[Version 9, 03/2022] corr. 11/2022

ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Dinalgen 60 mg/ml solution for injection for pigs

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:
Active substance:
Ketoprofen 60 mg

Excipients:

Qualitative composition of excipients and other constituents	**Quantitative composition if that information is essential for proper administration of the veterinary medicinal product**
Benzyl alcohol (E1519)	10 mg
L-arginine	
Citric acid (for pH adjustment)	
Water for injection	

Clear colourless solution.

3. CLINICAL INFORMATION

3.1 Target species

Pigs

3.2 Indications for use for each target species

Reduction of pyrexia in cases of respiratory disease and Postpartum Dysglactia Syndrome/Mastitis, Metritis, Agalactiae (MMA syndrome) in sows, in combination with anti-infective therapy, as appropriate.

3.3 Contraindications

Do not use in animals where there is the possibility of gastro-intestinal ulceration or bleeding, in order not to aggravate their situation.
Do not use in animals suffering from cardiac, hepatic, or renal disease.
Do not use in dehydrated or hypovolemic or hypotensive animals due to the potential risk of increased renal toxicity.
Do not use in cases of hypersensitivity to the active substance, acetylsalicylic acid or to any of the excipients.
Do not use where there is evidence of blood dyscrasia or blood coagulation disturbances.
Do not use other non-steroidal anti-inflammatory drugs (NSAIDs) concurrently or within 24 hours of each other.
See also section 3.7

3.4 Special warnings

None.

3.5 Special precautions for use

Special precautions for use in the target species:
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.
Since gastric ulceration is a common finding in PMWS (Post-weaning Multisystemic Wasting Syndrome), the use of ketoprofen in pigs affected by this pathology is not recommended, in order not to aggravate their situation.
Avoid use in dehydrated, hypovolaemic or hypotensive animals as there is a potential risk of increased renal toxicity.

Special precautions to be taken by the person administering the veterinary medicinal product to animals:
Hypersensitivity reactions (skin rash, urticaria) could occur. People with known hypersensitivity to ketoprofen or to any of the excipients should avoid contact with the veterinary medicinal product.
Avoid contact with the skin, eyes and mucous membranes.
In case of accidental skin, eye or mucous membrane contact, irrigate the affected area thoroughly with clean running water immediately. Seek medical advice if irritation persists.
In case of accidental self-injection, seek medical advice immediately and show the package leaflet or the label to the physician.
Wash hands after use.

Special precautions for the protection of the environment:
Not applicable.

3.6 Adverse events

Pigs:

Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Injection site irritation[1] Digestive tract disorders[2]

[1]Intramuscular injection may be followed by transient irritation at the injection site.
[2]The administration of ketoprofen in pigs at the recommended therapeutic dosage may cause superficial erosion and/or superficial ulceration of the gastrointestinal tract.

Reporting adverse events is important. It allows continuous safety monitoring of a veterinary medicinal product. Reports should be sent, preferably via a veterinarian, to either the marketing authorisation holder or its local representative or the national competent authority via the national reporting system. See the package leaflet for respective contact details.

3.7 Use during pregnancy, lactation or lay

The safety of ketoprofen has been investigated in pregnant laboratory animals (rats, mice, rabbits) and cattle. No adverse effects were noted.

The safety of the veterinary medicinal product has not been established during pregnancy in sows. Use only according to the benefit-risk assessment by the responsible veterinarian.

3.8 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 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. 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 and may compete with other highly bound drugs which can lead to toxic effects.

3.9 Administration routes and dosage

Intramuscular use.
3 mg ketoprofen/kg bw, i.e. 1ml of veterinary medicinal product per 20 kg bw, administered once by deep intramuscular injection.
Depending on the response observed and based on the benefit-risk analysis by the responsible veterinarian treatment may be repeated at intervals of 24 hours for a maximum of three treatments. Each injection should be given at a different site.

3.10 Symptoms of overdose (and where applicable, emergency procedures, antidotes)

Overdose with NSAIDS can lead to gastro-intestinal ulceration, loss of proteins, hepatic and renal impairment. In tolerance studies performed in pigs with the product up to 25% of the animals treated at three times the maximum recommended dose (9 mg/kg) for three days or at the recommended dose (3 mg/kg) for triple the maximum recommended time (9 days) showed erosive and/or ulcerative lesions in both the aglandular (*pars oesophagica*) and glandular parts of the stomach. Early signs of toxicity include loss of appetite and pasty faeces or diarrhoea. If overdose symptoms are observed, symptomatic treatment should be initiated. The occurrence of ulcers is dose dependent to a limited extent.

3.11 Special restrictions for use and special conditions for use, including restrictions on the use of antimicrobial and antiparasitic veterinary medicinal products in order to limit the risk of development of resistance

3.12 Withdrawal periods

Meat and offal: 3 days

4. PHARMACOLOGICAL INFORMATION

4.1 ATCvet code:
QM01AE03

4.2 P**harmacodynamics**

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.

4.3 Pharmacokinetics

After intramuscular administration ketoprofen is rapidly absorbed, having a high bioavailability and binding extensively to plasma proteins (>90%). Its elimination from plasma is rapid, although in the inflammatory exudate, it is more persistent. Ketoprofen is metabolized in liver and it is excreted mainly in urine and, to a lesser extent, in faeces.

In pigs, following the intramuscular injection of a single dose of 3 mg/ketoprofen/kg bw, the active drug substance is rapidly absorbed, reaching its average Cmax in plasma (13 μg/ml) between 0,5 and 1 hour (Tmax) after initiation of the treatment. The bioavailability is high, of approximately 96%. Mean distribution volume is low (Vd=0.2 l/kg), and the average elimination half-life is short (T1/2=2 h).

5. PHARMACEUTICAL PARTICULARS

5.1 Major incompatibilities

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

5.2 Shelf life

Shelf-life of the veterinary medicinal product as packaged for sale: 5 years
Shelf-life after first opening the immediate packaging: 28 days

5.3 Special precautions for storage

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

5.4 Nature and composition of immediate packaging

Amber type II glass vials, closed with bromobutyl rubber stoppers and flip-off aluminium caps (100 ml) or aluminium caps (250 ml).

Pack sizes:
Box with 1 vial of 100 ml
Box with 1 vial of 250 ml
Box with 10 vials of 100 ml
Box with 10 vials of 250 ml

Not all pack sizes may be marketed.

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

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 national collection systems applicable to the veterinary medicinal product concerned.

6. MARKETING AUTHORISATION HOLDER

Ecuphar Veterinaria S.L.U.

7. MARKETING AUTHORISATION NUMBER(S)

8. DATE OF FIRST AUTHORISATION

Date of the first authorization:

9. DATE OF LAST REVISION OF THE SUMMARY OF THE PRODUCT CHARACTERISTICS

10. CLASSIFICATION OF VETERINARY MEDICINAL PRODUCTS

Veterinary medicinal product subject to prescription.

Detailed information on this veterinary medicinal product is available in the Union Product Database (https://medicines.health.europa.eu/veterinary).

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

Box with vial(s) of 100 ml/250 ml

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Dinalgen 60 mg/ml solution for injection

2. STATEMENT OF ACTIVE SUBSTANCES

Each ml contains:
Ketoprofen 60 mg

3. PACKAGE SIZE

100 ml
250 ml
10 x100 ml
10x250 ml

4. TARGET SPECIES

Pigs.

5. INDICATIONS

6. ROUTES OF ADMINISTRATION

Intramuscular use.

7. WITHDRAWAL PERIOD

Withdrawal period:
Meat and offal: 3 days

8. EXPIRY DATE

Exp. {mm/yyyy}
Once broached, use within: 28 days
Once broached, use by:…

9. SPECIAL STORAGE CONDITIONS

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

10. THE WORDS "READ THE PACKAGE LEAFLET BEFORE USE"

Read the package leaflet before use.

11. THE WORDS "FOR ANIMAL TREATMENT ONLY"

For animal treatment only.

12. THE WORDS "KEEP OUT OF THE SIGHT AND REACH OF CHILDREN"

Keep out of the sight and reach of children.

13. NAME AOF THE MARKETING AUTHORISATION HOLDER

Ecuphar
An Animalcare Company

14. MARKETING AUTHORISATION NUMBERS

15. BATCH NUMBER

Lot {number}

PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGE

Vials of 100 ml/250 ml

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Dinalgen 60 mg/ml solution for injection

2. STATEMENT OF ACTIVE SUBSTANCES

Each ml contains:
Ketoprofen 60 mg

3. TARGET SPECIES

Pigs.

4. ROUTES OF ADMINISTRATION

Intramuscular use.
Read the package leaflet before use.

5. WITHDRAWAL PERIOD

Withdrawal period:
Meat and offal: 3 days

6. EXPIRY DATE

Exp. {mm/yyyy}
Once broached, use within: 28 days
Once broached, use by …….

7. SPECIAL STORAGE CONDITIONS

8. NAME OF THE MARKETING AUTHORISATION HOLDER

Ecuphar
An Animalcare Company

9. BATCH NUMBER

Lot {number}

B. PACKAGE LEAFLET

PACKAGE LEAFLET

1. Name of the veterinary medicinal product

Dinalgen 60 mg/ml solution for injection for pigs

2. Composition

Each ml contains:

Active substance:
Ketoprofen 60 mg

Excipients:
Benzyl alcohol (E1519) 10 mg

Clear colourless solution.

3. Target species

Pigs.

4. Indications for use

Reduction of pyrexia in cases of respiratory disease and Postpartum Dysglactia Syndrome/Mastitis, Metritis, Agalactiae (MMA syndrome) in sows, in combination with anti-infective therapy, as appropriate.

5. Contraindications

Do not use in animals where there is the possibility of gastro-intestinal ulceration or bleeding, in order not to aggravate their situation.
Do not use in animals suffering from cardiac, hepatic, or renal disease.
Do not use in dehydrated or hypovolemic or hypotensive animals due to the potential risk of increased renal toxicity.
Do not use in cases of hypersensitivity to the active substance, acetylsalicylic acid or to any of the excipients.
Do not use where there is evidence of blood dyscrasia or blood coagulation disturbances.
Do not use other non-steroidal anti-inflammatory drugs (NSAIDs) concurrently or within 24 hours of each other.

6. Special warnings

Special precautions for use in the target species
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.

Since gastric ulceration is a common finding in PMWS (Post-weaning Multisystemic Wasting Syndrome), the use of ketoprofen in pigs affected by this pathology is not recommended, in order not to aggravate their situation.
Avoid use in dehydrated, hypovolaemic or hypotensive animals as there is a potential risk of increased renal toxicity.

Special precautions to be taken by the person administering the veterinary medicinal product to animals
Hypersensitivity reactions (skin rash, urticaria) could occur. People with known hypersensitivity to the ketoprofen or to any of the excipients should avoid contact with the veterinary medicinal product.
Avoid contact with the skin, eyes and mucous membranes.
In case of accidental skin, eye or mucous membrane contact, irrigate the affected area thoroughly with clean running water immediately. Seek medical advice if irritation persists.
In case of accidental self-injection, seek medical advice immediately and show the package leaflet or the label to the physician.
Wash hands after use.

Pregnancy and lactation
The safety of ketoprofen has been investigated in pregnant laboratory animals (rats, mice, rabbits) and cattle. No adverse effects were noted. The safety of the veterinary medicinal product has not been established during pregnancy in sows. Use only according to the benefit-risk assessment by the responsible veterinarian.

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 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. 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 and may compete with other highly bound drugs which can lead to toxic effects.

Overdose
Overdose with NSAIDS can lead to gastro-intestinal ulceration, loss of proteins, hepatic and renal impairment. In tolerance studies performed in pigs with the product up to 25% of the animals treated at three times the maximum recommended dose (9 mg/kg) for three days or at the recommended dose (3 mg/kg) for triple the maximum recommended time (9 days) showed erosive and/or ulcerative lesions in both the aglandular (*pars oesophagica*) and glandular parts of the stomach. Early signs of toxicity include loss of appetite and pasty faeces or diarrhoea. If overdose symptoms are observed, 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.

7. Adverse events

Pigs:

Very rare (<1 animal / 10,000 animals treated, including isolated reports):
Injection site irritation[1] Digestive tract disorders[2]

[1]Intramuscular injection may be followed by transient irritation at the injection site.
[2]The administration of ketoprofen in pigs at the recommended therapeutic dosage may cause superficial erosion and/or superficial ulceration of the gastrointestinal tract.

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

8. Dosage for each species, routes and method of administration

Intramuscular use
3 mg ketoprofen/kg bw, i.e. 1ml of veterinary medicinal product per 20 kg bw, administered once by deep intramuscular injection.
Depending on the response observed, treatment may be repeated at intervals of 24 hours for a maximum of three treatments, at the discretion of the attending veterinarian. Each injection should be given at a different site.

9. Advice on correct administration

In the absence of compatibility studies, this veterinary medicinal product must not be mixed with other substances in the same syringe.

10. Withdrawal period

Meat and offal: 3 days

11. Special storage precautions

Keep out of the sight and reach of children.
This veterinary medicinal product does not require any special storage conditions
Shelf life after first opening the inmediate packaging: 28 days.

Do not use this veterinary medicinal product after the expiry date which is stated on the label and carton after "Exp". The expiry date refers to the last day of that month.

12. Special precautions for the 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.

13. Classification of veterinary medicinal products

Veterinary medicinal product subject to prescription.

14. Marketing authorisation numbers and pack sizes

Marketing authorisation number:

Pack sizes:
Box with 1 vial of 100 ml
Box with 1 vial of 250 ml
Box with 10 vials of 100 ml
Box with 10 vials of 250 ml

Not all pack sizes may be marketed.

15. Date on which the package leaflet was last revised

Detailed information on this veterinary medicinal product is available in the Union Product Database (https://medicines.health.europa.eu/veterinary).

16. Contact details

Marketing authorisation holder and contact details to report suspected adverse reactions:

Ecuphar Veterinaria S.L.U.
C/ Cerdanya 10-12, planta 6
08173 Sant Cugat del Vallés, Barcelona (Spain)
Tel: +34 935955000
Email: info@ecuphar.es

Manufacturer responsible for batch release:

Zoetis Manufacturing & Research Spain, S.L.
Crta. Camprodón s/n, 17813 Vall de Bianya (Girona)

España