1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Tolfine 80 mg/ml (Austria, Belgium, Cyprus, Czech Republic, Estonia, France, Germany, Greece, Ireland, Italy, Latvia, Lithuania, Luxembourg, Netherlands, Poland, Portugal, Slovakia, Slovenia, Spain) solution for injection for cattle
Tolfacton (Denmark, Finland) solution for injection for cattle

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains:

Active substance:
Tolfenamic acid 80 mg

Excipients:
For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection.
Clear colourless to slightly yellow-brown solution.

4. CLINICAL PARTICULARS

4.1 Target species

Cattle

4.2 Indications for use, specifying the target species

The veterinary medicinal product is indicated as:
- Adjunct treatment for the reduction of acute inflammation associated with respiratory diseases.
- Adjunct treatment of acute mastitis.

4.3 Contraindications

Do not uses 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 or in cases of blood dyscrasia.
Do not use in cases of hypersensitivity to the active substance or to any of the excipients.
Do not administer other steroidal or non-steroidal anti-inflammatory drugs concurrently or within 24 hours of each other.
Do not use in dehydrated, hypovolaemia or hypotensive animals, due to its potential risk of renal toxicity.

4.4 Special warnings for each target species

Non-steroidal anti-inflammatory drugs (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

Do not exceed the stated dosage and duration of treatment. Use aseptic precautions when administering the product.
Concurrent administration of potential nephrotoxic drugs should be avoided.

Young and aged animals are more sensitive to the digestive and renal side-effects of NSAIDs. Such a use should be done with careful clinical management.
In case of undesirable effects (digestive or renal side-effects) occurring during the treatment, your veterinarian should be contacted for advice and the possibility of stopping treatment should be considered.

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

The veterinary medicinal product is irritant to eyes.
In case of accidental eye exposure, flush the eyes immediately with clean water and seek medical advice immediately.
The veterinary medicinal product is irritant to skin. In case of accidental spillage onto skin, wash the skin immediately with soap and water.
Seek medical attention if irritation persists.
Wash hands after use.
In case of accidental self-injection, seek medical advice immediately and show the package leaflet or label to the physician.
People with known hypersensitivity to non-steroidal anti-inflammatory drugs (NSAIDs) should avoid contact with the veterinary medicinal product.
In view of the risk of accidental self-injection and the known adverse class-effects of NSAIDs on pregnancy and/or embryofoetal development, pregnant women or women attempting to conceive should administer this veterinary medicinal product with care.

4.6 Adverse reactions (frequency and seriousness)

Transient inflammation and swelling may commonly occur at the injection site, lasting up to 38 days.
There are occasional reports of collapse following rapid intravenous injection in cattle.
Diarrhoea and hemorrhagic diarrhoea may occur during treatment. If relevant, the benefit-risk assessment should be re-assessed for the second administration.

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

Pregnancy: Use only accordingly to the benefit/risk assessment by the responsible veterinarian. NSAIDs might delay parturition through a tocolytic effect by inhibiting prostaglandins that are important in signalling the initiation of parturition.

Lactation: Can be used during lactation.

4.8 Interaction with other medicinal products and other forms of interaction

Do not administer other steroidal or non-steroidal anti-inflammatory drugs concurrently or within 24 hours of each other.
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

Intramuscular and intravenous use.

As an adjunct in the treatment of acute inflammation associated with respiratory disease in cattle, the recommended dosage is 2 mg tolfenamic acid per kg bodyweight (corresponding to 1 ml of the product/40 kg bodyweight) by intramuscular injection into the neck area. Treatment may be repeated once after 48 hours.

The maximum injected volume is 18 ml per intramuscular injection site.
If dose volume exceeds 18 ml, it should be divided and injected into two or more sites.

As an adjunct in the treatment of acute mastitis, the recommended dosage is 4 mg tolfenamic acid per kg bodyweight (corresponding to 1 ml of the product/20 kg bodyweight) as a single intravenous injection.

When administered intravenously, the product should be injected slowly. At the first signs of intolerance, the injection should be interrupted.

As the vial should not be broached more than 15 times, the user should select the most appropriate vial size according to the size and number of cattle to be treated.
When treating groups of animals in one run, use a draw-off needle that has been placed in the vial stopper to avoid excess broaching of the stopper. The draw-off needle should be removed after treatment.

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

At high dosages, neurological disorders have been observed.

Symptoms of overdose include: excitation, salivation, tremors, vibration of the eyelids and ataxia. These symptoms are short-term in nature. Reversible kidney damage resulting in elevated plasma urea and creatinine levels is also possible. An antidote is not known. In case of overdose, stop tolfenamic acid administration and administer symptomatic treatment.

4.11 Withdrawal period(s)

I.M. injection
Meat and offal: 20 days
Milk: 0 hours

I.V. injection
Meat and offal: 4 days
Milk: 12 hours

5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Anti-inflammatory and antirheumatic products non steroids, fenamates, tolfenamic acid.

ATC vet code: QM01AG02

5.1 Pharmacodynamic properties

Tolfenamic acid (N-(2-methyl-3-chlorophenyl) anthranilic acid) is a non-steroidal anti-inflammatory drug (NSAID) belonging to the fenamate group. Tolfenamic acid exerts anti-inflammatory, analgesic

and antipyretic activities.
The anti-inflammatory activity of tolfenamic acid is mainly due to an inhibition of cyclo-oxygenase and thus to a reduction of the synthesis of prostaglandins and thromboxanes, which are important inflammatory mediators.

5.2 Pharmacokinetic particulars

In cattle, tolfenamic acid injected by I.M. route at a dose of 2mg/kg is rapidly absorbed from the injection site with mean maximum plasma concentrations of 1.77 ± 0.45 µg/ml obtained at 2.4 hours (0.25-8 hours).

The volume of distribution is approximately 1.3 l/kg.
The absolute bioavailability is high.

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 8 to 15 hours.

Tolfenamic acid is eliminated mainly unchanged in faeces (~30%) and urine (~70%).

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Diethylene glycol monoethyl ether
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 type I glass vials closed with chlorobutyl rubber stoppers and oversealed with an aluminium seal with a polypropylene flip-off cap.

Each vial is packaged in a cardboard box.

Package sizes:
Cardboard box with 1 vial of 50 ml
Cardboard box with 1 vial of 100 ml
Cardboard box with 1 vial 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

To be completed according to application form for each Member State

8. MARKETING AUTHORISATION NUMBER(S)

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: DD/MM/YYYY

10 DATE OF REVISION OF THE TEXT

{DD/MM/YYYY}