[Version 9.1,11/2024]

ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

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

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

Active substance:
Flunixin 50.0 mg
(equivalent to 82.9 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
Disodium edetate	
Propylene glycol	207.2 mg
Trisodium phosphate dodecahydrate	
Hydrochloric acid, dilute	
Sodium hydroxide	
Water for injections	

Clear and colourless to light yellow solution, free from visible particles.

3. CLINICAL INFORMATION

3.1 Target species

Cattle, horses and pigs

3.2 Indications for use for each target species

Cattle
Adjunctive therapy in the treatment of bovine respiratory diseases, endotoxemia and acute mastitis.
Alleviation of acute inflammation and pain associated with musculoskeletal disorders.
Reduction of post-operative pain associated with dehorning in calves of less than 9 weeks.

Horses
Alleviation of acute inflammation and pain associated with musculoskeletal disorders.
Alleviation of visceral pain associated with colic.
Adjunctive therapy of endotoxemia due to or as a result of post-surgical or medical conditions or diseases that result in impaired blood circulation in the gastrointestinal tract.
Reduction of pyrexia.

Pigs
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. The use of the veterinary medicinal product in the immediate post-partum period may interfere with uterine involution and expulsion of foetal membranes resulting in retained placentae.
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 NSAIDs 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 (cattle, horses: less than 6 weeks old) 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, inflammation or colic 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 to 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

Cattle

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

[1] Particularly in hypovolaemic and hypotensive animals.
[2] After intravenous administration. At the onset of the first symptoms, administration should be stopped immediately and, if necessary, anti-shock treatment should be started.
[3] Blood count abnormalities.
[4] By a tocolytic effect induced by inhibition of the synthesis of prostaglandins, responsible for the initiation of parturition.
[5] If the product is used in the period following parturition.

Horses

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

[1] Particularly in hypovolaemic and hypotensive animals.
[2] After intravenous administration. At the onset of the first symptoms, administration should be stopped immediately and, if necessary, anti-shock treatment should be started.
[3] Blood count abnormalities.

[4] By a tocolytic effect induced by inhibition of the synthesis of prostaglandins, responsible for the initiation of parturition.
[5] If the product is used in the period following parturition.
[6] May occur through accidental intra-arterial injection.

Pigs

Uncommon (1 to 10 animals / 1 000 animals treated):	Injection site reaction (such as injection site skin discolouration, injection site pain, injection site irritation and injection site 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] Particularly in hypovolaemic and hypotensive animals.
[3] After intravenous administration. At the onset of the first symptoms, administration should be stopped immediately and, if necessary, anti-shock treatment should be started.
[4] Blood count abnormalities.
[5] By a tocolytic effect induced by inhibition of the synthesis of prostaglandins, responsible for the initiation of parturition.
[6] If the product is used in the period following parturition.

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 cows and sows.
Do not use the veterinary medicinal product within 48 hours before expected parturition in cows and sows.
The safety of the veterinary medicinal product has not been established in pregnant mares.
Do not use during the whole of the pregnancy.
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 bulls, stallions and boars intended for breeding.
Do not use in breeding bulls, breeding stallions and 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 and intravenous use in cattle.
Intravenous use in horses.
Intramuscular use in pigs.

Cattle

Adjunctive therapy in the treatment of bovine respiratory diseases, endotoxemia and acute mastitis and alleviation of acute inflammation and pain associated with musculoskeletal disorders

2.2 mg flunixin/kg bodyweight (2 ml per 45 kg) once daily via intramuscular or intravenous route. Repeat as necessary at 24-hour intervals for up to 3 consecutive days.

For intramuscular use, if dose volumes exceed 8 ml, it should be divided and injected into two or three sites. In case that more than three sites are necessary, the intravenous route should be used.

Reduction of post-operative pain associated with dehorning in calves of less than 9 weeks

A single intravenous administration of 2.2 mg of flunixin per kg bodyweight (2 ml per 45 kg), 15-20 minutes before the procedure.

Horses

Alleviation of acute inflammation and pain associated with musculoskeletal disorders and reduction of pyrexia

1.1 mg flunixin/kg bodyweight (1 ml per 45 kg) once daily for up to 5 days according to clinical response.

Alleviation of visceral pain associated with colic

1.1 mg flunixin/kg bodyweight (1 ml per 45 kg). Repeat once or twice if colic recurs.

Adjunctive therapy of endotoxemia due to or as a result of post-surgical or medical conditions or diseases that result in impaired blood circulation in the gastrointestinal tract

0.25 mg flunixin/kg bodyweight every 6-8 hours or 1.1 mg flunixin/kg bodyweight once daily for up to 5 consecutive days.

Pigs

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.

The stopper may be safely punctured up to 25 times with a 18 G needle size and up to 100 times with a 21 G needle size. For multiple vial entry, an aspirating needle or multi-dose syringe is recommended to avoid excessive broaching of the stopper.

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.

Cattle:
In cattle, intravenous administration of three times the recommended dose did not cause any adverse effects.

Horse:
Foals administered an overdose of 6.6 mg flunixin/kg bodyweight (i.e., 5X the recommended clinical dose) had more gastrointestinal ulceration, greater cecal pathology and cecal petechiation scores than control foals. Foals treated with 1.1 mg flunixin/kg bodyweight for 30 days intramuscularly, developed gastric ulceration, hypoproteinemia, and renal papillary necrosis. Renal crest necrosis was observed in 1 out of 4 horses treated with 1.1 mg flunixin/kg bodyweight for 12 days.
In horses, after intravenous injection of three times the recommended dose, a transient increase in blood pressure may be observed.

Pig:
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

Cattle:

Meat and offal:	4 days (intravenous use).
	31 days (intramuscular use).
Milk:	24 hours (intravenous use).
	36 hours (intramuscular use).

Horses:
Meat and offal: 5 days (intravenous use).
Not authorised for use in mares producing milk for human consumption.

Pigs:
Meat and offal: 24 days (intramuscular use).

4. PHARMACOLOGICAL INFORMATION

4.1 ATCvet code:
QM01AG90

4.2 Pharmacodynamics
Flunixin meglumine is a non-steroidal anti-inflammatory drug with analgesic and antipyretic activity. Flunixin meglumine acts as a reversible non-selective inhibitor of cyclo-oxygenase (both COX 1 and COX 2 forms), an 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 are reduced. 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 E2 synthesis in the hypothalamus. Although flunixin has no direct effect on endotoxins after they have been produced, it reduces prostaglandin production and hence reduces the many effects of the prostaglandin cascade. Prostaglandins are part of the complex processes involved in the development of endotoxic shock.
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
Following intravenous administration of flunixin meglumine to equines (horses and ponies) at a dose of 1.1 mg/kg, the drug kinetics fit a two-compartment model. It showed a rapid distribution (volume of distribution 0.16 l/kg), with a high proportion of binding to plasma proteins (greater than 99%). The elimination half-life was between 1 and 2 hours. An AUC0-15h of 19.43 μg·h/ml was determined. The excretion took place rapidly, mainly through the urine, reaching the maximum concentration therein 2 hours after administration.
After 12 hours of intravenous injection, 61% of the administered dose had been recovered in the urine.

In cattle, after administering a dose of 2.2 mg/kg intravenously, maximum plasma levels of between 15 and 18 μg/ml were obtained 5-10 minutes after injection. Between 2 and 4 hours later, a second plasma concentration peak was observed (possibly due to enterohepatic circulation), while at 24 hours the concentrations were less than 0.1 μg/ml. In cattle, after intramuscular administration of flunixin at a dose of 2 mg/kg, a maximum concentration is observed approximately 30 minutes after injection. Flunixin meglumine is rapidly distributed into organs and body fluids (with high persistence in inflammatory exudate), with a volume of distribution between 0.7 and 2.3 l/kg. The elimination half-life was approximately 4 to 7 hours. Regarding excretion, this took place mainly through urine and feces. In milk, the drug was not detected, and in the cases where it was detected, the levels were negligible (<10 ng/ml).

In pigs, following intramuscular administration of 2.2 mg/kg flunixin meglumine, a maximum plasma concentration of about 3 μg/ml was detected approximately 20 minutes after injection.
The bioavailability, expressed as a fraction of the absorbed dose, was found to be 93%. The Volume of distribution was 2 l/kg, while the elimination half-life was 3.6 hours. Excretion (most as unchanged drug) occurred primarily in the urine, although 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: 30 months.
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 temperature storage conditions.
Keep the vial in the outer carton in order to protect from light.

5.4 Nature and composition of immediate packaging

Colourless type II glass vials closed with bromobutyl rubber stoppers and sealed with flip-off cap or an aluminium cap in a cardboard box.

Pack sizes:
1 x 50 ml vial
1 x 100 ml vial
1 x 250 ml vial

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

Industrial Veterinaria, S.A.

7. MARKETING AUTHORISATION NUMBER(S)

VPA10509/009/001

8. DATE OF FIRST AUTHORISATION

19/07/2024

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

25/04/2025

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).