TECHNICAL NOTES

Flunixin Injection

Active Constituent

50 mg/mL FLUNIXIN (as MEGLUMINE)

Indications

A non-steroidal, anti-inflammatory, analgesic and antipyretic, with anti-prostaglandin effects for use in horses, cattle, pigs and dogs.

Contraindications

This product is contraindicated for use in cats.

This product is contraindicated for concomitant use with other anti-inflammatory drugs, or with nephrotoxic substances.

This product is contraindicated when admixed in a syringe with other compounds.

Precautions

Use with caution in animals with pre-existing gastrointestinal ulceration, renal, hepatic or haematological disorders.

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. Do not use in cases of pre-existing gastrointestinal ulceration or renal disease, 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 other 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 sulphonamides.

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.

Side Effects

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

Dosage and Administration

Use the contents within 28 days of first broaching of the vial. Discard the unused portion.

Horses: 1.1 mg/kg (1 mL/45 kg) bodyweight daily for up to 5 days, by intravenous or intramuscular injection.

Cattle: 1.1-2.2 mg/kg (1-2 mL/45 kg) bodyweight daily for 3 to 5 days, by intravenous or intramuscular injection.

Pigs: 1.1-2.2 mg/kg (1-2 mL/45 kg) bodyweight daily for up to 3 days, by deep intramuscular injection.

Dogs: 1 mg/kg (0.2 mL/10 kg) bodyweight daily for up to 3 days, by intravenous or intramuscular injection.

General Directions

PHARMACOLOGY

Actions:

Flunixin meglumine is a non-steroidal anti-inflammatory agent with analgesic and antipyretic activity. Flunixin, through inhibition of cyclooxygenase, 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 cyclooxygenase inhibitor, in contrast to other NSAIDs, therapeutic pharmacological effects are associated with relatively low plasma levels of flunixin. It is reported to be a more potent analgesic than meclofenamic acid, phenylbutazone, naproxen, salicyclic 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 of colic in horses. In equine colic models, flunixin analgesia has been found 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 corticosteroids, 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 manifested within 2 hours and 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 PGE2 in inflammatory exudates for 12 to 24 hours after a single intravenous dose.

The 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 cyclooxygenase, the accumulation of flunixin at inflammatory sites, and the prolonged excretion of the agent from the body.

CLINICAL APPLICATION

elevet+ Flunixin Injection provides 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.

elevet+ Flunixin Injection 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 had 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. elevet+ Flunixin Injection 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.

Flunixin 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, elevet+ Flunixin Injection 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 been recommended as an adjunct to the treatment of persistent hyperthermia.

elevet+ Flunixin Injection 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 concentrations.

elevet+ Flunixin Injection has a wide margin of safety and reports of adverse reactions are rare at therapeutic dose rates and recommended treatment durations. Intravenous administrations 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.

Withholding Periods

MEAT (CATTLE AND PIGS)

DO NOT USE LESS THAN 7 days before slaughter for human consumption.

MEAT (HORSES)

DO NOT USE less than 28 days before slaughter for human consumption.

MILK

Milk collected from cows within 36 hours (3 milkings) following treatment MUST NOT BE USED or processed for human consumption or fed to bobby calves.

Trade Advice

EXPORT SLAUGHTER INTERVAL (ESI)

An ESI has not been established for this product. Note—observing the meat withholding period may not be sufficient to mitigate potential risks to export trade. Trade advice should be sought from AVet Health Ltd on 1300 28 38 28 before using this product.

Safety Data Sheet

For Safety Data Sheet see www.avet.health

First Aid Instructions

If poisoning occurs, contact a doctor or Poisons Information Centre. Phone Australia 13 11 26.

Disposal

Dispose of container by wrapping with paper and putting in garbage.

Storage

Store below 25°C (air conditioning).

Presentation

50 mL and 100 mL multidose vial

Poisons schedule

S4

Registration Numbers

APVMA Approval No.: 92610