Flunixin is a non-steroidal antiinflammatory 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 and, 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, salicylic acid, pentazocine lactate, pethidine, hydrochloride and codeine phosphate, and to provide comparative analgesia to clinically effective doses of morphine. Analgesic and antiinflammatory 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 antiinflammatory 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.

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, and 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 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 exudate 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.

INDICATIONS
A non-steroidal, anti-inflammatory, analgesic and antipyretic, with anti-prostaglandin effects, for use in horse, cattle, pigs and dogs. CaleFlunix may be used to treat a wide range of musculoskeletal disorders including arthritis, myelitis and traumatic injuries resulting from fractures and contusions.

CaleFlunix 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 antiinflammatory 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. CaleFlunix 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, antiinflammatory dose rates of flunixin.

In cattle, CaleFlunix Injection is used for its antiinflammatory 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 treatment of persistent hyperthermia.

CaleFlunix 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.
Flunixin has a wide margin of safety and reports of adverse reactions are rare at therapeutic dose rates and recommended treatment durations. Intravenous administration of flunixin at up to five times the recommended dose rate or 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.

**CONTRAINDICATIONS**
This product is contraindicated for use in cats.

**WARNINGS**
Concurrent administration with other antiinflammatory drugs or nephrotoxic agents should be avoided. The product should not be admixed in syringes 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 animals 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 antiinflammatory 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.
First Aid: If poisoning occurs, contact a doctor or Poisons Information Centre, Australia phone 131 126.
Dispose: Dispose of empty container by wrapping with paper and putting in garbage.

**WITHHOLDING PERIODS, EXPORT SLAUGHTER INTERVALS**
**Meat:** Cattle and Pigs 7 days, Horses 28 days. **Milk:** 36 hours.

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

**DOSEAGE AND ADMINISTRATION; DIRECTIONS FOR USE**
**HORSES:** 1.1 mg/kg (1 mL/45 kg) bodyweight daily for up to 5 days, by intravenous or intramuscular injection.
The recommended dose for the alleviation of pain associated with equine colic is 1.1 mg/kg bodyweight. Intravenous administration is recommended for prompt relief. Treatment may be repeated when signs of colic occur. The cause of colic should be determined and treated with concomitant therapy.
**CATTLE:** For infectious respiratory conditions and “downer cow” syndrome 2.2 mg/kg administered intravenously reduces body temperature. For optimum results, once daily dosage for 1 - 3 days may be required. Concomitant anti-infective therapy will be required in the presence of bacterial infections. Other uses in cattle include footrot, musculoskeletal indications such as gonitis in the bull and interdigital fibroma.
Visceral pain (colic) will respond to Caleflunix therapy as in the horse. The dose rate for these indications is 1.1 mg/kg administered intramuscularly or intravenously.
**PIGS:** Sows affected by MMA syndrome should receive 2.2 mg/kg (2 mL/45 kg) by deep intramuscular injection (5 cm). Caleflunix should not be deposited in fat tissue. One or two injections twelve hours apart can be administered depending on clinical response.
**DOGS:** A dose rate of 1.1 mg per kg bodyweight should not be exceeded in the canine.
Arthritis: For acute problems, administer one day only. For severe or chronic arthritis, administer Caleflunix for 2 - 3 days.
Heat Stroke: One administration IV at a dose rate not exceeding 1.1 mg/kg bodyweight will reduce temperature in one hour to normal level and maintain it. Supportive therapy is necessary following Caleflunix.

**PRESENTATION**
Injection (multidose vial): 50 mL.

**STORAGE**
Store below 30°C (room temperature).
Use the contents within 35 days of first broaching the vial. Discard the unused portion. Product should be stored in an upright position.

**POISONS SCHEDULES**
S4

**APVMA NUMBER**
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