 hour intervals for up to 5 consecutive days.

For intramuscular injection to pigs.

PIGS The recommended dose rate is 2 ml per 45 kg bodyweight (equivalent to 2.2 mg flunixin/kg) once by intramuscular injection, in the neck, in conjunction with appropriate antimicrobial therapy. The injection volume should be limited to a maximum of 5 ml per injection site.

An appropriate graduated syringe must be used to allow accurate administration of the required dose volume. This is particularly important when injecting small volumes.

The stopper should not be punctured more than 50 times. A draw-off needle should be used to avoid excessive puncturing of the stopper.

Do not exceed the stated dose or duration of treatment.

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

Overdosage is associated with gastrointestinal toxicity.

4.11 ***Withdrawal periods:***

Cattle: Meat and offal: 10 Days
Milk: 24 Hours

Horses: Meat and offal: 10 Days
Milk: The product is not authorised for use in lactating mares producing milk for human consumption.

Pigs: Meat and offal: 22 Days

5. Pharmacological Properties

Pharmacotherapeutic group: Anti-Inflammatory and antirheumatic products, non-steroids – Fenamates

ATCvet Code: QM01AG90

5.1 ***Pharmacodynamic properties:***

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 E_2 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.

5.2 ***Pharmacokinetic particulars:***

Flunixin was administered intravenously to horses as a single dose of 1.1 mg/kg. At the first timepoint measured (10 minutes after administration) the plasma concentration was 11.45 µg/ml, AUC was 21.45 µg.h/ml and the elimination half-life was approximately 2 hours.

Flunixin was administered intravenously to cattle as a single dose of 2.2 mg/kg. At the first timepoint measured (10 minutes after administration) the plasma concentration was 12.32 µg/ml, AUC was 14.87 µg.h/ml and the elimination half-life was approximately 4 hours.

In an experimental study, flunixin was administered intravenously to pigs as a single dose of 2.0 mg/kg. Flunixin was >98% protein bound at all physiologically relevant concentrations, but also had a large volume of distribution at steady-state. All plasma concentrations were below the limit of quantitation (0.02 µg/ml) by 48 hours and the elimination half-life was 7.76 hours.

Environmental properties:
None known.

6. Pharmaceutical Particulars

6.1 *List of excipients:*

Sodium Formaldehyde Sulphoxylate Dihydrate
Disodium Edetate
Phenol
Propylene Glycol
Sodium Hydroxide (for pH adjustment)
Hydrochloric Acid (for pH adjustment) Water for Injections

6.2 *Major Incompatibilities:*

In the absence of incompatibility studies, this medicinal product must not be mixed with other 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:*

Do not store above 25°C. Keep container in the outer carton to protect from light. Avoid introduction of contamination.
Discard unused product.

6.5 ***Nature and composition of immediate packaging:***

This product is available in cartons containing 1 vial; supplied in 50 ml, 100 ml and 250 ml Type I clear colourless glass vials, complete with bromobutyl 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, if appropriate:***

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**

Norbrook Laboratories (Ireland) Limited
Rossmore Industrial Estate
Monaghan
Ireland

Norbrook Laboratories Limited
Station Works Camlough Road Newry
Co. Down,
BT35 6JP
Northern
Ireland

8. **Marketing Authorisation Number**

Vm 02000/4253

9. **Date of First Authorisation**

23 February 2006

10. **Date of Revision of the Text**

July 2019

Approved: 30 July 2019