

ANNEX III
LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE AND THE IMMEDIATE PACKAGE

Individual box for a bottle of 500 ml
Label for a bottle of 500 ml

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

KETOPROCEN 300 mg/ml solution for use in drinking water for cattle and pigs (BG, EL, ES, HU, LT, LV, PL, PT, RO)
Kadir 300 mg/ml solution for use in drinking water for cattle and pigs (CZ, EE)

Ketoprofen

2. STATEMENT OF ACTIVE SUBSTANCES

Each ml contains:

Active substance:

Ketoprofen 300 mg

3. PHARMACEUTICAL FORM

Solution for use in drinking water.

4. PACKAGE SIZE

500 ml.

5. TARGET SPECIES

Cattle (calves) and pigs for fattening.

6. INDICATION(S)

7. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.

8. WITHDRAWAL PERIOD(S)

Withdrawal period(s):

Cattle (calves) and pigs for fattening: Meat and offal: 1 day.

9. SPECIAL WARNING(S), IF NECESSARY

Read the package leaflet before use.

10. EXPIRY DATE

EXP {month/year}

Once opened use by 9 months.

Once diluted use within 24 hours.

11. SPECIAL STORAGE CONDITIONS

12. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCTS OR WASTE MATERIALS, IF ANY

Dispose of waste material in accordance with local requirements.

Disposal: read package leaflet.

13. THE WORDS “FOR ANIMAL TREATMENT ONLY” AND CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE, IF APPLICABLE

For animal treatment only. To be supplied only on veterinary prescription.

Administration by a veterinarian surgeon or under their direct responsibility.

14. THE WORDS “KEEP OUT OF THE SIGHT AND REACH OF CHILDREN”

Keep out of the sight and reach of children.

15. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

CENAVISA S.L.

Camí Pedra Estela s/n

43205 Reus

SPAIN

16. MARKETING AUTHORISATION NUMBER(S)

17. MANUFACTURER’S BATCH NUMBER

Lot {number}

B. PACKAGE LEAFLET

PACKAGE LEAFLET:

KETOPROCEN 300 mg/ml solution for use in drinking water

1. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER AND OF THE MANUFACTURING AUTHORISATION HOLDER RESPONSIBLE FOR BATCH RELEASE, IF DIFFERENT

Marketing authorisation holder and manufacturer responsible for batch release:

CENAVISA S.L.
Camí Pedra Estela s/n
43205 Reus
SPAIN

2. NAME OF THE VETERINARY MEDICINAL PRODUCT

KETOPROCEN 300 mg/ml solution for use in drinking water for cattle and pigs (BG, EL, ES, HU, LT, LV, PL, PT, RO)

Kadir 300 mg/ml solution for use in drinking water for cattle and pigs (CZ, EE)

Ketoprofen

3. STATEMENT OF THE ACTIVE SUBSTANCE(S) AND OTHER INGREDIENT(S)

Each ml contains:
300 mg of Ketoprofen as active substance.

Clear yellowish solution.

4. INDICATION(S)

Cattle (calves) and pigs for fattening: Treatment for the reduction of pyrexia and dyspnoea associated with respiratory disease in combination with appropriate anti-infective therapy.

5. CONTRAINDICATIONS

Do not administer to suckling calves.

Do not administer to fasting animals or animals with limited access to feed.

Do not use in animals where there is the possibility of gastrointestinal alterations, ulceration or bleeding in order not to aggravate their situation.

Do not use in dehydrated or hypovolemic or hypotensive animal due to the potential risk of increased renal toxicity.

Do not administer to swine fattened at extensive or semi-extensive production farms with access to soil or foreign objects that may damage the gastric mucosa, or with a high parasite burden, or under a severe stress situation.

Do not use in animals suffering from cardiac, hepatic, or renal disease.

Do not use where there is evidence of blood dyscrasia.

Do not use in case of hypersensitivity to ketoprofen or aspirin or to any of the excipients.

Do not use other non-steroidal anti-inflammatory drugs (NSAIDs) concurrently or within 24 hours of each other.

6. ADVERSE REACTIONS

The administration of ketoprofen in pigs at the recommended therapeutic dosage may cause superficial and deep erosion of the gastrointestinal tract.

Serious adverse reactions of a gastric nature have very rarely been observed in weaning calves under severe stressful situations (transportation, dehydration, fasting, etc). Cases of gastric ulceration resulting in fatality have been observed in black Iberian pigs, which have been related to being fattened at soil stations with a high parasite burden and the ingestion of foreign bodies. Other cases in intensive farming have been related to forced fasting situations prior or during treatment.

Transitory softening of faeces may occur which, in any event, disappears during or at the end of the treatment.

If side effects occur treatment must be stopped for the whole group and the advice of a veterinarian should be sought.

The frequency of adverse reactions is defined using the following convention:

- very common (more than 1 in 10 animals treated displaying adverse reaction(s))
- common (more than 1 but less than 10 animals in 100 animals treated)
- uncommon (more than 1 but less than 10 animals in 1,000 animals treated)
- rare (more than 1 but less than 10 animals in 10,000 animals treated)
- very rare (less than 1 animal in 10,000 animals treated, including isolated reports).

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 inform your veterinary surgeon.

Alternatively you can report via your national reporting system {national system details}.

7. TARGET SPECIES

Cattle (calves) and pigs for fattening.

8. DOSAGE FOR EACH SPECIES, ROUTE(S) AND METHOD OF ADMINISTRATION

In drinking water use:

Cattle (calves):

3 mg of ketoprofen/kg bw/day (equivalent to 1 ml/100 kg bw/day of the veterinary medicinal product).

Pigs (pigs for fattening):

1.5 - 3 mg of ketoprofen/kg bw/day (equivalent to 0.5 - 1 ml/100 kg bw/day of the veterinary medicinal product). A dose of 1.5 mg/kg is effective for the treatment of mild to moderate inflammatory processes (body temperature < 41°C). Dose must be increased up to 3 mg of ketoprofen /kg bw to treat more severe cases.

Treatment should be given for one day. It can be continued for another 1-2 days after a risk/benefit assessment by the responsible veterinarian; see also special warnings for each target species and adverse reactions.

Method of Administration:

The veterinary medicinal product is administered by the oral route, diluted in drinking water. Administration over a 24 hour period is recommended. Medicated water should be the only water supply during the period of treatment and should be refreshed every 24 hours. The veterinary medicinal product may be put directly into the header tank or introduced via a

water proportioner pump. Once the treatment period has finished, the animals should be given unmedicated water.

The animals must have *ad libitum* access to food and medicated water before and during treatment. Start the treatment of recumbent animals with the parenteral form.

To prevent overdosing, pigs should be grouped according to bodyweight and an average bodyweight estimated as accurately as possible.

The water intake of the animals to be treated should be measured before calculating the total amount of veterinary medicinal product to be administered each day. In order to calculate accurately the rate of incorporation of the veterinary medicinal product in drinking water, it is necessary to estimate the mean weight and the consumption of water of the animals to be treated, based on the average for the days immediately before treatment.

If the veterinary medicinal product is administered by adding it directly into the drinking water tank, this must contain enough water for the level of consumption that is anticipated for the following 24 hours. Add the quantity of veterinary medicinal product that results from the following formula to the tank:

$$\begin{array}{lcl} \text{ml KETOPROCEN} & & \text{Mean animal weight (kg) x number of animals to be} \\ \text{300 mg/ml to be added} & & \text{treated x dose (ml/100 kg)} \\ \text{the water tank} & = & \hline \text{every 24 hours} & & 100 \end{array}$$

If the veterinary medicinal product is administered by a direct feeder into the water pipes, without first being diluted, the proper concentration of the veterinary medicinal product is obtained by applying the following formula:

$$\begin{array}{lcl} \text{ml KETOPROCEN} & & \text{Mean animal weight (kg) x dose (ml/100 kg)} \\ \text{300 mg/ml / L of} & & \\ \text{drinking water} & = & \hline & & \text{Mean daily water intake per animal (L) x 100} \end{array}$$

In the case of prior dilution being necessary, the resulting concentration has to be duly adapted.

In order to ensure the consumption of the proper dosage throughout the whole of the treatment, it will be necessary to adjust the incorporation rate into the drinking water on a daily basis.

9. ADVICE ON CORRECT ADMINISTRATION

Water intake of treated animals should be monitored to ensure adequate intake. Individual animal medication, preferably by injection, will be required if daily water intake is insufficient.

10. WITHDRAWAL PERIOD(S)

Cattle (calves) and pigs for fattening: Meat and offal: 1 day.

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 container: 9 months.

Shelf life after dilution according to directions: 24 hours.

12. SPECIAL WARNINGS

Special warnings for each target species:

None.

Special precautions for use in animals:

The presence of food or milk decreases oral absorption.

As ketoprofen may provoke gastrointestinal ulcerations, the use is not recommended in cases of PMWS (post-weaning multisystemic wasting syndrome) because ulcers are already frequently associated with this pathology.

To reduce the risk of adverse reactions do not exceed the recommended dose or duration of treatment.

When administering to pigs of less than 6 weeks of age or in aged animals it is necessary to adjust the dose accurately as well as to perform a close clinical follow-up.

To reduce the risk of ulceration treatment should be administered over 24 hours. For safety reasons the maximum treatment duration should not exceed 3 days. If side effects occur treatment must be stopped and the advice of a veterinarian should be sought. Treatment must be suspended for the whole group.

Water intake of treated animals should be monitored to ensure adequate intake. Individual animal medication, preferably by injection, will be required if daily water intake is insufficient.

Avoid use in dehydrated, hypovolaemic or hypotensive animals as there is a potential risk of increased renal toxicity.

This veterinary medicinal product does not contain any antimicrobial preservative.

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

The veterinary medicinal product may cause hypersensitivity reactions (skin, rash, urticaria). People with known hypersensitivity to ketoprofen or other non-steroidal anti-inflammatory drugs (NSAIDs) should avoid contact with the veterinary medicinal product.

Personal protective equipment consisting of rubber gloves and safety glasses should be worn when mixing the veterinary medicinal product. In case of accidental spillage onto skin, the affected area should be rinsed immediately with water. In case of accidental eye contact, irrigate the eyes thoroughly with clean running water immediately. Seek medical advice if the irritation persists. Contaminated clothing should be removed and any splashes on to the skin should be washed off immediately.

Wash hands after use.

Pregnancy:

Do not use in pregnant sows.

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 increased risk of renal disturbances. This is secondary to the diminished blood flow caused by the inhibition of prostaglandins.

This veterinary medicinal product should not be administered concurrently with other NSAIDs or glucocorticosteroids due to the risk of exacerbating gastrointestinal ulceration.

Concurrent treatment with other anti-inflammatory substances may result in additional or increased adverse effects. A period of at least 24 hours should be observed between treatment with other anti-inflammatories and this veterinary medicinal product.

The treatment-free period should, however, take into account the pharmacological properties of the products used previously.

Anticoagulants, particularly coumarin derivatives such as warfarin, should not be used in combination with ketoprofen.

Ketoprofen is highly bound to plasma proteins. The concomitant administration of substances that are also highly plasma protein bound may compete with ketoprofen with the possibility of consequent toxic effects due to the unbound fraction of the drug.

Overdose (symptoms, emergency procedures, antidotes):

Overdose with NSAIDS can lead to gastro-intestinal ulceration, loss of proteins, hepatic and renal impairment. In tolerance studies performed with the veterinary medicinal product when administered in drinking water to cattle and pigs, up to 25% of the animals treated at five times the maximum recommended dose (15 mg/kg) for three days or at the recommended dose (3 mg/kg) for triple the maximum recommended time (9 days) showed gastric ulcerative lesions. Early clinical signs of toxicity include loss of appetite and pasty faeces or diarrhoea. In case of overdosage, symptomatic treatment should be initiated. The occurrence of ulcers is dose dependent to a limited extent.

Incompatibilities:

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

13. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCT OR WASTE MATERIALS, IF ANY

Medicines should not be disposed of via wastewater or household waste.

Ask your veterinary surgeon or pharmacist how to dispose of medicines no longer required. These measures should help to protect the environment.

14. DATE ON WHICH THE PACKAGE LEAFLET WAS LAST APPROVED

15. OTHER INFORMATION

Pack size:

Cardboard box with 1 bottle containing 500 ml.

For animal treatment only. To be supplied only on veterinary prescription.

Administration by a veterinarian surgeon or under their direct responsibility.