[Version 8.2,01/2021]

ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

TOLFENIL 40 mg/ml solution for injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

Active substances:
Tolfenamic acid…….. 40.0 mg

Excipients:
Benzyl alcohol (E 1519) …… 10.4 mg
Sodium formaldehyde sulfoxylate……..... 5.0 mg

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection.
Clear, yellowish solution, free from visible particles.

4. CLINICAL PARTICULARS

4.1 Target species

Cattle, pigs, dogs, and cats.

4.2 Indications for use, specifying the target species

Cattle:
- As an adjunct in the reduction of acute inflammation associated with respiratory diseases.
- As an adjunct in the treatment of acute mastitis.

Pigs:
- As an adjunct in the treatment of Metritis, Mastitis and Agalactia syndrome.

Dogs:
- For the treatment of inflammatory and painful postoperative syndromes.
- For the reduction of postoperative pain.

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 hypersensitivity to the active substance or to any excipient.
Do not use in animals with cardiac disease, impaired hepatic function, or acute renal insufficiency.
Do not use in case of ulceration or digestive bleeding or in case of blood dyscrasia.
Do not inject intramuscularly in cats.
Avoid its use in dehydrated, hypovolemic, or hypotensive animals, due to its potential risk of increasing renal toxicity.

4.4 Special warnings for each target species

None.

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 animals undergoing general anaesthesia until fully recovered.
The scale of pain relief after pre-operative administration in dogs may be influenced by the severity and duration of the operation.
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.
To avoid renal insufficiency, an adequate drinking water supply for the animals has to be ensured during treatment.

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 drugs (NSAIDs) or to benzyl alcohol 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.

4.6 Adverse reactions (frequency and seriousness)

Rarely, calves may collapse after rapid intravenous injection. When administered intravenously, the product should be injected slowly. After the first signs of intolerance appear, stop the injection.
Anorexia, vomiting, diarrhoea, or blood in stools may occur in dogs and cats.
Polyuria and polydipsia may occur transiently. In most cases, these symptoms usually disappear spontaneously upon suppression of treatment.
Local reactions may appear at the injection site.

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 1,000 animals treated).
- rare (more than 1 but less than 10 animals in 10,000 animals treated).
- very rare (less than 1 animal in 10,000 animals treated, including isolated reports).

4.7 Use during pregnancy, lactation or lay

Cattle and pigs:
The results of the studies carried out in the rat and in the rabbit showed no teratogenic effect.
Peri and postnatal studies performed in the rat showed that tolfenamic acid has no influence on the evolution of viability, the gestation index, or the appearance of malformations.
Use only accordingly to the benefit/risk assessment by the responsible veterinarian.
Dogs and cats:
The safety of the veterinary medicinal product has not been established in dogs and cats during pregnancy and lactation.
The use is not recommended during pregnancy or lactation.

4.8 Interaction with other medicinal products and other forms of interaction

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) and intravenous (IV) use.
Pigs: Intramuscular use.
Dogs: Intramuscular and subcutaneous use.
Cats: Subcutaneous (SC) use.

Cattle:
- As an adjunct in the reduction of acute inflammation associated with respiratory diseases: 2 injections of 2 mg of tolfenamic acid /kg b.w. (equivalent to 1 ml of the product/20 kg b.w. each one), by IM route in the neck muscles, separate by 48 hours. Do not exceed 20 ml per injection site.
- As an adjunct in the treatment of acute mastitis: 4 mg of tolfenamic acid/kg b.w. (equivalent to 1 ml of the product/10 kg b.w.) by IV route, in a single dose.

Pigs:
- As an adjunct in the treatment of Metritis Mastitis Agalactia syndrome: 2 mg of tolfenamic acid/kg b.w. (equivalent to 1 ml of the product/20 kg b.w.) by IM route in the neck muscles, in a single dose. Do not exceed 20 ml per injection site.

Dogs:
- For the treatment of inflammatory and painful postoperative syndromes: 4 mg of tolfenamic acid/kg b.w. (equivalent to 1 ml of the product/10 kg b.w.) by IM or SC route. This dose can be repeated after 24 hours.
- For the reduction of postoperative pain: 4 mg of tolfenamic acid/kg b.w. (equivalent to 1 ml of the product/10 kg b.w.), by IM route, in a single dose, one hour before induction to anaesthesia.

Cats:
- As an adjunct in the treatment of upper respiratory disease in association with antimicrobial therapy, if appropriate: 4 mg of tolfenamic acid/kg b.w. (equivalent to 1 ml of the product /10 kg b.w.), by SC route. This dose can be repeated after 24 hours.
  Do not use IM route in cats.

In animals of reduced weight, it is advisable to use insulin-type syringes to ensure a correct dosage.

The stopper should not be punctured more than 50 times in 250 ml vials and 25 times in 20 ml and 100 ml vials. The user should choose the most appropriate vial size according to the target specie to treat.

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

Cattle:
Tolerance studies in cattle allowed to define that a dose 4 times higher than the therapeutic one (16 mg/kg b.w.) could constitute the margin of safety for administration of the product.
At doses of 18 and 20 mg/kg b.w. (4.5 and 5 times the therapeutic dose), signs of central toxicity in the form of agitation, balance disorders and motor incoordination were transiently recorded. Significant variations were recorded in haematological and biochemical parameters that corresponded to transient modifications of digestive and liver functions.
Pigs:
Tolfenamic acid is well tolerated (doses up to 5 times higher than the therapeutic dose), although there may be reactions at the injection site that are intense and spontaneously recover in 7-14 days.
Dogs and cats:
The symptoms described in the section 4.6 Adverse reactions may appear exacerbated. In this case, it is recommended to suspend the treatment and initiate a symptomatic treatment.

4.11 Withdrawal period

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

Pigs:
Meat and offal: 16 days

5. PHARMACOLOGICAL 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 cattle and pigs, tolfenamic acid, administered by IM route at a dose of 2 mg/kg b.w., is rapidly absorbed from the injection site, reaching maximum mean plasma concentrations of around 1.4 μg/ml in cattle and 2.3 μg/ml in pigs in approximately 1 hour, with a volume of distribution of about 1.3 l/kg in both species and a plasma albumin binding > 97%.

In dogs, tolfenamic acid is easily absorbed. After parenteral administration of a dose of 4 mg/kg b.w., a maximum plasma concentration of about 4 μg/ml (SC) and 3 μg/ml (IM) is obtained after two hours.

In cats, absorption is rapid. After one hour of parenteral administration of 4 mg/kg b.w., a peak of 3.9 μg/ml is recorded.

Tolfenamic acid is distributed in all organs with a higher concentration in plasma, digestive tract, liver, lungs, and kidneys, being on the contrary very weak in brain. Tolfenamic acid and its metabolites cross the placenta in a small proportion.

In extracellular fluids, concentrations are similar to those of plasma in both healthy and inflamed peripheral tissues.

It also appears in milk in active form, mainly associated with the curds.

Tolfenamic acid follows an enterohepatic cycle that ensures a longer duration of therapeutic concentrations in plasma.

The elimination half-life of tolfenamic acid varies between 3-5 hours in pigs and 8-15 hours in bovines.

It is excreted fundamentally unaltered by urinary (~ 70%), biliary and fecal (~ 30%) in both species. The milk excretion is negligible.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Benzyl alcohol (E 1519)
Sodium formaldehyde sulfoxylate
Ethanolamine
Diethylene glycol monoethyl ether
Water for injections

6.2 Major incompatibilities

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

6.3 Shelf life

Shelf life of the veterinary medicinal product as packaged for sale: 2 years.
Shelf life after first opening of 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

The veterinary medicinal product is packaged in type II amber glass vials closed with type I bromobutyl rubber stoppers and flip-off caps.

Pack sizes:
Cardboard box with 1 vial of 20 ml
Cardboard box with 1 vial of 100 ml
Cardboard box with 1 vial of 250 ml

Cardboard box with 5 vials of 20 ml
Cardboard box with 10 vials of 100 ml
Cardboard box with 15 vials of 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 product should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

MEVET S.A.U.
Polígono Industrial El Segre, p. 409-410,
25191 Lleida
Spain

8. MARKETING AUTHORISATION NUMBERS

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

10 DATE OF REVISION OF THE TEXT

PROHIBITION OF SALE, SUPPLY AND/OR USE