ANNEX III

LABELLING AND PACKAGE LEAFLET

B. PACKAGE LEAFLET

PACKAGE LEAFLET

1. Name of the veterinary medicinal product

KETOPROCEN 150 mg/ml solution for injection for cattle, pigs and horses

2. Composition

Each ml contains:

Active substance:
Ketoprofen 150 mg

Excipients:
Benzyl alcohol (E1519) 10 mg

Clear and colourless to yellowish solution free from visible particles.

3. Target species

Cattle, pigs and horses.

4. Indications for use

Cattle:
- Reduction of inflammation and pain associated with post-partum, musculoskeletal disorders and lameness.
- Reduction of fever associated with bovine respiratory disease.
- Reduction of inflammation, fever and pain in acute clinical mastitis in combination with antimicrobial therapy where appropriate.

Pigs:
- Reduction of pyrexia in cases of respiratory disease and Postpartum Dysgalactia Syndrome-PDS-(Metritis Mastitis Agalactia syndrome) in sows, in combination with antimicrobial therapy, where appropriate.

Horses:
- Reduction of inflammation and pain associated with osteoarticular and musculoskeletal disorders (lameness, laminitis, osteoarthritis, synovitis, tendinitis, etc.)
- Reduction of postoperative pain and inflammation.
- Reduction of visceral pain associated with colic.

5. Contraindications

Do not use in animals where there is the possibility of gastro-intestinal ulceration or bleeding, in order not to aggravate their situation.
Do not use in animals suffering from cardiac, hepatic, or renal disease.
Do not use in cases of hypersensitivity to the active substance, acetylsalicylic acid or to any of the excipients.
Do not use in animals with evidence of blood dyscrasia or coagulopathy.
Do not use with other non-steroidal antiinflammatory drugs (NSAIDs) concurrently or within 24 hours of each other.

6. Special warnings

Special warnings:

None.

Special precautions for safe use in the target species:

Do not exceed the recommended dose. Do not exceed the recommended treatment period.
The use of ketoprofen is not recommended in foals less than one month of age.
When administering to animals of less than 6 weeks of age, ponies or in aged animals it is necessary to adjust the dose accurately as well as to perform a close clinical follow-up.
Avoid intra-arterial injection.
Avoid use in any dehydrated, hypovolaemic or hypotensive animals as there is a potential risk of increased renal toxicity.
Since gastric ulceration is a common finding in PMWS (Post-weaning Multisystemic Wasting Syndrome), the use of ketoprofen in pigs affected by this pathology is not recommended, in order not to aggravate their situation.
In horses, avoid extravascular administration.

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

Hypersensitivity reactions (skin rash, urticaria) could occur. People with known hypersensitivity to the active substance or to any of the excipients should avoid contact with the veterinary medicinal product.
Avoid contact with the skin, eyes and mucous membranes.
In case of accidental skin, eye or mucous membrane contact, wash the affected area thoroughly with clean running water immediately. Seek medical advice if irritation persists.
Avoid accidental self-injection. 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.

Pregnancy:

Laboratory studies in rats, mice and rabbits, and in cattle have not produced any evidence of adverse effects. Can be used during pregnancy in cows.
The safety of the veterinary medicinal product has not been established during pregnancy in sows and mares. Use only according to the benefit-risk assessment by the responsible veterinarian.

Lactation:

Can be used during lactation in cows and sows.
The use is not recommended in lactating mares.

Interaction with other medicinal products and other forms of interaction:

Concurrent administration of diuretics or potentially nephrotoxic drugs should be avoided since there is an increase of renal disturbances, including renal failure. This is secondary to the diminished blood flow caused by the inhibition of prostaglandins synthesis.

Do not administer other non-steroidal anti-inflammatory drugs (NSAIDs), corticosteroids, anticoagulants or diuretics concurrently or within 24 hours of administration of the veterinary medicinal product since the risk of gastrointestinal ulceration and other adverse reactions may be exacerbated.

The treatment free period should however take into account the pharmacological properties of the veterinary medicinal products used previously.
Ketoprofen is highly bound to plasma proteins and may compete with other highly bound drugs which can lead to toxic effects.

Overdose:

Overdose with non-steroidal anti-inflammatory drugs can lead to gastro-intestinal ulceration, loss of proteins, hepatic and renal impairment.

In tolerance studies performed in pigs, up to 25% of the animals treated at three times the maximum recommended dose (9 mg/kg bw) for three days or at the recommended dose (3 mg/kg bw) for triple the maximum recommended time (9 days) showed erosive and/or ulcerative lesions in both the aglandular (pars oesophagica) and glandular parts of the stomach. Early signs of toxicity include loss of appetite and pasty faeces or diarrhoea.

The intramuscular administration of the veterinary medicinal product to cattle, at up to 3 times the recommended dose or for 3 times the recommended duration of the treatment (9 days) did not result in clinical signs of intolerance. However, inflammation mas well as necrotic subclinical lesions were detected at the injection site of the treated animals as well as an increase in CPK levels. The histopathological examination showed erosive or ulcerative abomasal lesions related to both dosage regimes.

Horses have been found to tolerate intravenous dosages of ketoprofen up to 5 times the recommended dose for three times the recommended duration (15 days) with no evidence of toxic effects.

If clinical signs of overdose are observed, there is no specific antidote, therefore symptomatic treatment should be initiated.

Special restrictions for use and special conditions for use:

Not applicable.

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 and pigs:

Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Injection site necrosis[1] Digestive tract disorder[2] Renal disorder

[1] When injected intramuscularly. Lesions are subclinical, mild and gradually resolve in the days after completion of treatment. Administration in the neck region minimizes the extension and severity of these lesions.
[2] Erosive and ulcerative lesions after repeated administrations, gastric intolerance.

Horses:

Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Injection site necrosis[1] Injection site reaction[2] Digestive tract disorder[3] Renal disorder

[1] When injected intramuscularly. Lesions are subclinical, mild and gradually resolve in the days after completion of treatment. Administration in the neck region minimizes the extension and severity of these lesions.

[2] Local reaction resolving after 5 days, after one administration of the veterinary medicinal product at the recommended volume by extravascular route.
[3] Erosive and ulcerative lesions after repeated administrations, gastric intolerance.

If side effects occur treatment must be stopped and the advice of a veterinarian should be sought. Reporting adverse events is important. It allows continuous safety monitoring of a veterinary medicinal 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

Intravenous or intramuscular use.

Cattle:
3 mg ketoprofen/kg body weight, i.e. 1 ml of the veterinary medicinal product per 50 kg body weight/day, administered via the intravenous or intramuscular route, preferably in the neck region.
The duration of treatment is 1-3 days and should be established according to the severity and duration of symptoms.

Pigs:
3 mg ketoprofen/kg body weight, i.e. 1 ml of the veterinary medicinal product per 50 kg body weight/day, administered via the intramuscular route on a single occasion.
Depending on the response observed and based on the benefit-risk analysis by the responsible veterinarian, the treatment may be repeated at 24-hour intervals for a maximum of three treatments. Each injection should be administered at a different site.

Horses:
2.2 mg ketoprofen/kg body weight, i.e. 0.75 ml of the veterinary medicinal product per 50 kg body weight/day, administered via the intravenous route.

The duration of treatment is 1-5 days, and should be established according to the severity and duration of symptoms. In the case of colic, one injection is usually sufficient. A second administration of ketoprofen requires a clinical re-examination.

To ensure a correct dosage, body weight should be determined as accurately as possible

9. Advice on correct administration

For multiple vial entry, an aspirating needle or multi-dose syringe is recommended to avoid excessive broaching of the stopper.

The cap may be safely punctured up to 30 times.

10. Withdrawal periods

Cattle:
Meat and offal: 2 days
Milk: zero hours

Horses:
Meat and offal: 1 day

Not authorised for use in animals producing milk for human consumption.

Pigs:
Meat and offal: 3 days

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 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 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 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

Marketing authorisation number:

Package sizes:
- Cardboard box with 1 glass vial of 100 ml
- Cardboard box with 1 glass vial of 250 ml
- Cardboard box with 1 PP vial of 100 ml
- Cardboard box with 1 PP vial of 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 manufacturer responsible for batch release and contact details to report suspected adverse reactions:
CENAVISA, S.L.
C/dels Boters 4
43205 Reus (SPAIN)

Tel: +34 977 75 72 73
E-mail: farmacovigilancia@cenavisa.com

17. Other information