[Version 9,03/2022]

ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

MEGANYL 50 mg/ml Solution for Injection for cattle, pigs and horses.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

Active substance:

Flunixin 50.0 mg
(equivalent to 83 mg of flunixin meglumine)

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, concentrated (*for pH adjustment*)	
Water for injection	

Clear, colourless solution and free from visible particles.

3. CLINICAL INFORMATION

3.1 Target species

Cattle, pigs and horses.

3.2 Indications for use, for eachtarget species

In cattle:
For the reduction of acute inflammation and pyrexia associated with the bovine respiratory disease.
For adjunctive therapy in the treatment of acute mastitis.

In pigs:
For adjunctive therapy in the treatment of Metritis-Mastitis-Agalactia (MMA).

In horses:
For the alleviation of inflammation and pain associated with musculoskeletal disorders.
For the alleviation of visceral pain associated with colic in the horse.

3.3 Contraindications

Do not use in animals with liver, cardiac or renal disease.
Do not use in animals where there is the possibility of gastro-intestinal ulceration or bleeding.

Do not use the product when there are signs of blood dyscrasias or haemostasis alteration.
Do not use in cases of hypersensitivity to the active substance, to other NSAIDs or to any of the excipients.
Do not use the product within 48 hours before expected parturition in cows.
Do not use in case of stomach cramps caused by ileus, associated to dehydration.
Do not use in animals that suffer chronic musculoskeletal disorders.

3.4 Special warnings

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

NSAIDs can cause phagocytosis inhibition and, therefore, in the treatment of inflammatory states associated with bacterial infections, appropriate concurrent antimicrobial therapy should be established.

3.5 Special precautions for use

Special precautions for safe use in the target species:

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.

Avoid use in dehydrated, hypovolaemic or hypotensive animals except in the case of endotoxaemia or septic shock. During treatment, water consumption and hydration status of the animal should be monitored, since in cases of dehydration the risk of kidney damage increases.

Intra-arterial injection must be avoided in cows and horses. Ataxia, incoordination, hyperventilation, excitability and muscles weakness could appear as clinical signs. These signs are transitory and disappear in few minutes without using antidote therapy.

Horses for racing and competition should be prevented for competition when they need treatment and horses that have been treated recently should be subject to local requirements. Necessary steps should be taken to ensure compliance with the rules of the competition. It is recommended a urine test, if in doubt.

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.

It is preferable that NSAIDs which inhibit prostaglandin synthesis are not administered to animals undergoing general anaesthesia until fully recovered.

In very rare cases, shock potentially lethal may appear after intravenous injections, due to high quantity of propylene glycol in the medicinal product. The product must be injected slowly and at body temperature. Stop injection at the first signs of intolerance and treat shock if necessary.

In intramuscular administration in pigs, it should be avoided to deposit the drug in adipose tissue.

NSAIDs are known to have the potential to delay calving through a tocolytic effect due to prostaglandin inhibition, which are important in signalling the initiate of calving. Use of the product in the period immediately following calving may interfere with uterine involution and expulsion of foetal membranes resulting in placental retention. See also section3.7.

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

People with known hypersensitivity to NSAIDs and/or to polyethylene glycol should avoid contact with the veterinary medicinal product.

The veterinary medicinal product may cause skin and eye irritation. Avoid contact with skin or eyes. Personal protective equipment consisting of gloves and protective goggles should be worn when handling the veterinary medicine. Wash your hands after using the product. In case of accidental skin contact, wash out the affected area immediately with plenty of water. In case of accidental eye contact, seek medical advice immediately and show the package leaflet or the label to the physician.

In case of accidental self-injection, acute pain and inflammation may appear. Clean and disinfect immediately the wound and seek medical advice and show the package leaflet or the label to the physician.

Special precautions for the protection of the environment:

Not applicable.

3.6 Adverse events

Cattle:

Rare 1 to 10 animals / 10,000 animals treated:	Application site reaction[1]
Very rare Less than1 animal / 10,000 animals treated, including isolated reports:	Haemorrhage[2] Digestive tract disorder[2] Renal and urinary disorders (Papillary necrosis)[2] Ataxia[2] Hyperventilation[2] Anaphylactic shock[3]

[1]Observed after intramuscular administration.
[2] Based on the literature available for non-steroidal anti-inflammatory drugs (NSAID).
[3]May occur after rapid intravenous injection. The medication should therefore be slowly injected and should be given at body temperature. The administration should be interrupted immediately if the signs of intolerance occur and, if necessary, initiate the treatment for shock.

Pigs:

Rare 1 to 10 animals / 10,000 animals treated:	Application site reaction[1]
Very rare Less than1 animal / 10,000 animals treated, including isolated reports:	Haemorrhage[2] Digestive tract disorder[2] Renal and urinary disorders (Papillary necrosis)[2] Ataxia[2] Hyperventilation[2]

[1]Observed after intramuscular administration.
[2] Based on the literature available for non-steroidal anti-inflammatory drugs (NSAID).

Horses:

Rare 1 to 10 animals / 10,000 animals treated:	Application site reaction[1]

Very rare Less than1 animal / 10,000 animals treated, including isolated reports:	Haemorrhage[2] Digestive tract disorder[2] Renal and urinary disorders (Papillary necrosis)[2] Ataxia[2] Hyperventilation[2] Anaphylactic shock[3]

[1]Observed after intramuscular administration.
[2] Based on the literature available for non-steroidal anti-inflammatory drugs (NSAID).
[3]May occur after rapid intravenous injection. The medication should therefore be slowly injected and should be given at body temperature. The administration should be interrupted immediately if the signs of intolerance occur and, if necessary, initiate the treatment for shock.

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 also the last section of the package leaflet for respective contact details

3.7 Use during pregnancy, lactation or lay

The safety of flunixin has not been assessed in pregnant mares, breeding stallions and bulls. Do not use in these animals.
The safety of flunixin was demonstrated in pregnant cows and sows, as well as boars. The product may be used in these animals except within 48 hours before parturition (see sections 3.3 and 3.6) in accordance with the benefit/risk assessment carried out by the responsible veterinarian before its use because calving could be delayed in gestating females.
The drug must be administered only during the first 36 hours after delivery in accordance with the benefit/risk assessment carried out by the responsible veterinarian and treated animals should be monitored for retention of the placenta.

3.8 Interaction with other medicinal products and other forms of interaction

The product should not be mixed with other drugs prior to administration.

Do not administer the product together with other non-steroid anti-inflammatory drugs (NSAIDs) because its toxicity is increased, especially gastrointestinal toxicity, even the use of low doses of acetylsalicylic acid.

The use in combination with corticoids can increase the toxicity of both of them, increasing the risk of gastrointestinal ulcers.

Pre-treatment with other anti-inflammatory substances may end up in additional or increase of adverse effects. Therefore, a free period of treatment with such substances should be left at least 24 hours prior to commence the treatment with flunixin. The free period of treatment, however, should take into account the pharmacokinetic properties of the products used previously.

Some NSAIDs may be highly bound to plasma proteins and compete with other highly bound drugs which can lead to toxic effects. This interaction is important for medicines with a narrow therapeutic margin: oral anticoagulants, methotrexate and some anticonvulsants as phenytoin.

It can reduce effects of some antihypertensive medicines due to the inhibition of prostaglandins synthesis. In this group of medicines stand out: diuretics, ACE inhibitors, ARA and β-blockers.
Avoid the administration jointly with potentially nephrotoxic medicines, standing out cyclosporine among them.

It can reduce renal elimination of some medicines increasing its toxicity, as it occurs with methotrexate, aminoglycosides and lithium salts.

Patients requiring joint therapy should be carefully controlled in order to determine flunixin compatibility with other drugs.

3.9 Administration routes and dosage

The product is administered by the intravenous route in cattle and horses, and by deep intramuscular injection in pigs.

Cattle: The recommended dose is 2.2 mg flunixin (meglumine)/kg body weight every 24 hours for a maximum period of three days (equivalent to 2 ml of the product/ 45 kg body weight, intravenously).

Pigs: The recommended daily dose is 2.2 mg flunixin (meglumine)/kg body weight (equivalent to 2 ml of the product/45 kg body weight) by deep intramuscular injection. It can be administered in 1 or 2 injections 12 hours apart. The number of treatments to be administered (one or two) will depend on the clinical response obtained.

The volume administered by injection point should not exceed 3 ml.

Horses: Relief of inflammation and pain associated with musculoskeletal disorders in acute and chronic conditions: 1.1 mg flunixin (meglumine)/ kg body weight every 24 hours for up to 5 days (equivalent to 1 ml of the product/ 45 kg body weight / Intravenously).

Relief of visceral pain associated with colic: 1.1 mg flunixin (meglumine) / kg body weight (equivalent to 1 ml of the product/ 45 kg body weight / Intravenously). In most cases, a single injection is sufficient to control the signs of colic, once the cause of the colic has been determined and the appropriate treatment has been established. However, if the clinical signs persist or reappear, a second or third injection may be administered with an interval of between 6 and 12 hours

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

Overdose is associated with gastrointestinal toxicity (vomiting, soft faeces/diarrhoea and faeces dyed with blood). Incoordination and ataxia signs also appear.
In horses, following 3 times the recommended dose (3 mg/kg bodyweight) administered by the intravenous route, a transient increase in blood pressure may be observed.
In cattle, administration of 3 times the recommended dose (6 mg/kg bodyweight) administered by the intravenous route did not induce untoward effects.
Dosages of 2.2 or 6.6 mg / kg body weight were administered 2 to 4 times, at 12 hour intervals to sows by deep intramuscular injection. Except some degree of local irritation at the injection site, flunixin had no adverse effect on sows or piglets. The muscular irritation was not serious enough to consider flunixin contraindicated in sows.

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

Administration under the control or direct responsibility of a veterinary surgeon.
Administration only by the veterinary surgeon in case of intravenous administration.

3.12 Withdrawal periods

Cattle:
Meat and offal: 4 days.
Milk: 24 hours.

Pigs:
Meat and offal: 24 days.

Horses:
Meat and offal: 4 days.
Milk: Not authorised for use in mares producing milk for human consumption.

4. PHARMACOLOGICAL INFORMATION

4.1 ATCvet code: QM01AG90.

4.2 Pharmacodynamics

Flunixin meglumine is a potent, non-steroidal, non-narcotic analgesic with anti-inflammatory and anti-pyretic activities.

Flunixin meglumine acts as a non-selective and reversible inhibitor of cyclooxygenase (COX), an enzyme that turn arachidonic acid into cyclic non-stable endoperoxides which turn into prostaglandins, prostacyclins and thromboxanes. Some of these prostanoids, such as prostaglandins, participate in the physiopathologic processes of inflammation, pain and fever; thus, its inhibition would be responsible of their therapeutic effects. Due to prostaglandins implication in other physiological processes, COX inhibition would be also responsible of different adverse reactions such as gastrointestinal or renal damage.

Although flunixin meglumine does not have a direct effect on endotoxins once they have been produced, it reduces the production of prostaglandins, which are part of the complex processes involved in the endotoxic shock development.

However, the lifetime of prostaglandins is extremely short (approximately 5 minutes) and, for this reason, this inhibition of synthesis has a very quick effect.
Flunixin has no influence on the prostaglandin F2 Alpha (PGF2Ŭ) injected, nor does it have immunosuppressive effect or other typical effects of glucocorticoids.

Prolonged bleeding time after the administration of flunixin is negligible compared to the effect of aspirin.

Flunixin strength effect in musculoskeletal disorders is 4 times greater than that of phenylbutazone.

4.3 Pharmacokinetics

Bovine
Flunixin meglumine has a plasmatic half-life of 4 hours when it is administered by intravenous route in one single dose of 2.2 mg/kg bw. After administered to calves, intravenously, at a dose of 2.2 mg / kg bw, the maximum plasma level of flunixin of between 15 and 18 µg/ml is obtained after 5-10 minutes of injection. Between 2 and 4 hours later a second peak of plasma concentration was observed (due, possibly, to the enterohepatic circulation), whereas, at 24 hours, the concentrations were inferior to 0.1 µg/ml. Flunixin meglumine is rapidly distributed in body organs and fluids (with high persistence in inflammatory exudate), with a distribution volume of between 0.7 and 2.3 l/kg. The elimination half-life was approximately 4 to 7 hours. In relation to excretion, this took place mainly through urine and faeces. In milk, the drug was not detected, and in the cases in which it was detected, the levels were < 10 ng/ml.

Porcine
One I.M. injection was administered to pigs with 2,2 mg/kg of flunixin meglumine. A maximum plasma concentration of about 3 µg /ml was detected approximately 20 minutes after injection. Bioavailability, expressed as a fraction of the absorbed dose, was 93%. The distribution volume was 2 l/kg, while the elimination half-life was 3.6 hours. Excretion (most of them as unaltered drug) took place primarily in the urine, although was also detected in the faeces.

Equine
After flunixin meglumine administration intravenously to horses, in a single dose of 1.1 mg /kg, the kinetics of the drug were adjusted to a bicompartmental model. It showed a rapid distribution (distribution volume of 0.16 l/kg), with a high proportion of plasma protein binding (above 99%). The elimination half-life was between 1 and 2 hours.
An AUC 0-15 h of 19.43 µg.h/ml was determined. Excretion took place quickly, mainly through the urine, reaching the maximum concentration in urine within 2 hours of administration. After 12 hours of intravenous injection, 61% of the administered dose had been recovered in the urine.

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

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

5.4 Nature and composition of immediate packaging

Type II colourless glass vial, with bromobutyl rubber stopper and aluminium cap.

Pack sizes:
Box with 1 vial of 100 ml
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 product 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

Laboratorios Syva, S.A..

7. MARKETING AUTHORISATION NUMBER(S)

8. DATE OF FIRST AUTHORISATION

Date of first authorisation:> <{DD/MM/YYYY}><{DD month YYYY}.>

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

<{MM/YYYY}>
<{DD/MM/YYYY}>
<{DD month YYYY}>

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.