SUMMARY OF THE PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

KetoProPig 100 mg/ml Oral Solution for use in drinking water for Pigs

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

- **Active substance**
  Ketoprofen: 100 mg

- **Excipients**
  Benzyl Alcohol (E1519): 20 mg

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Oral solution

Transparent and colourless liquid.

4. CLINICAL PARTICULARS

4.1 Target species

Pigs (fattening pigs)

4.2 Indications for use, specifying the target species

Symptomatic treatment for reduction of pyrexia in cases of acute infectious respiratory disease in fattening pigs in combination with an appropriate anti-infective therapy.

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 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 animals with a history of hypersensitivity to ketoprofen, aspirin or any of the excipients.

See also section 4.7

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

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 very young 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.

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

- Personal protective equipment consisting of rubber 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, 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)

Feed intake may decrease due to the treatment and the gastric ulcers induced by the treatment.
In tolerance studies ulcers have been observed in up to 70% of the treated animals.
Where administration is performed over a 24 hour period, no severe ulcers were identified. In a punctuated administration of the product (maximal 3 hours for administration), at least 12% of severe ulcers were identified. 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.

4.7 Use during pregnancy, lactation or lay

Pregnancy: Do not use in pregnant animals.
Lactation: Not applicable.

4.8 Interaction with other medicinal products and other forms of interaction

Interactions between Ketoprofen and the most commonly used antibiotics have not been investigated.
Pre-treatment with other anti-inflammatory substances may result in additional or increased adverse effects. Do not administer corticosteroids or other NSAIDs concurrently or within 24 hours of each other. The treatment-free period, however, should take into account the pharmacological properties of the products used previously the product must not be administered in conjunction with other NSAIDs or glucocorticosteroids. 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.
Avoid combining with anticoagulant drugs, particularly coumarin derivatives such as warfarin.
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 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. 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. Once the treatment period has finished, the pigs should be given unmedicated water.

The recommended daily dose is 3 mg of ketoprofen/kg bodyweight equivalent to 0.03 ml of KetoProPig 10% Oral Solution per kg bodyweight.

Duration of treatment: 1 day. Based on the risk-benefit assessment of the veterinarian additional administration for another 1-2 days at the most can be considered; see also 4.4 and 4.6 .

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 KetoProPig 100 mg/ml Oral Solution in ml to be added to the daily consumption of drinking water:

$$\frac{\text{0.03 ml KetoProPig 100 mg/ml / kg bodyweight / day} \times \text{Average body weight (kg) of the animals to be treated}}{\text{Average amount of drinking water / animal (l)}} = \text{ml KetoPro Pig 100 mg/ml / l of drinking water}$$

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 GI 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

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

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. Although it is a cyclooxygenase inhibitor, ketoprofen is said to stabilize lysosomal membranes and antagonizes the actions of bradykinin.

Ketoprofen is a mixture of (R) and (S) enantiomers and possesses anti-inflammatory, analgesic and antipyretic activity. The (R) enantiomer appears to be a more potent analgesic, whilst the (S) form is known to support the major anti-inflammatory activity of ketoprofen. The anti-inflammatory activity is increased by an enantiomer conversion from the (R) to the (S) form."

5.2 Pharmacokinetic particulars

After a single oral administration, the mean C_{max} observed was 10.1 $\mu g.mL^{-1}$ at a mean Tmax of 0.8 h.
The mean ± SD total AUC was 30.5 $\mu g.h.mL^{-1}$. The mean ± SD bioavailability was 93 %.
After repeated oral administration of the same dose in drinking water, 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 8 hours after offering 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.
The mean ± SD observed C_{max} was 1.9 $\mu g.mL^{-1}$. The T_{max} fluctuate between 5 and 32 hours after the beginning of administrations.
After absorption, ketoprofen binds extensively to plasma proteins, mainly albumina, proving that this union is enantioselective. Mean distribution volume was 223.2 mL/kg.
The predominant metabolic route is by glucoconjugation, forming the corresponding ketoprofen metabolites (50-80% of the parent drug), which are rapidly excreted through urine. Liver is the main organ involved in the elimination of the drug. Mean elimination lifetime value was 2.1 hours and MRT 3.1 hours.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Benzyl alcohol (E1519)
Arginine base
Citric Acid Monohydrate
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: 3 years
- Shelf-life after first opening the immediate packaging: 4 months
- Shelf-life after dilution: 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 products should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Labiana Life Sciences S.A.U.
C/Venus 26
Can Parellada Industrial
08228 Terrassa
Barcelona
Spain

8. MARKETING AUTHORISATION NUMBER

Vm 32112/4000

9. DATE OF THE FIRST AUTHORISATION

Date: 16 July 2008

10. DATE OF REVISION OF THE TEXT

Date: October 2013

Approved:  **31/10/2013**