Part II
SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Tolfine, 4% solution for injection for cattle and pigs

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains 4.0% w/v tolfenamic acid as active ingredient with 1.04% w/v benzyl alcohol and 0.50% w/v sodium formaldehyde sulphoxylate as preservatives.

For a full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Solution for injection. Clear, colourless to slightly yellow, slightly viscous solution

4. CLINICAL PARTICULARS

4.1 Target species

Cattle and pigs.

4.2 Indications for use, specifying the target species

An anti-inflammatory, antipyretic and analgesic agent indicated:-

In cattle:
-as an adjunct in the treatment of acute mastitis, used in conjunction with antibacterial therapy
-as an aid in the control of acute inflammation associated with bacterial respiratory disease, used in conjunction with antibacterial therapy.

In pigs, as an adjunct in the treatment of Metritis Mastitis Agalactia syndrome, used in conjunction with antibacterial therapy.

4.3 Contra-indications

Not for IM administration in cattle.
Not for IV or SC administration in pigs.
Not for SC administration in dairy cows

4.4 Special warnings for each target species

Do not exceed 20ml per intramuscular injection site.

Do not exceed the stated dose or the duration of treatment.

Use is contra-indicated in animals suffering from cardiac, hepatic or renal disease, where there is the possibility of gastro-intestinal ulceration or bleeding, or where there is evidence of hypersensitivity to the product.

Do not administer other NSAIDs concurrently or within 24 hours of each other. Some NSAIDs may be highly bound to plasma proteins and compete with other highly bound drugs which can lead to toxic effects.

Use in any animal less than 6 weeks of age or in aged animals may involve additional risk. If such use cannot be avoided animals may require a reduced dosage and careful clinical management.

Avoid use in any dehydrated, hypovolaemic or hypotensive animal as there is a potential risk of increased renal toxicity.

It is preferable that NSAIDs which inhibit prostaglandin synthesis are not administered to animals undergoing general anaesthesia until fully recovered.

Concurrent administration of potentially nephrotoxic drugs should be avoided.

4.5 Special precautions for use

(i) Special precautions for use in animals

Do not exceed the stated dosage and duration of treatment.

Use aseptic precautions when administering the product.

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

Take care to avoid self-injection. In case of eye or skin contact, wash immediately with water.

4.6 Adverse reactions (frequency and seriousness)

Transient swelling and inflammation can occur at the injection site.

4.7 Use during pregnancy, lactation or lay

The product may be used during lactation. As there is limited data to support use during pregnancy, use of the product in pregnant animals should be at the discretion of the veterinary surgeon after the risks and benefits have been considered.

4.8 Interaction with other medicinal products and other forms of interaction

Do not administer other NSAIDs concurrently or within 24 hours of each other. Tolfenamic acid is highly bound to plasma proteins and may compete with other highly bound drugs.

4.9 Amounts to be administered and administration route

For use in bovine mastitis, the recommended dosage is 4mg/kg bw (1ml per 10kg bw) as a single IV injection.

For use in bovine respiratory disease, the recommended dosage is 2mg/kg bw (1ml per 20kg bw) by IV or SC injection. Treatment may be repeated once after 48 hours. If a second injection is needed this should be given in the opposite side of the animal's body.

In pigs, the recommended dosage is 2mg/kg (1ml/20kg bw) as a single intramuscular injection, in the neck musculature.

When treating a number of animals the use of a draw-off needle is recommended to avoid excessive broaching of the closure.

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

None

4.11 Withdrawal period(s)

PIGS
Meat: 3 days

CATTLE
Meat: Following intravenous administration – 3 days
Meat: Following subcutaneous administration – 7 days
Milk: 24 hours

Milk from treated cattle must only be used for human consumption after 24 hours, i.e. at the second milking. Milk from the first milking after treatment should be discarded.

5. PHARMACOLOGICAL 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 in the synthesis of prostaglandins and thromboxanes, which are important inflammatory mediators.

Pharmacokinetic Properties

Pigs

In pigs, tolfenamic acid injected by IM route at a dose of 2mg/kg is rapidly absorbed from the injection site with a mean maximum plasma concentration of about 2.3ug/ml obtained at about 1 hour.
The volume of distribution is approximately 1.3 l/kg in pigs.
It is extensively bound to plasma albumin (>97%).

Tolfenamic acid distribution involves extracellular fluids where concentrations similar to plasma are achieved both in healthy and inflamed peripheral tissues.

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.

In pigs, tolfenamic acid is eliminated mainly unchanged in faeces (~30%) and urine (~70%).

Cattle

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 placental barrier 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 - 15 hours in cattle.

In cattle, tolfenamic acid is eliminated mainly unchanged in faeces (~30%) and urine (~70%).

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Benzyl alcohol
Sodium Formaldehyde Sulfoxlylate Anhydrous
Ethyl digol
Ethanolamine
Water for Injections

6.2 Incompatibilities

None Known

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

Do not store above 25°C. Protect from light.

Following withdrawal of the first dose, use the product within 28 days. Avoid the introduction of contamination during use. Discard unused material.

6.5 Nature and composition of immediate packaging

Cardboard box with 1 amber glass vial of 50ml or 100ml with a rubber chlorobutyl bung with aluminium overseal, or flip caps made of aluminium with a plastic disc. 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 of waste materials derived from such veterinary medicinal products should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Vétoquinol UK Limited
Vetoquinol House
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Buckingham
MK18 1PA

8. MARKETING AUTHORISATION NUMBER(S)

Vm 08007/4063

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

19/5/99/19/5/04

10. DATE OF REVISION OF THE TEXT

14 May 2008