Tolfedine™
(tolfenamic acid)

Actions: Tolfenamic acid is a nonsteroidal anti-inflammatory drug (nsaid) of the fenamate group. It has a double action on prostaglandins:
- inhibits prostaglandin synthesis from arachidonic acid
- inhibits tissue response to prostaglandins by occupying receptor sites

It is a potent analgesic, antipyretic and anti-inflammatory. The anti-inflammatory activity of tolfenamic acid is due to inhibition of cyclooxygenase leading to a reduction in prostaglandin and thromboxane synthesis, major inflammatory mediators.

Pharmacokinetics: Tolfenamic acid is rapidly absorbed both orally and following injection.

Cats
- Maximum plasma concentrations after administration of 4mg/kg results in mean maximum plasma concentration (Cmax) of 5.6µg/ml reached in about 1 hour. Plasma levels in cats are higher due to a high level of entro hepatic recycling which prolongs the therapeutic action.

Injection – A injection of 4mg/kg of tolfenamic acid results in mean maximum plasma concentration (Cmax) of 1.9µg/ml in about 1 hour. Levels persist (concentration >0.1µg/ml) for 24-48 hours. Absorption is particularly fast in cats.

Dogs
- After a single oral administration of 4mg/kg mean maximum plasma concentration (Cmax) of 4µg/ml is reached in 1 hour. At the same dosage taken with food Cmax is 2.5µg/ml.

Injection – Following administration of 4mg/kg by either IM or SC injection the mean maximum plasma concentration (Cmax) is 4µg/ml (SC) and 3µg/ml (IM) is reached in 2 hours.


• post operative pain and inflammation
• upper respiratory infections together with antimicrobials (in cats)
• for acute and chronic inflammatory conditions
• febrile syndromes (abcess, fever of unknown origin)
• inflammation and locomotor disease.

Contraindications: Do not use in food producing animals or horses.

Do not use in animals with cardiac, hepatic, or renal disease, showing signs of gastrointestinal ulceration, bleeding, blood dyscrasia or hypersensitivity to the product. Do not administer NSAID’s concurrently or within 24 hours of each other.

DO NOT ADMINISTER BY INTRAMUSCULAR INJECTION IN CATS.

Undesirable effects: Diarrhoea or vomiting may occur in rare cases during treatment. A temporary increase in thirst and/or diuresis may occur. In most cases these signs cease after treatment.

Precautions: Use in animals under six weeks of age and aged animals may involve additional risks. If such cases cannot be avoided animals may require a reduced dose and careful clinical management. Avoid use in dehydrated, hypovolemic, hypertensive animals as there is potential risk of increased renal toxicity. Do not use in cases where there is acute renal insufficiency. Although studies in laboratory animals did not show any effects on reproduction, it is advisable not to administer nsaid’s during gestation.

DOSAGE & ADMINISTRATION:

Tolfedine acid 4mg/kg bodyweight once daily for cats and dog by injection or orally.

Injection: Cats 1mL/10kg bodyweight by subcutaneous injection only

Dogs 1mL/10kg bodyweight by intramuscular or subcutaneous injection

The use of an insulin syringe is advisable in low weight animals to ensure accurate dosing. A subsequent dose after 24 hours of 1mL/10kg bodyweight by injection or tablets may be administered.

Tablets:
- Cats and Dogs: Tolfedine 6mg tablets/1 tablet per 1.5 kg body-weight,
- Tolfedine Tablets 6mg tolfenamic acid,
- For Cats and Dogs 4mg/kg bodyweight once daily for 3-5 days
- Tablets: Tolfedine 60mg tablets/1 tablet per 15kg bodyweight

A subsequent dose after 24 hours of 1mL/10kg bodyweight by injection or tablets may be administered.

A suggested regime is an initial injection of Tolfedine Injectable followed by Tolfedine tablets on subsequent days.

Longterm therapy: A three month study evaluated a dosage regime of 4mg/kg for 3 consecutive days a week for painful locomotor disease in dogs. The clinical improvement (p<0.05) was significant.

Additional information: For Dosage & Administration information see pack insert and pack label.

Presentation: Injection: Tolfedine Injectable 40mg/mL tolfenamic acid,
- 10 mL (multi-dose) vial
- For Cats and Dogs
- Tablets: Tolfedine Tablets 6mg tolfenamic acid,
- For Cats and Miniature Dogs 20’s,
- Tolfedine Tablets 60mg tolfenamic acid,
- For Dogs (7 – 45>kg) 16’s.

Disposal: Dispose of empty container by wrapping with paper and putting in the garbage.

Storage: Store below 25°C (air conditioning).

Manufacturer by: Vétoquinol
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Email ausrichter@bigpond.com

For Dogs (7 – 45>kg) 16’s.
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Rapid action in post-operative analgesia

Tolfedine provides effective post-operative analgesic cover due to its proven 24 hour action.

Three studies were carried out in dogs following orthopaedic surgery, under the same environmental and experimental conditions and the same anaesthetic protocols, to ascertain the analgesic effect of various drugs. The analgesic effect of tolfenamic acid (4mg/kg) was shown to be equal to that of pethidine (fig. 8).

Rapid pain relief in acute flare-ups of osteoarthritis

Tolfedine has been clinically proven to relieve arthritis effectively. A 3 month study to evaluate the dosage regime of 3 consecutive days a week for dogs with painful or locomotor disorders showed significant clinical improvement (p<0.05)(10).

Tolfedine® is a Non-Steroidal Anti-inflammatory Drug licenced for use in both cats and dogs.

Tolfenamic acid delivers the anti-inflammatory power expected of a modern NSAID and has been shown to have strong antipyretic and analgesic activity7). The maximum plasma concentration is reached within 2 hours for both injectable and oral routes in cats and dogs.

A dosage regime of 4mg/kg tolfenamic acid (either by the subcutaneous or the oral route) leads to an effective plasma concentration for 24 hours, without accumulation of the drug in the body. This prolonged action is due to the entero-hepatic recirculation of tolfenamic acid (fig. 1).

REFERENCES:
Proven Safety

When Tolfedine was administered to cats and dogs for 10 days at double the therapeutic dosage (8 mg/kg/day) by the oral route, it did not lead to digestive disorders or haemorrhagic diarrhoea and it did not modify blood clotting time (2).

In field trials carried out under routine veterinary practice conditions (287 dogs & 180 cats), adverse effects were monitored (3). The results are shown in figure 2.

Excellent Renal Tolerance

A study to assess the influence of tolfenamic acid on renally impaired dogs showed that there was no accumulation of the drug in the body and elimination of tolfenamic acid actually increased in renally impaired dogs. Tolfenamic acid can therefore be used safely in the renally impaired or geriatric dog, with no adjustment to the dosage regime necessary (4). It is however contra-indicated in acute renal insufficiency.

Low gastro-ulcerative effect

NSAIDs substantially more selective for inhibiting COX2 (cyclo-oxygenase 2) than COX1 (cyclo-oxygenase 1) have been shown to be well tolerated with regard to adverse effects on the gastrointestinal system during clinical trials in humans (5).

In a recent study, tolfenamic acid was shown to be 15 times more potent in inhibiting canine COX2 than COX1, ranked second highest among the veterinary licenced products (6)(fig.3).

Higher value for the ratio indicates greater selectivity for canine COX2

Tolfedine® - Proven Efficacy in DOGS

“I bet the dog will need his Tolfedine® soon!”
Cats are particularly sensitive to infections of the upper respiratory tract, often resulting in an impaired sense of smell and subsequent appetite loss. Loss of appetite is a critical symptom for the cat and also for the owner, who judges the cat to be in recovery only when it is eating again. A quick return to appetite is therefore desirable.

In a clinical trial, 55 cats suffering from acute feline influenza were treated; 25 with Tolfedine 4% injection and 30 with a placebo injectable solution. Both groups also received amoxycillin (30mg/kg/48hr on D0, D2 & D4).

Tolfedine promoted return to appetite and increased the success rate of therapy due to its fast action and anti-pyretic power (fig. 4 & 5).

Fever in cats is a common and non-specific condition and, if left untreated, can lead to anorexia, weight loss and anaemia. Loss of appetite is often the first indication of fever and presents a common and frequently frustrating clinical scenario.

A clinical trial of 36 cats with anorexia and pyrexia showed that Tolfedine increases the rate of recovery in cats with febrile syndromes due to its rapid anti-pyretic action.

Tolfedine produced a significant decrease in temperature from Day 1 regardless of the cause of pyrexia (fig. 6).

The average time for return to appetite with Tolfedine was significantly less than the placebo, occurring 24 hours earlier (fig. 7).

Both results were particularly notable in non-abscess-linked fevers, where the symptoms of fever are evident but diagnosis is often very difficult. The fast reduction in temperature and return to appetite achieved with Tolfedine is of considerable benefit in these cases.
Rapid Recovery in Upper Respiratory Tract Infections

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- Injection: Following administration of 4mg/kg by either IM or SC injection the mean maximum plasma concentration (Cmax) is 4µg/ml (SC) and 3µg/ml (IM) is reached in 2 hours.

**Indications:** Conditions requiring non steroidal anti-inflammatory-analgesic-antipyretic therapy in cats and dogs.

- post operative pain and inflammation
- upper respiratory infections together with antimicrobials (in cats)
- for acute and chronic inflammatory conditions
- febrile syndromes (abcess, fever of unknown origin)
- inflammation and locomotor disease.

**Contraindications:** Do not use in food producing animals or horses.

- Do not use in animals with cardiac, hepatic, or renal disease, showing signs of gastrointestinal ulceration, bleeding, blood dyscrasia or hypersensitivity to the product. Do not administer NSAID’s concurrently or within 24 hours of each other

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Tolfenamic acid 4mg/kg bodyweight once daily for cats and dog by injection or orally.

**Injection:** Cats 1mL/10kg bodyweight by intramuscular or subcutaneous injection only

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**Storage:** Store below 25°C (air conditioning).

**Manufactured by:**

Vétoquinol SA 72004 Lure Cedex France

**Distributed by:**

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