

## **SUMMARY OF PRODUCT CHARACTERISTICS**

### **1. NAME OF THE VETERINARY MEDICINAL PRODUCT**

DANIDOL 60 mg/ml solution for injection for pigs (all countries except ES)  
EDERAL 60 mg/ml solution for injection for pigs (ES)

### **2. QUALITATIVE AND QUANTITATIVE COMPOSITION**

Each 1 ml of the product contains:

Ketoprofen	60 mg
Benzyl alcohol (E1519)	10 mg

For a full list of excipients, see section 6.1.

### **3. PHARMACEUTICAL FORM**

Solution for injection  
Clear colourless solution

### **4. CLINICAL PARTICULARS**

#### **4.1 Target species**

Pigs

#### **4.2 Indications for use, specifying the target species**

Pigs:

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

#### **4.3 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 animals that have previously shown signs of hypersensitivity to ketoprofen or aspirin or any of the excipients.

Do not use where there is evidence of blood dyscrasia or blood coagulation disturbances

See also section 4.7

#### **4.4 Special warnings for each target species**

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.

#### **4.5 Special precautions for use**

##### **Special precautions for use in animals**

Do not exceed the recommended dose or duration of treatment

When administering to pigs of less than 6 weeks of age it is necessary to adjust the dose accurately as well as to perform a close clinical follow-up.

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

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.

Hypersensitivity reactions (skin rash, urticaria) could occur. People with known hypersensitivity to the active substance should avoid contact with this product.

#### **4.6 Adverse reactions (frequency and seriousness)**

Intramuscular injection may be followed by transient irritation at the injection site.

The administration of ketoprofen in pigs at the recommended therapeutic dosage may cause superficial erosion and/or superficial ulceration of the gastrointestinal tract.

If side effects occur treatment must be stopped and the advice of a veterinarian should be sought.

#### **4.7 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. As the safety of ketoprofen has not been assessed in pregnant sows, the product should be used in this case only according to the benefit/risk assessment by the responsible veterinarian.

#### **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. Concurrent administration of diuretics or potentially nephrotoxic drugs should be avoided since there is an increase of renal disturbances. This is secondary to the diminished blood flow caused by the inhibition of prostaglandins.

This product must not be administered in conjunction with other NSAIDs or glucocorticosteroids since gastrointestinal ulceration may be exacerbated.

Pre-treatment with other anti-inflammatory substances may result in additional or increased adverse effects and accordingly a treatment-free period with such drugs should be observed for at least 24 hours before the commencement of treatment. 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.

#### **4.9 Amounts to be administered and administration route**

Intramuscular use.

Administer the product via the intramuscular route at a dose of 3mg/Kg bodyweight of ketoprofen, equivalent to 1ml/20Kg bodyweight of product, on a single occasion. 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.

#### **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 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.

#### **4.11 Withdrawal period(s)**

Meat & offal: 3 days

### **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 (PGE<sub>2</sub> and PGF<sub>2</sub>α) without affecting the ratio of PGE<sub>2</sub>/PGF<sub>2</sub>α 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 anti-inflammatory effect of ketoprofen.

#### **5.2 Pharmacokinetic particulars**

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 body weight, the active drug substance is rapidly absorbed, reaching its average C<sub>max</sub> in plasma (13 µg/ml) between 0,5 and 1 hour (T<sub>max</sub>) after initiation of the treatment. The bioavailability is high, of approximately 96%. Mean distribution volume is low (V<sub>d</sub>=0.2 l/kg), and the average elimination half-life is short (T<sub>1/2</sub>=2 h).

## **6. PHARMACEUTICAL PARTICULARS**

### **6.1 List of excipients**

L-arginine  
Benzyl alcohol (E1519)  
Citric acid anhydrous for pH adjustment  
Water for injection

### **6.2 Incompatibilities**

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

### **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: 28 days

### **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**

#### Nature of the container:

Amber type II glass vials, closed with bromobutyl rubber stoppers and aluminium caps.

#### Presentations:

Vial containing 100 ml  
Vial containing 250 ml  
10 x vial containing 100 ml  
10 x vial containing 250 ml

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**

Laboratorios Dr. ESTEVE, S.A.  
Avda. Mare de Déu de Montserrat, 221  
08041 – Barcelona (Spain)

**8. MARKETING AUTHORISATION NUMBER(S)**

**9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION**

**10. DATE OF REVISION OF THE TEXT**

**PROHIBITION OF SALE, SUPPLY AND/OR USE**

Dispensing conditions:  
Veterinary prescription  
For animal treatment only

## **LABELLING**

### **<PARTICULARS TO APPEAR ON THE OUTER PACKAGE>**

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

### **1. NAME OF THE VETERINARY MEDICINAL PRODUCT**

DANIDOL 60 mg/ml solution for injection for pigs (all countries except ES)

EDERAL 60 mg/ml solution for injection for pigs (ES)

Ketoprofen

### **2. STATEMENT OF ACTIVE AND OTHER SUBSTANCES**

Each 1 ml contains:

Ketoprofen 60 mg

Benzyl alcohol (E1519) 10 mg

### **3. PHARMACEUTICAL FORM**

Solution for injection

### **4. PACKAGE SIZE**

100 ml

250 ml

10 x100 ml

10x250 ml

### **5. TARGET SPECIES**

Pigs.

### **6. INDICATION(S)**

### **7. METHOD AND ROUTE(S) OF ADMINISTRATION**

Intramuscular use. Read the package leaflet before use.

### **8. WITHDRAWAL PERIOD**

Meat and offal: 3 days

### **9. SPECIAL WARNING(S), IF NECESSARY**

Read the package leaflet before use.

**10. EXPIRY DATE**

<EXP {month/year}>

Shelf-life after first opening the immediate packaging: 28 days

**11. SPECIAL STORAGE CONDITIONS**

This veterinary medicinal 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.

Veterinary prescription.

**14. THE WORDS “KEEP OUT OF THE REACH AND SIGHT OF CHILDREN”**

Keep out of the reach and sight of children.

**15. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER**

Laboratorios Dr. ESTEVE, S.A.

Avda. Mare de Déu de Montserrat, 221

08041 – Barcelona (Spain)

**16. MARKETING AUTHORISATION NUMBER(S)**

**17. MANUFACTURER’S BATCH NUMBER**

<Batch> <Lot> <BN> {number}

**<PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGE>**

Vials containing 100 ml/250 ml

**1. NAME OF THE VETERINARY MEDICINAL PRODUCT**

DANIDOL 60 mg/ml solution for injection for pigs (all countries except ES)  
EDERAL 60 mg/ml solution for injection for pigs (ES)

Ketoprofen

**2. STATEMENT OF ACTIVE AND OTHER SUBSTANCES**

Each 1 ml contains: Ketoprofen 60 mg, Benzyl alcohol (E1519) 10 mg

**3. PACKAGE SIZE**

100 ml  
250 ml

**4. TARGET SPECIES**

Pigs.

**5. METHOD AND ROUTE(S) OF ADMINISTRATION**

Intramuscular use

**6. WITHDRAWAL PERIOD**

Meat and offal: 3 days

**7. SPECIAL WARNING(S), IF NECESSARY**

Read the package leaflet before use.

**8. EXPIRY DATE**

<EXP {month/year}>

Shelf-life after first opening the immediate packaging: 28 days

Once broached, use by .....

**9. SPECIAL STORAGE CONDITIONS**

Keep out of the reach and sight of children.

**10. THE WORDS “FOR ANIMAL TREATMENT ONLY” AND CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE, if applicable**



For animal treatment only.

<b>11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER</b>
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Laboratorios Dr. ESTEVE, S.A.  
Avda. Mare de Déu de Montserrat, 221  
08041 – Barcelona (Spain)

<b>12. MANUFACTURER'S BATCH NUMBER</b>
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<Batch> <Lot> <BN> {number}

## **PACKAGE LEAFLET**

DANIDOL 60 mg/ml solution for injection for pigs (all countries except ES)  
EDERAL 60 mg/ml solution for injection for pigs (ES)

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

Marketing authorisation holder:

Laboratorios DR. ESTEVE, S.A.

Avda. Mare de Déu de Montserrat, 221. 08041 Barcelona

Spain

Manufacturer for the batch release:

Pfizer Olot, S.L.U.

Crta. Camprodón s/n, 17813 Vall de Bianya (Girona)

Spain

### **2. NAME OF THE VETERINARY MEDICINAL PRODUCT**

DANIDOL 60 mg/ml solution for injection for pigs (AT, DE, FR, UK)

EDERAL 60 mg/ml solution for injection for pigs (only ES)

Ketoprofen

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

Each 1 ml contains:

Ketoprofen	60 mg
Benzyl alcohol (E1519)	10 mg

### **4. INDICATION(S)**

Pigs:

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

### **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 animals that have previously shown signs of hypersensitivity to ketoprofen or aspirin or any of the excipients.

Do not use where there is evidence of blood dyscrasia or blood coagulation disturbances.

## **6. ADVERSE REACTIONS**

Intramuscular injection may be followed by transient irritation at the injection site.

The administration of ketoprofen in pigs at the recommended therapeutic dose may cause superficial erosion and/or superficial ulceration of the gastrointestinal tract.

If side effects occur treatment must be stopped and the advice of a veterinarian should be sought.

## **7. TARGET SPECIES**

Pigs.

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

Intramuscular use.

Administer via the intramuscular route at a dose of 3mg/Kg bodyweight, equivalent to 1ml/20Kg bodyweight of product, on a single occasion. 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 reach and sight of children.

This veterinary medicinal product does not require any special storage conditions

Shelf life after first opening the immediate packaging: 28 days.

Do not use after the expiry date stated on the label and carton

## **12. SPECIAL WARNING(S)**

Do not exceed the recommended dose or duration of treatment

When administering to pigs of less than 6 weeks of age 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

The safety of ketoprofen has been investigated in pregnant laboratory animals (rats, mice, rabbits) and cattle. No adverse effects were noted. As the safety of ketoprofen has not been assessed in pregnant sows, the product should be used in this case only according to the benefit/risk assessment by the responsible veterinarian.

Interactions between Ketoprofen and the most commonly used antibiotics have not been investigated.

Concurrent administration of diuretics or potentially nephrotoxic drugs should be avoided since there is an increase of renal disturbances. This is secondary to the diminished blood flow caused by the inhibition of prostaglandins.

Danidol 60 mg/ml solution for injection must not be administered in conjunction with other NSAIDs or glucocorticosteroids since gastrointestinal ulceration may be exacerbated.

Pre-treatment with other anti-inflammatory substances may result in additional or increased adverse effects and accordingly a treatment-free period with such drugs should be observed for at least 24 hours before the commencement of treatment. 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 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.

#### USER WARNINGS

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.

Hypersensitivity reactions (skin rash, urticaria) could occur. People with known hypersensitivity to the active substance should avoid contact with this product.

#### **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**

Vial containing 100 ml

Vial containing 250 ml

10 x vial containing 100 ml

10 x vial containing 250 ml

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

Not all pack sizes may be marketed.