ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

<PARTICULARS TO APPEAR ON THE OUTER PACKAGE>
Cardboard box of 1 litre HDPE bottle

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

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

2. STATEMENT OF ACTIVE AND OTHER SUBSTANCES

Each ml contains:
Ketoprofen: 100 mg
Benzyl Alcohol (E1519): 20 mg

3. PHARMACEUTICAL FORM

Oral Solution

4. PACKAGE SIZE

1 litre

5. TARGET SPECIES

Pigs (fattening pigs)

6. INDICATION(S)

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

7. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.

Administration by oral route, diluted in drinking water. Administration over a 24 hour period is recommended.

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.

8. WITHDRAWAL PERIOD

Meat and offal: 2 days.

9. SPECIAL WARNING(S), IF NECESSARY

Read the package leaflet before use.

USER WARNINGS
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.

10. EXPIRY DATE

EXP {month/year}
Shelf-life after first opening the container: 4 months
Shelf-life after dilution: 24 hours

11. SPECIAL STORAGE CONDITIONS

This product does not require any special storage conditions

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

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

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.

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

Labiana Life Sciences S.A.U.
C/Venus 26
Can Parellada Industrial
Terrassa
08228 Barcelona
Spain
Local representative
Huvepharma NV
Uitbreidingsstraat 80,
2600 Antwerp, Belgium

16. MARKETING AUTHORISATION NUMBER(S)

VM 32112/4000

17. MANUFACTURER'S BATCH NUMBER

Batch: {number}

<PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGE>

1 litre HDPE bottle

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

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

2. STATEMENT OF ACTIVE AND OTHER SUBSTANCES

Each ml contains:
Ketoprofen: 100 mg
Benzyl Alcohol (E1519): 20 mg

3. PHARMACEUTICAL FORM

Oral Solution

4. PACKAGE SIZE

1 litre

5. TARGET SPECIES

Pigs (fattening pigs)

6. INDICATION(S)

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

7. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.

Administration by oral route, diluted in drinking water. Administration over a 24 hour period is recommended.

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.

8. WITHDRAWAL PERIOD

Meat and offal: 2 days.

9. SPECIAL WARNING(S), IF NECESSARY

USER WARNINGS
Read the user warnings in the package leaflet before using the 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.

10. EXPIRY DATE

EXP {month/year}
Shelf-life after first opening the container: 4 months
Shelf-life after dilution: 24 hours

Once broached, use by:

11. SPECIAL STORAGE CONDITIONS

This product does not require any special storage conditions

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

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

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.

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

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

Local representative
Huvepharma NV
Uitbreidingsstraat 80,
2600 Antwerp, Belgium

16. MARKETING AUTHORISATION NUMBER(S)

VM 32112/4000

17. MANUFACTURER'S BATCH NUMBER

Batch: {number}

B. PACKAGE LEAFLET

PACKAGE LEAFLET

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

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

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

Local representative:
Huvepharma NV
Uitbreidingsstraat 80,
2600 Antwerp, Belgium

Manufacturer for the batch release:
Laboratorios Labiana Life Sciences, S.A.
c/ Venus 26 - Can Perellada- 08228 Terrasa - Barcelona
Spain

2. NAME OF THE VETERINARY MEDICINAL PRODUCT

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

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

Each ml contains:
- Active substance: Ketoprofen: 100 mg
- Excipients: Benzyl Alcohol (E1519): 20 mg

4. INDICATION(S)

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

5. 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.

6. ADVERSE REACTIONS

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

7. TARGET SPECIES

Pigs (fattening pigs).

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

The veterinary medicinal product is administered by oral route, diluted in drinking water. Administration over a 24 hour period is recommended.

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.

9. ADVICE ON CORRECT ADMINISTRATION

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 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:

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

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

10. WITHDRAWAL PERIOD

Meat and offal: 2 days.

11. SPECIAL STORAGE PRECAUTIONS

Keep out of the reach and sight of children.
This veterinary medicinal product does not require any special storage conditions.

Shelf-life after first opening the container: 4 months
Shelf-life after dilution: 24 hours
Do not use this veterinary medicinal product after the expiry date which is stated on the label after EXP

12. SPECIAL WARNING(S)

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

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

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.

Overdose (symptoms, emergency procedures, antidotes:

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.

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

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

14. DATE ON WHICH THE PACKAGE LEAFLET WAS LAST APPROVED

15. OTHER INFORMATION

To be supplied only on veterinary prescription.

For any information about this veterinary medicinal product, please contact the local representative of the marketing authorisation holder.

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."

Each container is provided with a plastic cup measuring device graduated from 10 up to 75 ml.

When the container is broached (opened) for the first time, using the in-use shelf-life which is specified on this package leaflet, the date on which any product remaining in the container should be discarded should be worked out. This discard date should be written in the space provided on the label.