WARNING
KEEP OUT OF REACH OF CHILDREN
FOR ANIMAL TREATMENT ONLY

RESTRICTED VETERINARY MEDICINE

Norflunix

Active Ingredient:
FLUNIXIN 50 mg/mL (as Flunixin meglumine)

READ THE ENTIRE LABEL BEFORE USE

PHARMACOLOGY

Actions

Flunixin meglumine is a non-steroidal anti-inflammatory agent with analgesic and antipyretic activity.

Flunixin, through inhibition of cyclo-oxygenase, blocks synthesis of eicosanoids, including prostaglandins, thromboxane, and prostacyclin (PG12), which are chemical mediators of inflammation. Of the NSAIDs, flunixin is considered to be the most potent cyclo-oxygenase inhibitor, in contrast to other NSAIDs, therapeutic pharmacological effects are associated with relatively low plasma levels of flunixin. It is reported to be more analgesic than mecofenamic acid, phenylbutazone, naproxen, salicylic acid, pentazocine lactate, pethidine hydrochloride and codeine phosphate, and to provide comparable analgesia to clinically effective doses of morphine. Analgesic and anti-inflammatory effects of flunixin are dose related and tolerance, as occurs with narcotic agents, apparently does not develop to the action of flunixin.

Clinical studies have confirmed the analgesic and anti-inflammatory efficacy of flunixin in the therapy of musculoskeletal disorders in horses and dogs and colic in horses. In equine colic models flunixin analgesia has been found to be superior to that of pethidine. Flunixin does not significantly alter gastrointestinal motility, blood pressure, or cardiac rhythm in horses.

Thromboxane and prostacyclin are involved in the adverse haemodynamic changes associated with endotoxic shock. Flunixin administration decreases endotoxin-induced lactic acidosis, reduces severity of arterial hypotension and endothelial cell injury, and improves venous return. Flunixin treatment of dogs with experimental E.coli, septicaemia prevents arterial hypotension and hypoxaemia and has resulted in improved animal survival.

Vascular changes in uveitis may be mediated at least in part by endogenous prostaglandin release, and a cause and effect relationship between prostaglandin release and subsequent increase in aqueous protein concentration has been established. Administration of flunixin prior to intraocular surgery is effective in reducing aqueous humour prostacyclin accumulation in the horse. Intravenous flunixin, alone or in combination with corticosteroid, has been shown to reduce aqueous flare in dogs after intraocular surgery.

PHARMACOKINETICS

Flunixin has a rapid onset and long duration of action. Therapeutic effects are manifest within 2 hours after parenteral or oral administration. Peak response is reached between 12 and 16 hours after administration, and duration of action is up to 36 hours. The plasma half life is reported to be 1.6 hours in horses, 3.7 hours in dogs, and 8.1 hours in cattle.

Flunixin is widely distributed throughout body tissues and fluids. Renal excretion is significant in the elimination of flunixin, which is excreted in the urine largely in conjugated form. Excretion via bile and other gastrointestinal secretions may also occur. Flunixin is detectable by conventional analytical methods, in equine urine for at least 72 hours after dosing and may be detectable by some techniques for up to 15 days after administration. Drug clearance time after sequential doses does not differ significantly from that following a single dose.

Flunixin apparently does not accumulate in body tissues. NSAIDs however, being acidic, have a propensity to accumulate at sites of low pH such as at regions of inflammation. In experimental models of acute inflammation in horses, concentrations of flunixin in inflammatory exudates have been found to be higher than those in plasma by 6 hours after intravenous administration of a single therapeutic dose. Flunixin suppresses the production of PG12 in inflammatory exudates for 12 to 24 hours after a single intravenous dose.

This long pharmacological action of flunixin is at variance with its short plasma half-life in the horse. This may be attributable to the capacity of NSAIDs to irreversibly bind to cyclo-oxygenase, the accumulation of flunixin at inflammatory sites, and the prolonged excretion of the agent from the body.

CLINICAL APPLICATION

Norflunix produces effective anti-inflammatory and analgesic action in a wide range of musculoskeletal disorders in horses, dogs, cattle and pigs. In those species it may be used in the therapy of arthritis, myelitis and traumatic injuries resulting in fractures and contusions.

Norflunix administration results in effective visceral analgesia in cases of equine colic due to flatulence or inflammatory causes. Flunixin is considered to be a more potent analgesic than many of the narcotic or other non-steroidal anti-inflammatory drugs and is widely used in the therapy of equine colic.

Intravenous administration of flunixin has been advocated in the therapy of ocular inflammatory conditions, and may be employed pre-and post-operatively to reduce inflammation resulting from intraocular surgery in the horse and dog. Norflunix may be a useful alternative, or adjunct, to corticosteroids in such cases. Flunixin may be administered subconjunctivally prior to intraocular surgery in the horse to reduce aqueous humour prostacyclin accumulation.

Norflunix has been used successfully to reduce the adverse haemodynamic changes which characterise endotoxic shock in both horses and dogs. The agent is also recommended as an adjunct to the therapy of Mastitis-Metritis-Agalactia (MMA) syndrome in sows. Therapeutic effects in such cases are observed at or below, anti-inflammatory dose rates of flunixin.

In cattle, Norflunix is used for its anti-inflammatory and analgesic actions in the therapy of aseptic laminitis and peripheral nerve injury resulting from direct trauma or pressure. Flunixin administered intravenously at 1.1 mg/kg daily has also been recommended as an adjunct to treatment of persistent hyperthermia.

Norflunix may be administered either intravenously or intramuscularly with comparable efficacy, and onset and duration of action. Flunixin has a long pharmacological action, and therapeutic effects are maintained even at low plasma concentration.

Flunixin has a wide margin of safety and reports of adverse reactions are rare at therapeutic dose rates and recommended treatment duration. Intravenous administration of flunixin at up to five times the recommended dose rate and for twice the recommended treatment period have been reported to produce no gross clinical abnormalities and no changes in haematological, biochemical or urinary parameters. Parenteral administration of the agent rarely causes tissue irritation.

DOSAGE & ADMINISTRATION:
Do not use in cats.
Do not admix in syringe with other compounds.
Do not use concomitantly with other anti-inflammatory drugs, or with nephrotoxic substances.
Use with caution in animals with pre-existing gastrointestinal ulceration, renal, hepatic or haematologic disorders.

Horses: 1.1 mg/kg (1 mL/45 kg) bodyweight daily for up to 5 days, by IV or IM injection.
Cattle: 1.1-2.2 mg/kg (1-2 mL/45 kg) bodyweight daily for 3-5 days, by IV or IM injection.
Pigs: 1.1-2.2 mg/kg (1-2 mL/45 kg) bodyweight daily for up to 3 days, by deep IM injection.
Dogs: 1 mg/kg (0.2 mL/10 kg) bodyweight daily for up to 3 days, by IV or IM injection.

All potentially irritant substances given by intramuscular injection may result in the tissue damage necessary for clostridial bacteria to proliferate.

WITHHOLDING PERIODS:
It is an offence for users of this product to cause residues exceeding the relevant MRL in the Food Notice: Maximum Residue Levels for Agricultural Compounds.

MILK: Nil
MEAT: **Cattle** producing meat or offal for human consumption must not be sold for slaughter either during treatment or within **1 day** of the last treatment.
Pigs producing meat or offal for human consumption must not be sold for slaughter either during treatment or within **3 days** of the last treatment.
Horses producing meat or offal for human consumption must not be sold for slaughter either during treatment or within **63 days** of the last treatment.

PRECAUTIONS:
Prostaglandins have a cytoprotective action on the gastric mucosa, and in some species maintenance of renal blood flow in hypovolaemic states is prostaglandin dependent, flunixin should therefore be used with caution in conjunction with ulcerogenic or nephrotoxic agents; in cases of pre-existing gastrointestinal ulceration or renal diseases, and in hypovolaemic patients. Care should be exercised in the use of flunixin in patients with hepatic disease, haematological disorders or severe cardiac failure.
As with NSAIDs, flunixin should be used cautiously in conjunction with highly protein-bound drugs such as phenytoin, valproic acid, oral anticoagulants, other anti-inflammatory agents, and sulfonamides.
A case of flunixin toxicity has been reported in a pony mare after intravenous administration of flunixin at greater than 5 times the recommended dose for 5 days. Clinical signs observed included anorexia, depression, gastrointestinal ulceration, hypoproteinaemia and neutropaenia.
In dogs treated with flunixin at excessive doses or for prolonged periods, vomiting, diarrhoea, and gastrointestinal ulceration may occur.
Flunixin, when used in the therapy of equine colic, may mask the behavioural and cardiopulmonary signs associated with endotoxaemia or intestinal devitalisation. Care should be taken to avoid intra-arterial injection of flunixin as it may cause transient CNS stimulation, ataxia, hyperventilation, and muscle weakness.
Flunixin may be slightly irritant when administered by intramuscular injection to young animals or if injected too superficially into older animals.
Safety of the use of flunixin during pregnancy has not been established.

ADVERSE EFFECTS
Occasional cases of localised swelling, induration, muscle stiffness, and sweating have been reported following intramuscular injection of flunixin in horses.

PRESENTATION:
Cartons of 12 x 50 mL and 12 x 100 mL glass bottles.

WARNING
Dangerous to the Environment

Handling Precautions:
May be harmful if swallowed or absorbed through the skin. May possibly affect many organs. Wash hands and exposed skin before meals and after use. Avoid skin contact.

First Aid:
IF swallowed do NOT induce vomiting. For advice contact the National Poisons Centre 0800 POISON (0800 764 766) or a doctor immediately. If skin or hair contact occurs remove contaminated clothing and flush skin and hair with running water.

Environmental Protection:
Harmful to terrestrial vertebrates. Avoid release to the environment.

Disposal:
Preferably dispose of product by use. Otherwise dispose of product, packaging and waste at an approved landfill or equivalent facility.

STORAGE
Store below 25°C (air conditioning).

Registered pursuant to the ACVM Act 1997 No. A7861
See www.foodsafety.govt.nz for registration conditions.

Registered to and distributed by:
Norbrook NZ Ltd
KPMG Centre,
18 Viaduct Harbour Avenue,
Auckland
Ph: 0800 224 022

052460I08

Norbrook®