[Version 8, 10/2012]

ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS (SPC)

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

DINALGEN 300 mg/ml oral solution for cattle and pigs (All countries except UK, IE and ES)
DINALGEN 300 mg/ml oral solution for use in drinking water for cattle and pigs (UK and IE)
DINALGEN CONCENTRADO 300 mg/ml oral solution for cattle and pigs (ES)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

Active substance
Ketoprofen 300 mg

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Oral solution.

Clear yellowish solution.

4. CLINICAL PARTICULARS

4.1 Target species

Fattening Cattle and Pigs

4.2 Indications for use, specifying the target species

Fattening Cattle and Pigs:
Treatment for the reduction of pyrexia and dyspnoea associated with respiratory disease in combination with anti-infective therapy, as appropriate.

4.3 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.
See also section 4.7

4.4 Special warnings for each target species

None.

4.5 Special precautions for use

Special precautions for use in animals

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

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 irritation persists. Contaminated clothing should be removed and any splashes on to the skin should be washed off immediately. Wash hands after use. Hypersensitivity reactions (skin rash, urticaria) could occur. People with known hypersensitivity to the active substance should avoid contact with the veterinary medicinal product.

4.6 Adverse reactions (frequency and seriousness)

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 feces 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

4.7 Use during pregnancy, lactation or lay

Do not use in pregnant sows.

4.8 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 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 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.

4.9 Amounts to be administered and administration route

Oral use:

Cattle
3 mg of ketoprofen/kg bw/d (equivalent to 1 ml/100 kg bw/d of the finished product)

Pigs
1.5 - 3 mg of ketoprofen/kg bw/d (equivalent to 0.5 - 1 ml/100 kg bw/d of the finished product). Dose of 1.5 mg/kg is effective in the treatment of mild to moderate processes (body temperature <41ºC). Dose must be increased up to 3mg 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 4.4 and 4.6.

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 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 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. Add the quantity of product that results from the following formula to the tank:

$$\text{ml DINALGEN 300 mg/ml Oral Sol. to be added to the water tank every 24h} = \frac{\text{Mean animal weight (kg) x number of animals to be treated x Dose (ml/100 kg)}}{100}$$

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

$$\text{ml DINALGEN 300 mg/ml Oral Sol./ L of drinking water} = \frac{\text{Mean animal weight (kg) x Dose (ml/100 kg)}}{\text{Mean daily water intake per animal (L) x 100}}$$

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.

4.10 Overdose (symptoms, emergency procedures, antidotes), if necessary

Overdose with NSAIDS can lead to gastro-intestinal ulceration, loss of proteins, hepatic and renal impairment. In tolerance studies performed with the 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.

4.11 Withdrawal period(s)

Meat and offal: 1 day

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Anti-inflammatory and Antirheumatic Products, Non-Steroids, Propionic acid derivatives.
ATCvet code: QM01 AE 03

5.1 Pharmacodynamic properties

Ketoprofen, 2-(phenyl 3-benzoyl) propionic acid is a non-steroidal anti-inflammatory drug belonging to the arylpropionic acid group. Ketoprofen inhibits the biosynthesis of prostaglandins (PGE2 and PGF2α) without affecting the ratio of PGE2/PGF2α 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.
The antiinflammatory effect is enhanced by the conversion of the (R)-enantiomer to (S)-enantiomer. It is known that the (S)-enantiomer supports the ant-inflammatory effect of ketoprofen.

5.2 Pharmacokinetic particulars

Following oral administration, ketoprofen is readily absorbed and binds strongly to plasma proteins. Ketoprofen is metabolised in the liver and converted into a carbonil-reduced derivation, the RP69400 metabolite.It is excreted primarily through the kidneys and, to a lesser extent, in the faeces.

Cattle:
Following oral gavage administration at a dosage of 3 mg/kg to fattening calves, ketoprofen is absorbed readily (F=100%). Maximum concentrations (Cmax) of 3.7 µg/ml (2.5 to 4.5 µg/ml) are achieved at 72 min (0.33 to 2h) after administration. (Tmax). Following absorption, the pharmacokinetics of ketoprofen are characterised by a low volume of distribution (0.5 l/kg) and a short plasma elimination half-life (2.2 hours).

After repeated oral administration in drinking water in calves, the kinetic profile presents principally 2 different phases per administration day, clearly related to the day-night cycle, which influenced the animal's water consumption. The first phase (first 9 hours post-treatment) corresponded to the absorption phase of the product. Considering the rapid absorption phase for the single administration, the longer phase observed for repeated administrations is due to the administration route: ketoprofen administered via drinking water is consumed by the animals sparsely during the day. The elimination phase observed in the following hours is directly related to the low drinking water consumption by the animals during the night time. When administering the product at 3 mg ketoprofen/kg/d during 3 days in drinking water, the Cmax observed was 1.9 µg/ml (1.6 to 2.4 µg/ml) and Tmax was of 32h (9 to 57 h) after beginning of administrations.

Pigs:
In swine, after oral gavage administration at a dosage of 3 mg ketoprofen/kg, a maximum mean concentration (Cmax) of 10.6 µg/ml (2.2 to 17.2 µg/ml) is attained, in average, at 60 min (0.33 to 2h) after administration (Tmax). Absolute bioavailability is high (84%).

Volume of Distribution following IV administration is low (Vd=0.2 l/kg) and its elimination half-life is short (t1/2= 2.0h). Plasma clearance is 0.06 l/kg.h.

When administering the product at 3 mg ketoprofen/kg/d during 3 days in drinking water in pigs, the kinetic profile is similar to that of cattle. The Cmax observed was 2.7 µg/ml (1.4 to 4.2 µg/ml) and the Tmax was of 16h (6 to 57h) after beginning of administrations

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

L-arginine
Citric acid anhydrous *for pH adjustment*
Purified water.

6.2 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: 5 years
Shelf life after first opening the immediate packaging: 3 months
Shelf life after reconstitution in drinking water: 24 hours

6.4. Special precautions for storage

Keep the bottle tightly closed.

6.5 Nature and composition of immediate packaging

Nature of the container:

White high density polyethylene bottle with high density polyethylene screw cap (100 and 500 ml)

Presentations:
Bottles of 100ml and 500 ml
Includes a 30 ml graduated dosing cup for precise dose adjustment.

Not all pack sizes may be marketed.

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 products should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Ecuphar Veterinaria S.L.U.
C/Cerdanya, 10-12 Planta 6º
08173 Sant Cugat del Vallés

Barcelona (Spain)

8. MARKETING AUTHORISATION NUMBER(S)

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

October 2008 / 13 October 2013

10 DATE OF REVISION OF THE TEXT

05/2022

PROHIBITION OF SALE, SUPPLY AND/OR USE

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