Do not use in pregnant, breeding, or lactating animals. The safety of Trocoxil has not been established during pregnancy and lactation. However, studies in laboratory animals administered other NSAIDs have shown increased pre- and post-implantation loss, embryo-foetal lethality, and malformations.

No drug interaction studies have been performed. In common with other NSAIDs, Trocoxil should not be administered simultaneously with other NSAIDs or glucocorticoids. Risks for interactions have to be accounted for throughout the effect period i.e. 1-2 months after administration of Trocoxil. Dogs should be carefully monitored if Trocoxil is administered simultaneously with an anticoagulant.

NSAIDs are highly bound to plasma proteins and may compete with other highly bound substances, such that concomitant administration may result in toxic effects.

Pre-treatment with other anti-inflammatory substances may result in additional or increased adverse effects. To avoid such effects when Trocoxil is to be administered in replacement of another NSAID, ensure an appropriate treatment-free period of at least 24 hours before administering the first dose of Trocoxil. The treatment-free period should however, take into account the pharmacology of the medicinal products used previously. Should another NSAID be administered after Trocoxil treatment, a treatment-free period of at least ONE MONTH should be ensured to avoid adverse effects.

In the overdose studies, in common with other NSAIDs, adverse pharmacodynamic events occur affecting the gastrointestinal system. Similarly adverse reactions occurring at the use dose in the animal population principally involved the gastrointestinal system.

In overdose safety studies, repeated doses of 5 mg/kg and 10 mg/kg were not associated with adverse clinical events, abnormal clinical chemistry or significant histological abnormalities. At 15 mg/kg there was evidence of vomiting, and softened/mucoid faeces and an increase in clinical chemistry parameters reflecting renal function. At 25 mg/kg there was evidence of gastrointestinal ulceration.

There is no specific antidote for mavacoxib overdosage, but general supportive therapy, as applied to clinical overdosage with NSAID's, should be given.

Operator warnings
In case of accidental self-administration, seek medical advice immediately and show the package leaflet or the label to the physician.

Ingestion of Trocoxil may be harmful for children, and prolonged pharmacological effects leading to e.g. gastrointestinal disorders may be observed. To avoid accidental ingestion administer the tablet to the dog immediately after removal from the blister packaging.

People with known hypersensitivity to NSAIDs should avoid contact with the veterinary medicinal product.

Do not eat, drink, or smoke when handling the product. Wash hands after handling the product.

Pharmaceutical precautions
Store in the original packaging.

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

For animal treatment only.

Keep out of the reach and sight of children.

Legal category
UK: POM-V

IE: POM

Package quantities
Cardboard carton containing a blister, each blister containing two tablets of 6 mg, 20 mg, 30 mg, 75 mg or 95 mg mavacoxib. Not all pack sizes may be marketed.

Further information
Mavacoxib is a non-steroidal anti-inflammatory drug (NSAID) of the coxib class. The principal mode of action is inhibition of cyclooxygenase (COX).

COX is a key enzyme in pathways of arachidonic acid metabolism. Its activity culminates in the synthesis of local hormones and inflammatory mediators, termed eicosanoids, which include several prostaglandins. There are two isoforms of COX, COX-1, and COX-2. COX-1 is a widely distributed constitutive enzyme, primarily involved in maintaining organ and tissue function, whilst COX-2 is inducible at sites of tissue damage but in some organs it is also constitutive. COX-2 exerts the major role in synthesising prostaglandins which have pivotal roles as mediators of pain, inflammation and fever. Mavacoxib acts by preferential inhibition of COX-2-mediated prostaglandin synthesis. It therefore possesses analgesic and anti-inflammatory properties. Both COX-1 and COX-2 are present constitutively in the kidney and are assumed to possess protective roles in adverse physiological circumstances.

Mavacoxib is well absorbed after oral administration; bioavailability was 87% in fed dogs and 46 % in fasted conditions and the recommended dose is based on administration with food. Therapeutic concentrations in fed dogs are reached rapidly and peak concentrations are obtained in less than 24 hours after administering a dose. Mavacoxib is approximately 98% bound to plasma proteins. It is extensively distributed throughout the body and almost all the mavacoxib-related residues in plasma comprise parent drug. The rate of body clearance of mavacoxib is slow and the major route of elimination is by biliary excretion of the parent drug.

In laboratory studies with young adult dogs, mean elimination half-life values ranged from 13.8 to 19.3 days. Mavacoxib possessed a longer elimination half-life in client owned animals. Population pharmacokinetic data derived from studies in dogs with a predominately older population with heavier dogs as compared to the experimental studies (mean 9 years of age) showed that the mean elimination half-life was 39 days with a small sub-population (<5%) having an elimination half-life of more than 80 days and correspondingly an increased exposure was recorded in these individuals.

Marketing authorisation number
6 mg EU/2/08/084/001, 20 mg EU/2/08/084/002, 30 mg EU/2/08/084/003, 75 mg EU/2/08/084/004, 95 mgEU/2/08/084/005

References: 1. Johnston SA. Osteoarthritis. Joint anatomy, physiology and pathobiology. In *Vet Clin of North Am: Small Anim Pract.* 1997; 27 (4):699-723 **2.** Hellyer P *et al.* AAHA/AAFP Pain management guidelines for dogs and cats. *J Am Anim Hosp Assoc.* 2007; 43 (5):235-248 **3.** Menetrey D and Besson JM. Electrophysiological characteristics of dorsal horn cells in rats with cutaneous inflammation resulting from chronic arthritis. *Pain.* 1982; 13:343-364 **4.** Neugebauer V *et al.* Evidence for a central component in the sensitization of spinal neurons with joint input during development of acute arthritis in cat's knee. *J of Neurophys* 1990; 64:299-311 **5.** Fiorentino PM *et al.* Spinal Interleukin-1-β in a mouse model of arthritis and joint pain. *Arthritis Rheum.* 2008; 58 (10):3100-3109 **6.** Sluka KA *et al.* Joint inflammation is reduced by dorsal rhizotomy and not by sympathectomy or spinal cord transection. *Ann Rheum Dis.* 1994; 53 (5):309-314 **7.** Veiga APC *et al.* Prevention by celecoxib of secondary hyperalgesia induced by formalin in rats. *Life Sci* 2004; 75 (23):2807-2817 **8.** Sluka KA *et al.* Reduction in joint swelling and hyperalgesia following post-treatment with a non NMDA glutamate receptor antagonist. *Pain.* 1994; 59 (1):95-100 **9.** Innes JF *et al.* Systematic review of the safety and efficacy of long-term NSAID use in treatment of canine osteoarthritis. *Vet Rec* In Press **10.** Pfizer Study Number 2167A-10-97-003

Pfizer Animal Health

For further information please contact Pfizer Animal Health, Walton Oaks, Tadworth, Surrey KT20 7NS POM-V
Pfizer Animal Health, 9 Riverwalk, National Digital Park, Citywest Business Campus, Dublin 24 POM
Trocoxil contains mavacoxib.
AH388/09

Managing pain is integral to the treatment of osteoarthritis[1]

- If pain is not appropriately managed, central sensitisation can occur[2-4]
- Central sensitisation can be involved in joint inflammation and pathology[5-7, 9]
- Continuous pain control may:
  - Prevent the development of central sensitisation[7,9]
  - Reduce joint inflammation[8]
  - Progressively reduce pain[9]
  - Reduce the number of relapses[10]

Trocoxil® –The continuous path of pain relief

in a monthly dose*

- Delivers a full month's pain relief in a single dose*
- Continuous pain relief*
- Chewable tablet with beef flavouring
- Convenient dosing – 2 mg/kg, available in 5 strengths (6 mg, 20 mg, 30 mg, 75 mg and 95 mg)
- Peace of mind for your clients with assured continuous pain relief in a monthly dose*

*Trocoxil is dosed once monthly. An additional dose should be given on day 14 after treatment is initiated – the 'jump-start' dosing regime. This thereby provides continuous pain relief within the treatment cycle (7 consecutive doses).

Trocoxil® DATA SHEET

Trocoxil® chewable tablets for dogs

Presentation

Trocoxil chewable tablets are triangular tablets containing 6, 20, 30, 75 or 95 mg mavacoxib. Each tablet has a mottled brown appearance embossed with the tablet strength on one side and the word "Pfizer" on the other.

Uses

For the treatment of pain and inflammation associated with degenerative joint disease in dogs aged 12 months or more in cases where continuous treatment exceeding one month is indicated.

Dosage and administration

For oral use.

THIS IS NOT A DAILY NSAID. The dose is 2 mg mavacoxib per kg body weight given immediately before or with the dog's main meal. Care should be taken to ensure that the tablet is ingested. The treatment should be repeated 14 days later, thereafter the dosing interval is ONE MONTH. A treatment cycle should not exceed 7 consecutive doses (6.5 months).

Bodyweight (kg)	Number and strength of tablets to be administered				
	6 mg	20 mg	30 mg	75 mg	95 mg
5-6	2				
7-10		1			
11-15			1		
16-20		2			
21-23		1	1		
24-30			2		
31-37				1	
38-47					1
48-52			1	1	
53-62			1		1
63-75				2	

Contra-indications, warnings, etc

Do not use in dogs less than 12 months of age and/or less than 5 kg body weight.
Do not use in dogs suffering from gastro-intestinal disorders including ulceration and bleeding.
Do not use where there is evidence of a haemorrhagic disorder.
Do not use in cases of impaired renal or hepatic function.
Do not use in cases of cardiac insufficiency.
Do not use in pregnant, breeding or lactating animals.
Do not use in cases of hypersensitivity to the active substance or to any of the excipients.
Do not use in cases of known hypersensitivity to sulphonamides.
Do not use concomitantly with glucocorticoids or other NSAIDs.
Do not administer other NSAIDs within 1 month of the last administration of Trocoxil.

Mavacoxib exhibits an extended plasma half life due to its low rate of elimination. This corresponds to a duration of effect of 1-2 months after administration of the second dose (and following doses). Care should be taken to avoid treatment of animals that might not tolerate prolonged NSAID exposure. A maximum treatment administration of 6.5 months continuous therapy is recommended so as to manage plasma levels of mavacoxib in animals which exhibit reduced elimination.

Animals should undergo a thorough clinical examination before commencing treatment with Trocoxil. Animals with evidence of impaired renal or hepatic function, or with evidence of a protein or blood-losing enteropathy are not suitable for treatment with Trocoxil. It is recommended to repeat the clinical examination one month after commencing treatment with Trocoxil and prior to administration of the third dose.

Mavacoxib is excreted via bile and in dogs with hepatic disorders reduced elimination and thus excessive accumulation could occur. For this reason dogs with hepatic disorders should not be treated.

Avoid use in any dehydrated, hypovolaemic or hypotensive animal, as there is a potential risk of increased renal toxicity. Concurrent administration of potentially nephrotoxic medicinal products should be avoided.

Ensure appropriate hydration and haemodynamic status when animals receiving Trocoxil undergo anaesthesia and/or surgical procedures or develop conditions which may result in dehydration or compromised haemodynamic status. The key aim of intervention is to maintain renal perfusion.

Adverse reactions of NSAIDs such as loss of appetite, diarrhoea, vomiting, apathy and degradation of renal biochemistry parameters and impaired renal function have occasionally been reported. In rare cases these may be fatal.

If an adverse reaction to the administration of Trocoxil occurs, no further tablets should be administered and general supportive therapy, as applied to clinical overdosage with NSAIDs, should be applied. Particular attention should be paid to maintaining haemodynamic status. Veterinarians should be aware that clinical signs of adverse reactions may continue when supportive therapy (such as gastro protectants) is discontinued.