

**ANNEX I**  
**SUMMARY OF PRODUCT CHARACTERISTICS**

## 1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Emdofluxin 50 mg/mL solution for injection for cattle, horses and pigs [BE, BG, DE, DK, EE, ES, FR, HR, HU, IE, IT, LT, LU, LV, NL, SI, UK]

Inflanixim 50 mg/mL solution for injection for cattle, horses and pigs [AT]

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each mL contains:

### Active substance:

Flunixin (as flunixin meglumine) 50.00 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	5.00 mg
Sodium formaldehyde sulfoxylate	2.50 mg
Disodium edetate	0.10 mg
Propylene glycol	207.20 mg
Hydrochloric acid, dilute (for pH adjustment)	
Sodium hydroxide (for pH adjustment)	
Water for injections	

Colourless to yellow solution, clear and 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 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 threatening 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

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

<sup>1</sup> Particularly in hypovolaemic and hypotensive animals.

<sup>2</sup> After intravenous administration. At the onset of the first symptoms, administration should be stopped immediately and, if necessary, anti-shock treatment should be started.

<sup>3</sup> Blood count abnormalities.

<sup>4</sup> By a tocolytic effect induced by inhibition of the synthesis of prostaglandins, responsible for the initiation of parturition.

<sup>5</sup> If the product is used in the period following parturition.

#### Horses

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

<sup>1</sup> Particularly in hypovolaemic and hypotensive animals.

<sup>2</sup> After intravenous administration. At the onset of the first symptoms, administration should be stopped immediately and, if necessary, anti-shock treatment should be started.

<sup>3</sup> Blood count abnormalities.

<sup>4</sup> By a tocolytic effect induced by inhibition of the synthesis of prostaglandins, responsible for the initiation of parturition.

<sup>5</sup> If the product is used in the period following parturition.

<sup>6</sup> May occur through accidental intra-arterial injection.

#### Pigs

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

<sup>1</sup> Resolves spontaneously within 14 days.

<sup>2</sup> Particularly in hypovolaemic and hypotensive animals.<sup>3</sup> After intravenous administration. At the onset of the first symptoms, administration should be stopped immediately and, if necessary, anti-shock treatment should be started.

<sup>4</sup> Blood count abnormalities.

<sup>5</sup> By a tocolytic effect induced by inhibition of the synthesis of prostaglandins, responsible for the initiation of parturition.

<sup>6</sup> 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 or 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  $\beta$ -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.

The maximal volume to be administered per injection site is 20 mL.

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 5 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 vial should not be broached more than 25 times.

Therefore the user should select the most appropriate vial size according to the target species to be treated.

When treating several animals in one run, use a draw-off needle that has been placed in the vial stopper to avoid excess broaching of the stopper. The draw-off needle should be removed after treatment.

### **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 animals 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 AUC<sub>0-15h</sub> 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: 3 years.  
Shelf life after first opening the immediate packaging: 28 days.

## **5.3 Special precautions for storage**

Keep the vial in the outer carton in order to protect from light.

## **5.4 Nature and composition of immediate packaging**

50, 100 or 250 mL colourless type I glass vials closed with bromobutyl rubber stoppers and sealed with an aluminium cap in a cardboard box.

### Pack sizes:

Cardboard box containing one vial of 50 mL

Cardboard box containing one vial of 100 mL

Cardboard box containing one vial of 250 mL

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 systems applicable to the veterinary medicinal product concerned.

## **6. NAME OF THE MARKETING AUTHORISATION HOLDER**

Emdoka

## **7. MARKETING AUTHORISATION NUMBER(S)**

## **8. DATE OF FIRST AUTHORISATION**

Date of first authorisation: 07 August 2020

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

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>).

**ANNEX III**  
**LABELLING AND PACKAGE LEAFLET**

## **A. LABELLING**

**PARTICULARS TO APPEAR ON THE OUTER PACKAGE****Cardboard box****1. NAME OF THE VETERINARY MEDICINAL PRODUCT**

Emdoflixin 50 mg/mL solution for injection [BE, BG, DE, DK, EE, ES, FR, HR, HU, IE, IT, LT, LU, LV, NL, SI, UK]  
Inflanixim 50 mg/mL solution for injection [AT]

**2. STATEMENT OF ACTIVE SUBSTANCES**

Each ml contains: 50 mg Flunixin (as Flunixin meglumine)

**3. PACKAGE SIZE**

50 mL

100 mL

250 mL

**4. TARGET SPECIES**

Cattle, horses, pigs

**5. INDICATIONS****6. ROUTES OF ADMINISTRATION**

Cattle: intramuscular or intravenous use.

Horse: intravenous use.

Pig: intramuscular use.

**7. WITHDRAWAL PERIODS**

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 animals producing milk for human consumption.

Pigs

Meat and offal: 24 days (intramuscular use).

**8. EXPIRY DATE**

Exp. {mm/yyyy}

Once broached, use within 28 days.

Use by...

**9. SPECIAL STORAGE PRECAUTIONS**

Keep the vial in the outer carton in order to protect from light.

**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**

Emdokta

**14. MARKETING AUTHORISATION NUMBERS**

**15. BATCH NUMBER**

Lot {number}

**PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGE**

**Vial** (label for 100, 250 ml)

**1. NAME OF THE VETERINARY MEDICINAL PRODUCT**

Emdoflixin 50 mg/mL solution for injection [BE, BG, DE, DK, EE, ES, FR, HR, HU, IE, IT, LT, LU, LV, NL, SI, UK]

Inflanixim 50 mg/mL solution for injection [AT]

**2. STATEMENT OF ACTIVE SUBSTANCES**

Each ml contains 50 mg Flunixin (as Flunixin meglumine)

**3. TARGET SPECIES**

Cattle, horses, pigs

**4. ROUTES OF ADMINISTRATION**

Cattle: i.m. or i.v. use.

Horses: i.v. use.

Pigs: i.m. use.

Read the package leaflet before use.

**5. WITHDRAWAL PERIODS**

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 animals producing milk for human consumption.

Pigs

Meat and offal: 24 days (intramuscular use).

**6. EXPIRY DATE**

Exp. {mm/yyyy}

Once broached, use within 28 days.

Use by...

**7. SPECIAL STORAGE PRECAUTIONS**

Keep the vial in the outer carton in order to protect from light.

**8. NAME OF THE MARKETING AUTHORISATION HOLDER**

Emdoka

**9. BATCH NUMBER**

Lot {number}

**MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS****Vial** (label for 50 ml)**1. NAME OF THE VETERINARY MEDICINAL PRODUCT**

Emdofluxin 50 mg/mL solution for injection for cattle, horses and pigs [BE, BG, DE, DK, EE, ES, FR, HR, HU, IE, IT, LT, LU, LV, NL, SI, UK]

Inflanixim 50 mg/mL solution for injection for cattle, horses and pigs [AT]

**2. QUANTITATIVE PARTICULARS OF THE ACTIVE SUBSTANCES**

Each ml contains 50 mg Flunixin (as Flunixin meglumine)

**3. BATCH NUMBER**

Lot {number}

**4. EXPIRY DATE**

Exp. {mm/yyyy}

Once broached, use within 28 days.

Use by...

**B. PACKAGE LEAFLET**

## PACKAGE LEAFLET

### 1. Name of the veterinary medicinal product

Emdofluxin 50 mg/mL solution for injection for cattle, horses and pigs [BE, BG, DE, DK, EE, ES, FR, HR, HU, IE, IT, LT, LU, LV, NL, SI, UK]

Inflanixim 50 mg/mL solution for injection for cattle, horses and pigs [AT]

### 2. Composition

Each ml contains:

50.00 mg Flunixin, equivalent to 83 mg Flunixin meglumine	
Phenol	5.00 mg
Sodium formaldehyde sulfoxylate	2.50 mg
Disodium edetate	0.10 mg
Propylene glycol	207.20 mg

Colourless to yellow solution, clear and free from particles.

### 3. Target species

Cattle, horses, pigs

### 4. Indications for use

Cattle

Adjunctive therapy in the treatment of bovine respiratory diseases, endotoxemia (severe illness due to bacterial poisons in the bloodstream) and acute mastitis (infection of the udder).

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 fever.

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 disorder, liver disorder or renal disorder 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 in case of colic caused by ileus and associated with dehydration.

Do not use if haematopoiesis or coagulation is impaired.

### 6. Special warnings

Special precautions for safe use in the target species:

Inject slowly as life threatening 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.

**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.

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.

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 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.

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**

<b>Uncommon</b> (1 to 10 animals / 1,000 animals treated):	Injection site reaction (such as injection site irritation and injection site swelling).
<b>Rare</b> (1 to 10 animals / 10,000 animals treated):	Liver disorder; Renal disorder (Nephropathy, Papillary necrosis) <sup>1</sup> . Anaphylaxis (e.g. Anaphylactic shock, Hyperventilation, Convulsion, Collapse, Death) <sup>2</sup>
<b>Very rare</b>	Ataxia <sup>2</sup> ; Blood and lymphatic system disorder <sup>3</sup> , Haemorrhage;

(<1 animal / 10,000 animals treated, including isolated reports):	Digestive tract disorder (gastrointestinal irritation, gastrointestinal ulceration, digestive tract haemorrhage, nausea, blood in faeces, diarrhoea) <sup>1</sup> ; Delay of parturition <sup>4</sup> , stillbirth <sup>4</sup> , retained placenta <sup>5</sup> ; Appetite loss.
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<sup>1</sup> Particularly in hypovolaemic and hypotensive animals.

<sup>2</sup> After intravenous administration. At the onset of the first symptoms, administration should be stopped immediately and, if necessary, anti-shock treatment should be started.

<sup>3</sup> Blood count abnormalities.

<sup>4</sup> By a tocolytic effect induced by inhibition of the synthesis of prostaglandins, responsible for the initiation of parturition.

<sup>5</sup> If the product is used in the period following parturition.

#### Horses

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

<sup>1</sup> Particularly in hypovolaemic and hypotensive animals.

<sup>2</sup> After intravenous administration. At the onset of the first symptoms, administration should be stopped immediately and, if necessary, anti-shock treatment should be started.

<sup>3</sup> Blood count abnormalities.

<sup>4</sup> By a tocolytic effect induced by inhibition of the synthesis of prostaglandins, responsible for the initiation of parturition.

<sup>5</sup> If the product is used in the period following parturition.

<sup>6</sup> May occur through accidental intra-arterial injection.

#### Pigs

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

<sup>1</sup> Resolves spontaneously within 14 days.

<sup>2</sup> Particularly in hypovolaemic and hypotensive animals.

<sup>3</sup> After intravenous administration. At the onset of the first symptoms, administration should be stopped immediately and, if necessary, anti-shock treatment should be started.

<sup>4</sup> Blood count abnormalities.

<sup>5</sup> By a tocolytic effect induced by inhibition of the synthesis of prostaglandins, responsible for the initiation of parturition.

<sup>6</sup> 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**

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 the intramuscular or intravenous route.

Repeat as necessary at 24 hour intervals for up to 3 consecutive days.

The maximal volume to be administered per injection site is 20 mL.

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 every 6-8 hours or 1.1 mg flunixin/ kg once 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 per bodyweight (2 ml per 45 kg) once daily for up to 3 consecutive days. The injection volume should be limited to a maximum of 5 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 vial should not be broached more than 25 times.

Therefore the user should select the most appropriate vial size according to the target species to be treated.

When treating several animals in one run, use a draw-off needle that has been placed in the vial stopper to avoid excess broaching of the stopper. The draw-off needle should be removed after treatment.

## **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).

Horses:

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

Pigs

Meat and offal: 24 days (intramuscular use).

## **11. Special storage precautions**

Keep out of the sight and reach of children.

Keep the vial in the outer carton in order to protect from light.

Do not use this veterinary medicinal product after the expiry date which is stated on the label 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 wastewater or household waste.

Use take-back schemes for the disposal of any unused veterinary medicinal product or waste materials derived therefrom 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 authorisation numbers and pack sizes**

Pack sizes:

Cardboard box containing one vial of 50 mL  
Cardboard box containing one vial of 100 mL  
Cardboard box containing one vial of 250 mL

Not all pack sizes may be marketed.

**15. Date on which the package leaflet was last revised**

DD month YYYY

Detailed information on this veterinary medicinal product is available in the [Union Product Database](https://medicines.health.europa.eu/veterinary) (<https://medicines.health.europa.eu/veterinary>).

**16. Contact details**

Marketing authorisation holder:

Emdoka , John Lijsenstraat 16, B-2321 Hoogstraten, Belgium

Manufacturer responsible for batch release:

Produlab Pharma bv, NL-4941 SJ Raamsdonksveer, Nederland

Local representatives and contact details to report suspected adverse reactions:

For any information about this veterinary medicinal product, please contact the local representative of the marketing authorisation holder.

**17. Other information**

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