SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

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

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

Active substance:
Flunixin ..... 50 mg
(as 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 mg
Sodium formaldehyde sulfoxylate	2.5 mg
Disodium edetate	0.1 mg
Sodium hydroxide	
Propylene glycol	
Dilute hydrochloric acid for pH-adjustment	
Water for injections	

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

3. CLINICAL INFORMATION

3.1 Target species

Cattle, pigs and horses.

3.2 Indications for use for each target species

Cattle:
Alleviation of clinical signs of respiratory disease when used concurrently with appropriate anti-infective therapy.

Pigs:
To support appropriate antibiotic therapy in the treatment of Mastitis-Metritis-Agalactia syndrome.

Alleviation of fever associated with respiratory disease when used in conjunction with specific antibiotic therapy.

Horses:

Alleviation of inflammation and pain associated with musculo-skeletal disorders.

Alleviation of visceral pain associated with colic.

3.3 Contraindications

Do not use in animals suffering from chronic musculo-skeletal disorders.
Do not use in animals suffering from cardiac, hepatic or renal disease.
Do not use in animals with gastro-intestinal lesions (gastro-intestinal ulceration or bleeding).

Do not use in cases of haemorrhagic disorders.
Do not use in cases of hypersensitivity to flunixine meglumine, other NSAIDs or any of the excipients.

Do not use in animals suffering from colic caused by ileus and associated with dehydration.

Do not use the veterinary medicinal product within 48 hours before expected parturition in cows. In such cases an increase in the number of stillbirths has been observed.
Do not exceed the stated dose or the duration of treatment.

See also section 3.7.

3.4 Special warnings

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

3.5 Special precautions for use

Special precautions for safe use in the target species

Use in any animal less than 6 weeks of age (cattle and horses) 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.
Avoid use in any dehydrated, hypovolaemic or hypotensive animal except in the case of endotoxaemia or septic shock.

In rare cases, shock (potentially fatal), may occur after intravenous injection, due to a high quantity of propylene glycol in the veterinary medicinal product. The veterinary

medicinal product must be injected slowly and at body temperature. Stop injection at the first signs of intolerance and treat for shock if necessary.

Due to its anti-inflammatory properties, flunixin may mask clinical signs and therefore possible resistance to antibiotic treatment.

NSAIDs are known to have the potential to delay parturition through a tocolytic effect by inhibiting prostaglandins that are important in signaling 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 fetal membranes resulting in retained placentae.

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.
See also section 3.7

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

Flunixin meglumine is a non-steroidal anti-inflammatory drug (NSAID). The veterinary medicinal product may cause an allergic reaction in people sensitised to NSAIDs. People with known hypersensitivity to NSAIDs should avoid contact with the veterinary medicinal product.

Hypersensitivity reactions may be serious.

This veterinary medicinal product may cause skin and eye irritation.
Avoid contact with skin or eyes.

In case of skin contact, wash exposed area with soap and plenty of water. If symptoms persist, seek medical advice.

In case of contact with the eyes, wash eyes thoroughly with clean water and seek medical advice.

Avoid risk of ingestion, do not eat or drink when using the veterinary medicinal product and wash hands after use. In case of ingestion of the veterinary medicinal product seek medical advice.

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.

Special precautions for the protection of the environment:

Not applicable

3.6 Adverse events

Cattle:

Rare (1 to 10 animals / 10,000 animals treated):	Anaphylaxis (with collapse)[1] Death[1]
Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Bleeding[2], gastrointestinal irritation[2], gastric ulceration[2] Renal damage[2] Injection site reaction[3]
Undetermined frequency (cannot be estimated from the available data)	Renal and hepatic disorders[4] Delayed parturition[5], increase of stillbirths[5], retained placenta[6]

[1]mainly during rapid intravenous injection
[2] mainly in dehydrated or hypovolaemic animals
[3] following intramuscular injection
[4] idiosyncratic effects
[5] through a tocolytic effect by inhibiting prostaglandins that are important in signalling the initiation of parturition
[6] in cases of the use of the veterinary medicinal product in the immediate post-partum period

Horses:

Rare (1 to 10 animals / 10,000 animals treated):	Anaphylaxis (with collapse)[1] Death[1]
Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Bleeding[2], gastrointestinal irritation[2], gastric ulceration[2], blood in faeces, diarrhea (liquid) Renal damage[2]
Undetermined frequency (cannot be estimated from the available data)	Renal and hepatic disorders[3] Delayed parturition[4], increase of stillbirths[4], retained placenta[5]

[1]mainly during rapid intravenous injection
[2] mainly in dehydrated or hypovolaemic animals
[3] idiosyncratic effects
[4] through a tocolytic effect by inhibiting prostaglandins that are important in signalling the initiation of parturition

[5] in cases of the use of the veterinary medicinal product in the immediate post-partum period

Pigs:

Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Bleeding[1], gastrointestinal irritation[1], gastric ulceration[1], vomiting[1] Renal damage[1]
Undetermined frequency (cannot be estimated from the available data)	Renal and hepatic disorders[2] Delayed parturition[3], increase of stillbirths[3], retained placenta[4]

[1] mainly in dehydrated or hypovolaemic animals
[2] idiosyncratic effects
[3] through a tocolytic effect by inhibiting prostaglandins that are important in signalling the initiation of parturition
[4] in cases of the use of the veterinary medicinal product in the immediate post-partum period

In case of untowards effects stop treatment and seek medical advice.
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 and lactation:

Studies in laboratory animals have produced evidence of foetotoxicity from flunixin after oral administration (rabbit and rat) and intramuscular administration (rat) at maternotoxic doses as well as an increase in the gestation period (rat).

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 veterinary medicinal product may be used in these animals except within the 48 hours preceding parturition (see sections 3.3 and 3.6).

The veterinary medicinal 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.

3.8 Interaction with other medicinal products and other forms of interaction

Do not administer other 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.

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 products, such as diuretics, Angiotensin Conversion Enzyme (ACE) inhibitors, and beta blockers, by inhibition of prostaglandin synthesis.

Concurrent administration of potentially nephrotoxic drugs, particularly aminoglycosides, should be avoided.

Flunixin may reduce renal elimination of some drugs and increase their toxicity, such as aminoglycosides for example.

3.9 Administration routes and dosage

Cattle: intramuscular and intravenous uses
Pigs: intramuscular use
Horses: intravenous use
The bodyweight should be accurately determined before the administration

Cattle:

2 mg of flunixin per kg bodyweight, equivalent to 2 ml of solution per 50 kg bodyweight, administered once daily by intravenous or intramuscular injection for 1 to 3 consecutive days.

Volumes greater than 20 ml should be divided and administered at least at 2 different injection sites.

Pigs:

To support appropriate antibiotic therapy in the treatment of Mastitis-Metritis-Agalactia syndrome:

2 mg of flunixin per kg bodyweight, equivalent to 2 ml of solution per 50 kg bodyweight, administered once daily for 1 to 3 consecutive days.

Alleviation of fever associated with respiratory diseases:

2 mg of flunixin per kg bodyweight, equivalent to 2 ml of solution per 50 kg bodyweight, administered once daily.

Maximum dosage volume per injection site should not exceed 5 ml. Volumes greater than 5 ml should be divided and administered at different injection sites.

Horses:
Alleviation of inflammation and pain associated with musculo-skeletal disorders: 1 mg of flunixin per kg bodyweight, equivalent to 1 ml of solution per 50 kg bodyweight, administered once daily for 1 to 5 consecutive days.

Alleviation of visceral pain associated with colic:
1 mg of flunixin per kg bodyweight, equivalent to 1 ml of solution per 50 kg bodyweight, administered once daily. Treatment may be repeated once or twice if colic recurs.

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. Signs of ataxia and incoordination may 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.
In pigs, following a dose of 2 mg flunixin/kg, administered twice a day, painful reactions at the injection site and an increase in the number of leucocytes was reported.

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: 10 days (IV route) / 31 days (IM route).
Milk: 24 hours (IV route) / 36 hours (IM route).

Pigs:
Meat and offal: 20 days.

Horses:
Meat and offal: 10 days.
Milk: the veterinary medicinal product is not authorised for use in lactating animals producing milk for human consumption.

4. PHARMACOLOGICAL INFORMATION

4.1 ATCvet code:

QM01AG90

4.2 Pharmacodynamics

Flunixin (as meglumine) demonstrates potent inhibition of the cyclo-oxygenase system (COX). The enzyme converts arachidonic acid to unstable cyclic endoperoxides, which are converted to prostaglandins, prostacyclin and thromboxane. Some of these prostanoids, such as prostaglandins are mediators for inflammation, pain and fever. The inhibition of the synthesis of such components would be responsible for the therapeutic effects of flunixin meglumine.

Since prostaglandins also play a part in other physiological processes, COX inhibitors may be responsible for some untoward effects such as gastrointestinal and renal damage.
Prostaglandins are involved in the complex process of endotoxaemic shock.

4.3 Pharmacokinetics

In cattle, after intramuscular injection at a dose of 2 mg/kg, a maximum concentration of 2.5 µg/ml is observed approximately 30 minutes after injection.
After intravenous injection flunixin distributes rapidly. The elimination is slow (approximately 4 hours).
Flunixin is highly bound to plasma proteins (>99%).

In pigs, after intramuscular injection at a dose of 2 mg/kg, a maximum concentration of 4 µg/ml is observed approximately 30 minutes after injection.
After intravenous injection flunixin distributes rapidly. The elimination is slow (approximately 8 hours).
Flunixin is highly bound to plasma proteins (>98%).

In the horse, after intravenous injection at a dose of 1 mg/kg flunixin distributes rapidly. The elimination half-life is 1.6 hours.
Flunixin is eliminated mainly via the kidneys as conjuguated form.

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 in a glass bottle: 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

Ceva Animal Health Ltd

7. MARKETING AUTHORISATION NUMBER

Vm 15052/3010

8. DATE OF FIRST AUTHORISATION

16 April 2013

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

July 2023

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).

Approved 12 March 2024