SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Wellicox 50 mg/ml solution for injection for cattle, horses, pigs (FR, BE, DE, DK, HU, IT, NL, PL, RO, SE)
Allevinix 50 mg/ml solution for injection for cattle, horses, pigs (UK(NI))

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

Active substance:
Flunixin (as flunixin meglumine) 50 mg
(equivalent to 83 mg 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	0.1 mg
Sodium hydroxide	
Propylene glycol	207.2 mg
Dilute hydrochloric acid for pH-adjustment	
Water for injections	

Colourless to pale yellow solution, clear and practically free from particles.

3. CLINICAL INFORMATION

3.1 Target species

Cattle, horses, 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 musculo-skeletal 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.
Non-steroidal anti-inflammatory drugs (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]. Anaphylaxis (e.g. Anaphylactic shock, Hyperventilation, Convulsion, Collapse, Death)[2];
Very rare (<1 animal / 10,000 animals treated, including isolated reports):	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]. Anaphylaxis (e.g. Anaphylactic shock, Hyperventilation, Convulsion, Collapse, Death)[2];
Very rare (<1 animal / 10,000 animals treated, including isolated reports):	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 post-partum 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 beta blockers.
Concomitant administration of potentially nephrotoxic drugs (e.g., aminoglycoside antibiotics), should be avoided.

3.9 Administration routes and dosage

Cattle: intramuscular and intravenous uses
Horses: intravenous use
Pigs: intramuscular use

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 site 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 cap can be broached up to 10 times. When treating large groups of animals at one time, use an automatic dosing device.

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.

Horses:
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.

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

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

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 of about 2.5 µg/ml 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: 3 years
Shelf-life after first opening the immediate packaging: 28 days

5.3 Special precautions for storage

Do not store above 25°C after first opening the immediate packaging.

5.4 Nature and composition of immediate packaging

50, 100 or 250 ml colourless Type II glass vial sealed with chlorobutyl rubber stoppers and a flip-off cap on top of an aluminium crimp seal.
50, 100 or 250 ml translucent PP/Ethylene vinyl alcohol/PP multi-layer plastic vials with bromobutyl rubber stopper with aluminium cap.
1 vial per cardboard box.
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 system applicable to the veterinary medicinal product concerned.

6. NAME OF THE MARKETING AUTHORISATION HOLDER

7. MARKETING AUTHORISATION NUMBER(S)

8. DATE OF FIRST AUTHORISATION

Date of first authorisation: {DD/MM/YYYY}

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

{DD/MM/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 (https://medicines.health.europa.eu/veterinary).

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

Cardboard box of 50 ml, 100 ml or 250 ml

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Wellicox 50 mg/ml solution for injection
Allevinix 50 mg/ml solution for injection (UK(NI))

2. STATEMENT OF ACTIVE SUBSTANCES

1 ml contains 50 mg of flunixin, equivalent to 83 mg flunixin meglumine

3. PACKAGE SIZE

50 ml
100 ml
250 ml

4. TARGET SPECIES

Cattle, horses, pigs

5. INDICATIONS

6. ROUTES OF ADMINISTRATION

Cattle/pigs: Intramuscular use
Cattle/horses: Intravenous use

7. WITHDRAWAL PERIODS

Withdrawal period:
Cattle:
Meat and offal: 4 days (IV use).
31 days (IM use).
Milk: 24 hours (IV use).
36 hours (IM use).
Pigs:
Meat and offal: 24 days (IM use).
Horses:
Meat and offal: 5 days (IV use).
Not authorised for use in animals producing milk for human consumption.

8. EXPIRY DATE

Exp. {mm/yyyy}
Once broached, use within 28 days.

9. SPECIAL STORAGE PRECAUTIONS

Do not store above 25^0 C after first opening the immediate packaging.

10. THE WORDS "READ THE PACKAGE LEAFLET BEFORE USE"

Read the package leaflet before use.

11. THE WORDS "FOR ANIMAL TREATMENT ONLY"

For animal treatment only.

12. THE WORDS "KEEP OUT OF THE SIGHT AND REACH OF CHILDREN"

Keep out of the sight and reach of children.

13. NAME OF THE MARKETING AUTHORISATION HOLDER

14. MARKETING AUTHORISATION NUMBERS

15. BATCH NUMBER

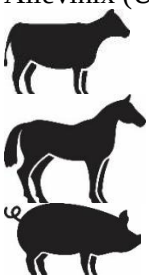
Lot {number}

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

Label of 50 ml

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Wellicox
Allevinix (UK(NI))



2. QUANTITATIVE PARTICULARS OF THE ACTIVE SUBSTANCE

Flunixin 50 mg/ml

3. BATCH NUMBER

Lot {number}

4. EXPIRY DATE

Exp. {mm/yyyy}
Once broached, use within 28 days by: ___/___/___

PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGE

Label of 100 ml or 250 ml

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Wellicox 50 mg/ml solution for injection
Allevinix 50 mg/ml solution for injection (UK(NI))

2. STATEMENT OF ACTIVE SUBSTANCES

1 ml contains 50 mg of Flunixin, equivalent to 83 mg flunixin meglumine

3. TARGET SPECIES

Cattle, horses, pigs.

4. ROUTES OF ADMINISTRATION

Cattle/pigs: IM.
Cattle/horses: IV.
Read the package leaflet before use.

5. WITHDRAWAL PERIODS

Withdrawal period:
Cattle:
Meat and offal: 4 days (IV use).
31 days (IM use).
Milk: 24 hours (IV use).
36 hours (IM use).
Pigs:
Meat and offal: 24 days (IM use).
Horses:
Meat and offal: 5 days (IV use).
Not authorised for use in animals producing milk for human consumption.

6. EXPIRY DATE

Exp. {mm/yyyy}
Once broached, use within 28 days by: __/__/__

7. SPECIAL STORAGE PRECAUTIONS

Do not store above 25°C after first opening the immediate packaging.

8. NAME OF THE MARKETING AUTHORISATION HOLDER

9. BATCH NUMBER

Lot {number}

B. PACKAGE LEAFLET

PACKAGE LEAFLET

1. Name of the veterinary medicinal product

Wellicox 50 mg/ml solution for injection for cattle, horses and pigs
Allevinix 50 mg/ml solution for injection for cattle, horses and pigs (UK (NI))

2. Composition

Each ml contains:

Active substance:
50 mg flunixin equivalent to 83 mg flunixin meglumine.
Excipients:

Phenol.....	5.0	mg
Sodium formaldehyde sulfoxylate.....	2.5	mg
Disodium edetate.....	0.1	mg
Propylene glycol……	207.2	mg

Colourless to pale yellow solution, clear and practically free from particles.

3. Target species

Cattle, horses, pigs.

4. Indications for use

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 musculo-skeletal 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.

5. 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.

6. Special warnings

Special warnings
None.

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.
Non-steroidal anti-inflammatory drugs (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 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 (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 skin contact, wash affected area immediately with plenty of water. If symptoms persist, seek medical advice.
In case of accidental eye contact, rinse eyes immediately with plenty of water.
If skin and /or eye irritation persists, seek medical advice 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.

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 post-partum 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.

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 beta blockers.
Concomitant administration of potentially nephrotoxic drugs (e.g. aminoglycosides antibiotics), should be avoided.

Overdose

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 injection of three times the recommended dose did not cause any adverse effects.

Horses:

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.

Pigs:

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.

Major incompatibilities

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

7. 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]. Anaphylaxis (e.g. Anaphylactic shock, Hyperventilation, Convulsion, Collapse, Death)[2];
Very rare (<1 animal / 10,000 animals treated, including isolated reports):	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]. Anaphylaxis (e.g. Anaphylactic shock, Hyperventilation, Convulsion, Collapse, Death)[2];
Very rare (<1 animal / 10,000 animals treated, including isolated reports):	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 product. If you notice any side effects, even those not already listed in this package leaflet, or you think that the medicine has not worked, please contact, in the first instance, your veterinarian. You can also report any adverse events to the marketing authorisation holder or the local representative of the marketing authorisation holder using the contact details at the end of this leaflet, or via your national reporting system.

8. Dosage for each species, routes and method of administration

Cattle: Intramuscular and intravenous uses.
Horses: Intravenous use.
Pigs: intramuscular use

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 site 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 cap can be broached up to 10 times. When treating large groups of animals at one time, use an automatic dosing device.

9. Advice on correct administration

10. Withdrawal periods

Cattle:
Meat and offal: 4 days (intravenous use).
31 days (intramuscular use).
Milk: 24 hours (intravenous use).
36 hours (intramuscular use).
Pigs:
Meat and offal: 24 days (intramuscular use).
Horses:
Meat and offal: 5 days (intravenous use).
Not authorised for use in animals producing milk for human consumption.

11. Special storage precautions

Keep out of the sight and reach of children.
Do not store above 25°C after first opening the immediate packaging.

Do not use this veterinary medicinal product after the expiry date stated on the label or carton after Exp. The expiry date refers to the last day of that month.
Shelf-life after first opening the immediate packaging: 28 days.

12. Special precautions for disposal

Medicines should not be disposed of via waste water 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 applicable national collection systems. These measures should help to protect the environment.
Ask your veterinary surgeon or pharmacist how to dispose of medicines no longer required

13. Classification of veterinary medicinal products

Veterinary medicinal product subject to prescription.

14. Marketing authorization numbers and pack sizes

Cardboard box of 1 glass vial of 50 ml, 100 ml or 250 ml
Cardboard box of 1 plastic vial of 50 ml, 100 ml or 250 ml
Not all pack sizes may be marketed.

15. Date on which the package leaflet was last revised

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

16. Contact details

Marketing authorisation holder and contact details to report suspected adverse reactions:
(Name and address to be completed nationally)
Tel: +800 35 22 11 51
E-mail: pharmacovigilance@ceva.com

Manufacturer responsible for batch release:
Ceva Santé Animale- 10, av. de la Ballastière- 33500 Libourne- France
or
Vetem S.p.A.- Lungomare L. Pirandello 8,- 92014 Porto Empedocle (AG)- Italy

17. Other information

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