B. PACKAGE LEAFLET

PACKAGE LEAFLET

1. Name of the veterinary medicinal product

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

2. Composition

Each ml contains:

Active substance:	
Flunixin	50.0 mg
(equivalent to 83 mg of flunixin meglumine)	
Excipients:	
Phenol	5.0 mg
Sodium formaldehyde sulfoxylate	2.5 mg
Propylene glycol	207.2 mg

Clear, colourless solution and free from visible 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 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.

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

None.

Special precautions for safe use in animals the target species:

The underlying cause of pain, inflammation or colic should be determined and, when appropriate, antibiotic or re-hydration therapy should be given concurrently

Inject slowly as life threating symptoms of shock can occur due to the content of propylene glycol.
NSAIDs are known to have the potential to delay parturition through a tocolytic effect by inhibiting prostaglandins that are important in signalling the initiation of parturition. The use of the veterinary medicinal product in the immediate post-partum period may interfere with uterine involution and expulsion of foetal membranes resulting in retained placentae.

The veterinary medicinal product should have a temperature close to body temperature. Stop injection immediately after first symptoms of shock and start shock treatment if necessary.

Use of 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 risk. 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 propylenee 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.

The 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 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 inhibitingprostaglandin synthesis, such as diuretics, ACE inhibitors (angiotensin converting enzyme inhibitors) and β-blockers.
Concomitant administration of potentially nephrotoxic drugs (e.g., aminoglycoside antibiotics) should be avoided.

Overdose.
Overdose is associated with gastrointestinal toxicity.Ataxia and incoordination may also occur.
In case of overdose, symptomatic treatment should be administered.

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.

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

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 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].
Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Anaphylaxis (e.g. Anaphylactic shock, Hyperventilation, Convulsion, Collapse, Death)[2] Ataxia (incoordination)[2] Blood and lymphatic system disorder[3], Haemorrhage Digestive tract disorder (gastrointestinal irritation, gastrointestinal ulceration, digestive tract haemorrhage, nausea, blood in faeces, diarrhoea)[1] Delay of parturition[4], stillbirth[4], retained placenta[5] Appetite loss.

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

Horses:

Uncommon (1 to 10 animals / 1,000 animals treated):	Injection site reaction (such as injection site irritation and injection site swelling).
Rare (1 to 10 animals / 10,000 animals treated):	Liver disorder; Renal disorder (Nephropathy, Papillary necrosis)[1].
Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Anaphylaxis (e.g. Anaphylactic shock, Hyperventilation, Convulsion, Collapse, Death)[2]; Ataxia(incoordination)[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 (incoordination)[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: <{national system details}*[listed in Appendix I*]*>.

*[*For the printed material, please refer to the guidance of the annotated QRD template.]*

8 Dosage for each species, routes and method of administration

Intravenous use in cattle.
Intramuscular use in pigs.
Intravenous use in horses.

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

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.

9. Advice on correct administration

10. Withdrawal periods

Cattle:
Meat and offal: 4 days (intravenous use)

Milk: 24 hours(intravenous use).

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

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

11. Special storage precautions

Keep out of the sight and reach of children.

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

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 thereof in accordance with local requirements and with any applicable national collection systems. These measures should help to protect the environment.

Ask your veterinary 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:
Box with one vial of 100 ml,
Box with one vial of 250 ml.

Not all pack sizes may be marketed.

15. Date on which the package leaflet was last revised

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

Laboratorios Syva, S.A.
Calle Marqués de la Ensenada, 16
28004 MADRID
ESPAÑA

Manufacturer responsible for batch release:

Laboratorios Syva S.A.
Avenida del Párroco Pablo Díez, 49-57
San Andrés del Rabanedo
24010 LEÓN
ESPAÑA

<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.