**ANNEX III**

**LABELLING AND PACKAGE LEAFLET**

**PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGE - <u>COMBINED LABEL AND PACKAGE LEAFLET</u>**

**BOTTLE 500 ml**

## 1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Ketink 300 mg/ml solution for use in drinking water for cattle and pigs [AT, BG, CY, DE, ES, HU, NL, PL, PT, RO, SI]
Ainil 300 mg/ml solution for use in drinking water for cattle and pigs [EL, IT]
Aristal 300 mg/ml solution for use in drinking water for cattle and pigs [BE]
Ketisio 300 mg/ml solution for use in drinking water for cattle and pigs [ES]

## 2. COMPOSITION

Each ml contains:

**Active substance:**
Ketoprofen 300 mg

Clear yellowish solution

## 3. PACKAGE SIZE

500 ml

## 4. TARGET SPECIES

Cattle (calf) and pigs (for fattening).

## 5. INDICATIONS FOR USE

**Indications for use**
Treatment for the reduction of pyrexia and dyspnoea associated with respiratory disease in combination with anti-infective therapy, as appropriate.

## 6. CONTRAINDICATIONS

**Contraindications**
Do not use in suckling calves.
Do not use in fasting animals or animals with limited access to feed.
Do not use in animals in which there is the possibility of gastrointestinal alterations, ulceration or bleeding in order to not aggravate their situation.
Do not use in dehydrated, hypovolemic or hypotensive animals due to the potential increased risk of renal toxicity.
Do not use in 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 in animals when there is evidence of blood dyscrasia.
Do not use in cases of hypersensitivity to ketoprofen, to acetylsalicylic acid or to any of the excipients.

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

## 7. SPECIAL WARNINGS

**Special warnings**

Special warnings:
Water intake of treated animals should be monitored to ensure adequate intake. Individual animal medication, preferably by injection with a veterinary medicinal product, which is intended for injection, will be required if daily water intake is insufficient.

Special precautions for safe use in the target species:
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 administered to pigs less than 6 weeks old or to elderly pigs it is necessary to adjust the dose accurately as well as to perform a close clinical follow-up.
It is recommended that the daily dose is administered over a period of 24 hours. The total daily dose should not be administered over a shorter period than recommended as this has been shown to result in more severe gastric ulceration. 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.
Avoid use in dehydrated, hypovolemic or hypotensive animals as there potentially is an increased risk of a 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 any of the excipients should avoid contact with the veterinary medicinal product.
Handle the veterinary medicinal product with care to avoid contact with skin and eyes while adding it to water.
Personal protective equipment consisting of rubber gloves and safety glasses should be worn when handling 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 irritation persists.
Contaminated clothing should be removed and any splashes on to the skin should be washed off immediately.
Wash hands after use.
Do not smoke, eat or drink while handling the veterinary medicinal product.

Pregnancy:
Do not use in pregnant sows.

Interactions 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. Consequently, 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:
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 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.

Special restrictions for use and special conditions for use:

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

## 8. ADVERSE EVENTS

**Adverse events**
Cattle (calf):

| | |
|---|---|
| Very rare<br>(<1 animal / 10,000 animals treated, including isolated reports): | Gastric ulcer[1], soft stool[2] |

[1] Serious adverse event observed under severe stressful situations (transportation, dehydration, fasting, etc)
[2] Transitory, which disappears during or at the end of the treatment

Pigs (for fattening):

| | |
|---|---|
| Very rare<br>(<1 animal / 10,000 animals treated, including isolated reports): | Gastric ulcer[3], soft stool[4] |

[3] At the recommended therapeutic dose may cause superficial and deep erosion of the gastrointestinal tract. Observed also in black Iberian pigs resulting in fatality related to being fattened at soil stations with a high parasite burden and the ingestion of foreign bodies. In intensive farming have been related to forced fasting situations prior or during treatment.
[4] Transitory, which 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.

Reporting adverse events is important. It allows continuous safety monitoring of a product. If you notice any side effects, even those not already listed on this label, 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 on this label, or via your national reporting system {national system details}.

## 9. DOSAGE FOR EACH TARGET SPECIES, ROUTES AND METHOD OF ADMINISTRATION

**Dosage for each species, routes and method of administration**

In drinking water use.

Cattle (calf)
3 mg ketoprofen/kg body weight/day (equivalent to 1 ml of the veterinary medicinal product/100 kg b.w./day)

Pig (for fattening)
1.5 - 3 mg ketoprofen/kg body weight/day (equivalent to 0.5 - 1 ml of the veterinary medicinal product/100 kg b.w./day).
The dose of 1.5 mg/kg is effective in the treatment of mild to moderate processes (body temperature < 41°C). The dose must be increased up to 3 mg ketoprofen/kg b.w. to treat more severe cases.
Treatment should be administered for one day. It can be extended for another 1-2 days after a risk/benefit assessment has been carried out by the responsible veterinarian; see also sections Special warnings and Adverse events.

## 10. ADVICE ON CORRECT ADMINISTRATION

**Advice on correct 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 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. Any medicated water which is not consumed within 24 hours should be discarded.
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 ensure a correct dosage, body weight should be determined as accurately as possible.

The water intake of the animals to be treated should be measured before calculating the total amount of product to be administered each day. In order to calculate accurately the rate of incorporation of the 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 it is administered by adding the product directly into the drinking water tank, this must contain enough water for the level of consumption that is anticipated for the following 24 hours.

Based on the recommended dose and the number and weight of animals to be treated, the exact daily concentration of the veterinary medicinal product should be calculated according to the following

formula:

$$\frac{\frac{ml\ veterinary\ medicinal\ product/}{kg\ body\ weight\ day}\ x\ \frac{average\ body\ weight\ (kg)}{of\ animals\ to\ be\ treated}}{average\ daily\ water\ intake\ (l/animal)} = \frac{ml\ veterinary\ medicinal\ product}{per\ litre\ of\ drinking\ water}$$

## 11. WITHDRAWAL PERIODS

**Withdrawal periods**

Cattle: Meat and offal: 1 day
Pigs: Meat and offal: 1 day

## 12. SPECIAL STORAGE PRECAUTIONS

**Special storage precautions**

Keep out of the sight and reach of children
Keep the bottle tightly closed.
Do not use this veterinary medicinal product after the expiry date which is stated on the bottle after Exp. The expiry date refers to the last day of that month.

## 13. SPECIAL PRECAUTIONS FOR DISPOSAL

**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.

## 14. CLASSIFICATION OF VETERINARY MEDICINAL PRODUCTS

**Classification of veterinary medicinal products**
Veterinary medicinal product subject to prescription.

## 15. MARKETING AUTHORISATION NUMBERS AND PACK SIZES

*To be completed nationally*

**Pack sizes**
500 ml

## 16. DATE ON WHICH THE LABEL WAS LAST REVISED

**Date on which the label was last revised**

DD/MM/YYY

Detailed information on this veterinary medicinal product is available in the Union Product Database.

## 17. CONTACT DETAILS

**Contact details**

Marketing authorisation holder:
LIVISTO Int'l, S.L.
Av. Universitat Autònoma, 29
08290 Cerdanyola del Vallès
(Barcelona), Spain

Manufacturer responsible for batch release:
Industrial Veterinaria, S.A.
Esmeralda, 19
E-08950 Esplugues de Llobregat (Barcelona) Spain

Local representatives <and contact details to report suspected adverse reactions>:
*To be completed nationally*

## 18. OTHER INFORMATION

## 19. THE WORDS "FOR ANIMAL TREATMENT ONLY"

For animal treatment only.

## 20. EXPIRY DATE

Exp {mm/yyyy}

Once broached use by…
Shelf life after first opening the immediate packaging: 3 months
Shelf life after dilution according to directions: 24 hours

## 21. BATCH NUMBER

Lot {number}