Summary of Product Characteristics

1 NAME OF THE VETERINARY MEDICINAL PRODUCT

TOLFEDOL, 40 mg/ml, solution for injection for cattle, pigs, cats and dogs

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

Active substance:

Tolfenamic acid ..... 40 mg

Excipients:

Benzyl alcohol (E1519).....10.4 mg
Sodium formaldehyde sulphoxylate..... 5 mg

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Solution for injection.
A clear yellowish solution.

4 CLINICAL PARTICULARS

4.1 Target Species

Cattle, pigs, cats and dogs.

4.2 Indications for use, specifying the target species

In cattle, as an adjunct in the treatment of pneumonia by improving general conditions and nasal discharge and as an adjunct in the treatment of acute mastitis.
In pigs, as an adjunct in the treatment of Metritis Mastitis Agalactia syndrome.
In dogs : for the treatment of inflammation associated with musculo-skeletal disorders and for the reduction of post-operative pain.
In cats : as an adjunct in the treatment of upper respiratory disease in association with antimicrobial therapy, if appropriate.

4.3 Contraindications

Do not use in cases of cardiac disease.
Do not use in cases of impaired hepatic function or acute renal insufficiency.
Do not use in cases of ulceration or digestive bleeding, in case of blood dyscrasia.
Do not inject intramuscularly in cats.
Do not use in known cases of hypersensitivity to the active substance or to any of the excipients.
Do not use in dehydrated, hypovolaemic or hypotonic animals (due to its potential risk of increasing renal toxicity).
Do not administer other steroidal or non – steroidal anti – inflammatory drugs concurrently or within 24 hours of each other.

4.4 Special warnings for each target species

NSAIDS can cause inhibition of phagocytosis and hence in the treatment of inflammatory conditions associated with bacterial infections appropriate concurrent antimicrobial therapy should be instigated.

4.5 Special precautions for use

Special precautions for use in animals

Use in animals less than 6 weeks of age, or in aged animals, may involve additional risk. If such a use cannot be avoided, animals may require a reduced dosage and careful clinical management is essential. Reduced metabolism and excretion in these animals should be considered.

Concurrent administration of potential nephrotoxic drugs should be avoided.

It is preferable that the product is not administered to cats undergoing general anaesthesia until fully recovered.

Do not exceed the prescribed dosage or duration of treatment. The scale of pain relief after pre-operative administration may be influenced by the severity and duration of the operation.

Animals suffering from a chronic renal insufficiency and requiring an anti-inflammatory treatment may be treated with tolfenamic acid without requiring an adjustment of the dosage. However, the use of this product is contra-indicated in acute cases of renal insufficiency.

In case of undesirable effects (anorexia, vomiting, diarrhoea, presence of blood in faeces) occurring during the treatment, your veterinarian should be contacted for advice and the possibility of stopping treatment should be considered.

Use aseptic precautions when administering the product.

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

The product may cause skin sensitisation. People with known hypersensitivity to non-steroidal anti-inflammatory (NSAID) or to any of the excipients should avoid contact with the veterinary medicinal product.

Administer the veterinary medicinal product with caution to avoid accidental self-injection. In case of accidental self-injection, seek medical advice immediately and show the package leaflet or the label to the physician.

This product may cause skin and eye irritation. Avoid contact with skin or eyes. In case of accidental contact, wash immediately exposed area with plenty of clean water.

Seek medical attention if irritation persists.

Wash hands after use.

4.6 Adverse reactions (frequency and seriousness)

Collapse following rapid intravenous injection in cattle may occur uncommonly.

A temporary increase in thirst and/or diuresis may occur very rarely. In most of the cases, these signs cease spontaneously after treatment.

Diarrhoea and vomiting may occur during treatment very rarely. Where either persists, treatment should be discontinued.

Local injection site reactions may occur very rarely.

The frequency of adverse reactions is defined using the following convention:

- Very common (more than 1 in 10 animals treated displaying adverse reaction(s))
- Common (more than 1 but less than 10 animals in 100 animals treated)
- Uncommon (more than 1 but less than 10 animals in 1000 animals treated)
- Rare (more than 1 but less than 10 animals in 10000 animals treated)
- Very rare (less than 1 animal in 10000 animals treated, including isolated reports).

4.7 Use during pregnancy, lactation or lay

Cats and dogs:

Do not use during pregnancy.

Cattle and pigs:

Pregnancy: Use only according to the benefit-risk assessment by the responsible veterinarian

Lactation: The product can be used during lactation.

4.8 Interaction with other medicinal products and other forms of interactions

Do not administer with other non-steroidal anti-inflammatory drugs simultaneously or with an interval of 24 hours between them. Other NSAIDs, diuretics, anticoagulants and substances with high affinity to plasma proteins may compete for binding and produce toxic effects.

Do not administer in conjunction with anticoagulants.

Avoid simultaneous administration of potentially nephrotoxic drugs.

Do not administer in conjunction with glucocorticoids

4.9 Amounts to be administered and administration route

Cattle: intramuscular (IM) or intravenous (IV) routes.
Pigs: intramuscular (IM) route.
Dogs: intramuscular or subcutaneous routes.
Cats: subcutaneous (SC) route.

Cats and dogs: The recommended dose is 4 mg/kg bodyweight (1 ml/10 kg bodyweight) given as a single injection and repeated once after 24 to 48 hours if required and depending upon clinical assessment. Alternatively, a single injection of 1 ml/10 kg can be given with the treatment being continued by the oral route, using tablets.
In dogs administer by intramuscular or subcutaneous injection.
For the reduction of post-operative pain, this is best given pre-operatively, at the time of premedication one hour before induction of anaesthesia
In cats, administer by the subcutaneous route only.

Cattle: For inflammation associated with respiratory disease in cattle, the recommended dosage is 2 mg/kg (1 ml/20 kg bodyweight) by intramuscular injection into the neck area. Treatment may be repeated once after 48 hours.
For use in mastitis, the recommended dosage is 4 mg/kg bodyweight (1ml per 10 kg bodyweight) as a single IV injection.
When administering intravenously, the product should be injected slowly. At the first signs of intolerance, the injection should be interrupted.

Pigs: the recommended dosage is 2 mg/kg (1ml/20kg bodyweight) as a single intramuscular injection.
The maximum injected volume is 20 ml per injection site.
The stopper for the 20 ml, 50 ml and 100 ml vial sizes may be safely punctured up to 20 times. The stopper for the 250 ml vial size may be safely punctured up to 50 times. The user should choose the most appropriate vial size according to the target species to be treated.
The use of an insulin-type needle/syringe is advisable particularly in low-weight animals to ensure an accurate dose.

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

At high dosages, neurological disorders have been observed.
In case of overdose, administer symptomatic treatment.

4.11 Withdrawal period(s)

Cattle:
Intramuscular injection
Meat and offal: 12 days.
Milk: zero hours
Intravenous injection
Meat and offal: 4 days.
Milk: 24 hours.

Pigs:
Meat and offal: 16 days.

5 PHARMACOLOGICAL or IMMUNOLOGICAL PROPERTIES

Pharmacotherapeutic group: Non-steroidal anti-inflammatory and antirheumatic products, Fenamates.
ATCvet code: QM01AG02.

5.1 Pharmacodynamic properties

Tolfenamic acid (N-(2-methyl-3-chlorophenyl) anthranilic acid) is a non-steroidal anti-inflammatory drug belonging to the fenamate group. Tolfenamic acid possesses anti-inflammatory, analgesic and antipyretic properties.
The anti-inflammatory activity of tolfenamic acid is due to inhibition of cyclooxygenase leading to a reduction in prostaglandin and thromboxane synthesis, which are important inflammatory mediators.

5.2 Pharmacokinetic particulars

In dogs, tolfenamic acid is readily absorbed by injectable administration. By injection, maximum plasma concentrations of about 4 µg/ml (subcutaneously) and about 3 µg/ml (intramuscularly) are obtained 2 hours after administration at 4 mg/kg
In cats, absorption is quite rapid. By injection, a peak of 3.9 µg/ml is obtained within 1 hour of administration at 4 mg/kg.
In dogs and cats**,** over 99% of tolfenamic acid is bound to plasma proteins.
In the dog, only tolfenamic acid and its conjugate with glucuronic acid are found in urine.
The hydroxylated metabolites and their conjugates are mainly excreted by the kidneys. The unchanged tolfenamic acid and its glucuronides are predominantly excreted into the bile. Moreover, tolfenamic acid undergoes an intensive enterohepatic recycling.
Tolfenamic acid is distributed to all organs with high concentrations in plasma, digestive tract, liver, lungs and kidneys. The concentration in the brain however is low.
In dogs with renal insufficiency, the elimination of tolfenamic acid is unchanged and accumulation does not occur.
In cattle and pigs, tolfenamic acid injected intramuscularly at a dose of 2mg/kg is rapidly absorbed from the injection site with mean maximum plasma concentrations of about 1.4 µg/ml in cattle and 2.3 µg/ml in pigs obtained at about 1 hour.
The volume of distribution is about 1.3 l/kg.
Tolfenamic acid is extensively bound to plasma albumin (>97%).
Tolfenamic acid is distributed in all the organs with a high concentration in the plasma, digestive tract, liver, lungs and kidneys. However, the concentration in the brain is low. Tolfenamic acid and its metabolites do not cross the placenta to any great extent.
Tolfenamic acid distribution involves extracellular fluids where concentrations similar to plasma are achieved both in healthy and inflamed peripheral tissues. It also appears in milk in the active form, mainly associated with the curds.
Tolfenamic acid undergoes extensive enterohepatic recirculation and, as a result prolonged concentrations are found in plasma. The elimination half-life varies from 3-5 hours in pigs to 8 - 15 hours in cattle.
In cattle and pigs, tolfenamic acid is eliminated mainly unchanged in faeces (~30%) and urine (~70%).

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Benzyl alcohol (E1519)
Sodium formaldehyde sulfoxylate
Diethylene glycol monoethylether
Ethanolamine
Water for injections

6.2 Major 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: 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

Amber polypropylene vials of 20 ml, 50 ml, 100 ml and 250 ml provided with a grey (20 ml, 50 ml and 100 ml) or pink (250 ml) bromobutyl stopper and aluminium seal with a flip-off sealing.
Each vial is packaged in an outer carton.
Not all pack sizes may be marketed.

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

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

7 MARKETING AUTHORISATION HOLDER

SP Veterinaria, S.A.
Ctra. Reus - Vinyols Km 4, 1
Riudoms 43330
Spain

8 MARKETING AUTHORISATION NUMBER(S)

VPA10790/006/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of the first authorisation: 21 August 2015
Date of last renewal: 21 August 2020