SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Ketoxyme 100 mg/ml Solution for Use in Drinking Water

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:
Active substance:
Ketoprofen 100 mg
Excipients:
Benzyl alcohol (E 1519) 20 mg

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for use in drinking water.
Clear and colourless solution.

4. CLINICAL PARTICULARS

4.1 Target species
Pigs.

4.2 Indications for use, specifying the target species
Symptomatic treatment for reduction of pyrexia associated with infectious respiratory diseases in pigs in combination with an appropriate anti-infective therapy, as appropriate.

4.3 Contraindications
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 animals 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 in cases of hypersensitivity to ketoprofen, or aspirin or to any of the excipients.
Do not use where there is evidence of blood dyscrasia.
Do not use other non-steroidal anti-inflammatory drugs (NSAIDs) concurrently or within 24 hours of each other.

4.4 Special warnings for each target species
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.

4.5 Special precautions for use

Special precautions for use in animals

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

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 animalsit 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.

Avoid use in animals with hypoproteinemia due to the increased risk of toxicity caused by the highly plasma protein bound nature of ketoprofen, which may result in toxic effects due to the unbound fraction of the drug.

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

People with known hypersensitivity to ketoprofen or benzyl alcohol should avoid the contact with the veterinary medicinal product.

Personal protective equipment consisting of impenetrable gloves and safety glasses should be worn when mixing the veterinary medicinal product.

In the case of accidental spillage onto skin, the affected area should be washed immediately with soap and water.

In case of accidental eye contact, flush the eyes thoroughly with clean running water immediately. Seek medical advice if irritation persists.

Hypersensitivity reactions (skin rash, urticaria) could occur. If irritation persists and you develop such symptoms following exposure, you should seek medical advice and show the label or package leaflet to the physician. Swelling of the face, lips, or eyes or difficulty breathing, are more serious symptoms and require urgent medical attention.

Contaminated clothing should be removed immediately.

Wash hands after use.

4.6 Adverse reactions (frequency and seriousness)

Using the veterinary medicinal product according with the proposed posology:

- In very rare occasions gastric symptoms (as gastritis, gastric erosion and gastric ulceration) may occur. Where administration is performed over a 24 hour period, no severe ulcers were identified.
- In very rare occasions the feed intake may decrease.

In tolerance studies, in which the treatment was carried out during 3 to 9 days, ulcers have been observed in very common occasions. It is recommended that the veterinary medicinal product is administered in accordance with the proposed posology to decrease the incidence of gastric ulcerations.

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.

Three days after the cessation of dosing, gastric ulcers generally recover (with some residual scarring) or are in the process of recovery/cicatrisation.

If serious adverse events such as signs of ulcers or gastrointestinal haemorrhage occur, use of the product should be stopped 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)

4.7 Use during pregnancy, lactation or lay

The safety of the veterinary medicinal product has not been established during pregnancy and lactation. The use is not recommended during pregnancy or lactation.

4.8 Interaction with other medicinal products and other forms of interaction

Do not administer in combination with anticoagulants., particularly coumarin derivatives such as warfarin
Concomitant administration of other drugs have to be assessed by the veterinarian responsible.
Do not administer corticosteroids or other NSAIDs concurrently or within 24 hours of each other.
Gastrointestinal tract ulceration may be exacerbated by corticosteroids in animals given non-steroidal anti-inflammatory drugs.
The concomitant administration of active substances that are highly plasma protein bound may demonstrate a competitive effect with the ketoprofen with the possibility of consequent toxic effects due to the unbound fraction of the drug.
Concurrent use with diuretics or potentially nephrotoxic drugs has a higher risk to develop renal disturbances secondary to the diminishing blood flow caused by the inhibition of prostaglandins.

4.9 Amounts to be administered and administration route

The veterinary medicinal product is administered by the oral route, diluted in drinking water at a dose of 3 mg of ketoprofen/kg bodyweight/day (equivalent to 0.3 ml of veterinary medicinal product/10 kg b.w./day). Based on the benefit-risk assessment of the veterinarian, additional administration for another 1-2 days at the most can be considered.
Administration over a 24 hour period is recommended.
Medicated water should be refreshed every 24 hours. The product may be put directly into the header tank or introduced via a water proportioner pump.
The water intake of the pigs to be treated should be measured before calculating the total amount of product to be administered each day.
The following calculation should be made to determine the quantity of product to be added in drinking water daily:

$$\frac{\text{0.03 ml veterinary medicinal product/ kg b.w. / day} \times \text{Average body weight (kg)}}{\text{Average amount of drinking water (L/animal)}} = \text{Total volume (ml)/L of drinking water/day}$$

Medicated water should be the only water supply during the period of treatment.
To prevent overdosing, pigs should be grouped according to bodyweight and an average bodyweight estimated as accurately as possible.

4.10 Overdose (symptoms, emergency procedures, antidotes), if necessary
Overdose up to 3x the recommended dose can cause gastrointestinal ulcers, protein loss, and kidney and liver damage. Early signs of toxicity include loss of appetite and depression. In case of overdosage, symptomatic treatment should be initiated.

4.11 Withdrawal period(s)
Meat and offal: 2 days

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Antiinflammatory and antirheumatic products, non-steroids
ATCvet code: QM01AE03.

5.1 Pharmacodynamic properties
Ketoprofen, 2-(phenyl 3benzoyl) propionic acid, is a nonsteroidal anti-inflammatory drug belonging to the arylpropionic acid group. Ketoprofen inhibits the biosynthesis of PGE2 and PGF2 alpha without affecting the ratio of PGE2/PGF2 alpha and thromboxanes. This mechanism of action results in its anti-inflammatory, anti-pyretic and analgesic activity. These properties are also attributed to its inhibiting effect on bradykinin and superoxide anions together with its stabilizing action on lysosomal membranes.

5.2 Pharmacokinetic particulars
Following oral administration, ketoprofen is readily absorbed and binds strongly to plasma proteins. Bioavailability is high (93%). It is excreted primarily through the kidneys and, to a lesser extent, in the faeces.
In pigs, after oral administration of ketoprofen at a dose rate of 3 mg/kg bw/day in drinking water, ad libitum during the whole day, for 3 consecutive days, the mean C_{max} (maximum plasma concentration) was 1.9 µg/ml and the elimination half-life was 3.77h. The distribution volume after intravenous administration is low (Vd=223.21 mg/kg) and the elimination half-life is short ($t_{1/2}$=2.04h). Plasma clearance is 97.91 ml/h.kg.

The predominant metabolic route is by glucoconjugation, forming the corresponding ketoprofen metabolites (50-80% of the parent drug), which are rapidly excreted through the urine. The liver is the main organ involved in the elimination of the drug. The mean elimination lifetime value was 2.1 hours and MRT 3.1 hours.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients
Benzyl alcohol (E 1519)
Arginine
Citric Acid Monohydrate
Purified Water

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

6.3 Shelf life
Shelf life of the veterinary medicinal product as packaged for sale: 3 years

Shelf life after first opening the immediate packaging: 4 months
Shelf life after dilution according to directions: 24 hours

6.4 Special precautions for storage

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

6.5 Nature and composition of immediate packaging

1 litre white HDPE containers coated with fluorinated polymers, provided with white polypropylene caps with screw top and sealed with a three layer-seal.
Each container is provided with a polypropylene cup measuring device graduated from 10 up to 75 ml.

6.6 Special precautions for the disposal of unused veterinary medicinal product or waste materials derived from the use of such products

Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal product should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Andersen, S.A.
Avda de la Llana 123
08191 Rubi (Barcelona)
Spain

8. MARKETING AUTHORISATION NUMBER

Vm 39897/4001

9. DATE OF FIRST AUTHORISATION

5 August 2014

10. DATE OF REVISION OF THE TEXT

July 2019

PROHIBITION OF SALE, SUPPLY AND/OR USE

Not applicable

Approved 02 July 2019