

FLUNIXIN (Veterinary—Systemic)

Some commonly used *brand names* for veterinary-labeled products are: *Banamine*; *Banamine-S*; *Cronyxin*; *Flumeglumine*; *Flunazine*; *Flu-nix*; *Flunixamine*; *Suppressor*; *Suppressor-Dairy*; and *Vedagesic*.

Note: For a listing of dosage forms and brand names by country availability, see the *Dosage Forms* section(s).

Category: Analgesic; anti-inflammatory (nonsteroidal); antipyretic.

Indications

Note: The text between ^{EL,US} and ^{EL} describes uses that are not included in U.S. product labeling. Text between ^{EL,CAN} and ^{EL} describes uses that are not included in Canadian product labeling.

The ^{EL,US} or ^{EL,CAN} designation can signify a lack of product availability in the country indicated. See the *Dosage Forms* section of this monograph to confirm availability.

Accepted

Fever (treatment)—

Cattle: Flunixin injection is indicated for control of fever associated with bovine respiratory disease, endotoxemia, and acute bovine mastitis. ^(R-1; 24; 42-46)

^{EL,CAN}**Pigs^{EL}:** Flunixin injection is indicated for control of fever associated with swine respiratory disease. ^(R-3)

^{EL,US,CAN}**Dogs^{EL}** and ^{EL,US,CAN}**horses^{EL}:** Flunixin is used for control of fever.

Inflammation, endotoxemia-associated (treatment)—

Cattle: Flunixin injection is indicated for control of inflammation in endotoxemia. ^(R-1; 24)

^{EL,US,CAN}**Dogs^{EL}** and ^{EL,US,CAN}**horses^{EL}:** Flunixin is used for control of inflammation in endotoxemia. ^(R-34-41)

Inflammation, musculoskeletal (treatment)—**Horses:** Flunixin

^{EL,US}granules^{EL}, ^{EL,CAN}paste^{EL}, and injection are indicated for control of inflammation associated with musculoskeletal disorders. ^(R-1; 2; 24; 25)

Pain, colic-associated (treatment)—**Horses:** Flunixin injection is indicated for control of pain associated with colic. ^(R-1; 24)

Pain, musculoskeletal (treatment)—**Horses:** Flunixin ^{EL,US}granules^{EL}, ^{EL,CAN}paste^{EL}, and injection are indicated for control of pain in equine musculoskeletal disorders. ^(R-1; 2; 4; 24; 25)

^{EL,US,CAN}**Sepsis (treatment adjunct)^{EL}**—**Cattle, dogs, and horses:**

Flunixin is used as adjunctive therapy in the treatment of sepsis. ^(R-21; 47)

Potentially effective

^{EL,US,CAN}**Emphysema, acute bovine pulmonary (treatment)^{EL}**—**Cattle:**

Although the efficacy has not been established, one study using an experimental model in calves suggests flunixin may reduce the pulmonary effects of this disorder. ^(R-27; 33)

Regulatory Considerations

U.S. and Canada—

Flunixin is not labeled for use in dry dairy cows, calves to be processed for veal, or horses to be slaughtered for food. ^(R-1; 2; 24) This drug is restricted to use by or on the order of a licensed veterinarian. ^(R-1; 2; 24)

Chemistry

Chemical name: Flunixin meglumine—3-Pyridinecarboxylic acid, 2-[[2-methyl-3-(trifluoromethyl)phenyl]amino]-, compd. with 1-deoxy-1-(methylamino)-D-glucitol (1:1). ^(R-6)

Molecular formula: Flunixin meglumine—C₁₄H₁₁F₃N₂O₂ · C₇H₁₇NO₅. ^(R-6; 24)

Molecular weight: Flunixin meglumine—491.46. ^(R-6; 24)

Description: Flunixin Meglumine USP—White to off-white crystalline powder. ^(R-20)

pKa: 5.82. ^(R-23; 24)

Solubility: Flunixin Meglumine USP—Soluble in water, in alcohol, and in methanol; practically insoluble in ethyl acetate. ^(R-20)

Pharmacology/Pharmacokinetics

Mechanism of action/Effect: The precise site and mode of action is unknown. Flunixin acts via analgesic and anti-inflammatory mechanisms. Analgesic actions may involve blocking pain impulse generation via a peripheral action by inhibition of the synthesis of prostaglandins and possibly inhibition of the synthesis or actions of other substances, which sensitize pain receptors to mechanical or chemical stimulation. Flunixin may act peripherally in inflamed tissue, probably by inhibiting the enzyme cyclooxygenase to decrease the formation of precursors of prostaglandins, and possibly by inhibiting other local mediators of the inflammatory response. ^(R-7)

Absorption: Flunixin is rapidly and relatively completely absorbed from the gastrointestinal tract of the horse. Flunixin has also been shown to be rapidly absorbed from the gastrointestinal tract following oral administration to dogs, monkeys, and rats. Rapid absorption following parenteral administration to cattle, dogs, monkeys, pigs, and rats has also been shown.

Pharmacokinetic data:

Species	Half-life of elimination (hours)	Vol _D , steady state (L/kg)	Clearance (mL/min/kg)
Cows ^(R-11)	3.8	0.42	2.4
^(R-14)	5.2	0.78 ± 0.24	1.9 ± 0.2
^(R-22)	8.1	0.50	1.5
Cows, lactating ^(R-28)	3.1	0.40 ± 0.11	2.5 ± 1.0
Dogs ^(R-12)	3.7 ± 1.2	0.18 ± 0.08	1.1 ± 0.2
^(R-29)	3.4 ± 1.1		1.0 ± 0.1
^(R-30)	4.2 ± 2.1	0.15 ± 0.05	1.1 ± 0.2
^(R-31)		0.15 ± 0.01	1.5 ± 0.002

Protein binding:

Cattle—Protein binding in bovine plasma has been determined to be >99% over a concentration range of 3 to 24 micrograms per milliliter (mcg/mL). ^(R-11)

Dogs—92.2% at 5 mcg/mL. ^(R-10)

Goats—84.8% at 5 mcg/mL. ^(R-10)

Horses—86.9% at 5 mcg/mL. ^(R-10)

Onset of action: Variable. ^(R-4; 13)

Concentrations:

Cattle—

Following a single intravenous dose of 2.2 mg per kg of body weight (mg/kg), plasma concentration was initially 16.16 ± 5.28 mcg/mL, declined to 1.22 ± 0.16 mcg/mL by 2 hours, and reached 0.5 ± 0.02 mcg/mL by 30 hours.

Following a single oral dose of 2.2 mg/kg, a peak concentration (C_{max}) of 0.9 ± 0.05 mcg/mL occurred 3.5 ± 1.0 hours (T_{max}) after the dose; serum concentration declined to 0.06 ± 0.01 mcg/mL by 30 hours. ^(R-14)

Dogs—

With intravenous administration of 1.1 mg/kg, serum concentration was approximately 6 mcg/mL at 1 hour post-injection and 0.3 mcg/mL at 8 hours post-

injection.^(R-12)

Following a single oral dose of 1.1 mg/kg, a peak serum concentration of 5.03 ± 0.99 mcg/mL at 1.10 ± 0.2 hours was measured.^(R-9) Twenty-four hours after dosing, serum concentration was below the level of detection (<0.05 mcg/mL).^(R-9)

Horses—

Following a single intravenous dose of 1.1 mg/kg, plasma concentration 1 hour post-injection was 1.6 mcg/mL (mean) and gradually diminished to 0.065 mcg/mL at 8 hours post-injection.^(R-13)

Following a single intravenous dose of 1 mg/kg, plasma concentration was initially 10 mcg/mL and decreased to 0.1 mcg/mL after 12 hours.

Peak plasma concentration of approximately 3 mcg/mL was reached about 30 minutes after a 1 mg/kg oral dose.

Elimination: *Cattle*—Hepatic, primarily by biliary secretion.^(R-15)

Precautions to Consider

Pregnancy/Reproduction

Cattle, horses, and pigs: The effects of flunixin on reproduction in bulls, horses, and pigs intended for breeding have not been studied.^(R-1-3) In cows, nonsteroidal anti-inflammatory drugs have the potential to affect the onset of the estrus cycle or of parturition.^(R-1)

Drug interactions and/or related problems

The following drug interactions and/or related problems have been selected on the basis of their potential clinical significance (possible mechanism in parentheses where appropriate)—not necessarily inclusive (» = major clinical significance):

Note: Combinations containing any of the following medications, depending on the amount present, may also interact with this medication.

- » Anti-inflammatory analgesics, nonsteroidal, other (concurrent use with other nonsteroidal anti-inflammatory medications may increase the risk of severe gastrointestinal side effects, including ulceration or hemorrhage, without providing additional improvement, and is generally not recommended) (because it is highly protein bound, the possibility exists that flunixin may displace other medications from their protein-binding sites or flunixin itself may be displaced, leading to increased action of the displaced medication; interactions based on this mechanism have not been documented.)

Medical considerations/Contraindications

The medical considerations/contraindications included have been selected on the basis of their potential clinical significance (reasons given in parentheses where appropriate)—not necessarily inclusive (» = major clinical significance).

Except under special circumstances, this medication should not be used when the following medical problems exist:

All species

Bleeding disorders

(because nonsteroidal anti-inflammatory drugs [NSAIDs] have been associated with inhibition of platelet aggregation, their administration to animals with bleeding problems, including coagulation or platelet function disorders, could increase the risk of adverse effects)

Gastrointestinal bleeding or ulceration

(many NSAIDs are known to increase the risk of gastrointestinal disease, particularly ulceration;^(R-1; 3) therefore, the presence of lesions before treatment may put an animal at risk of exacerbation or perforation)

Hypersensitivity to flunixin meglumine^(R-1; 3)

(previous development of adverse effects from flunixin may be an indication of increased risk of future sensitivity)

Risk-benefit should be carefully considered when the following medical problems exist:

All species

Cardiovascular disease or

Hepatic dysfunction or

Renal dysfunction

(because NSAIDs have been associated with renal toxicity, risk to patients with cardiovascular, hepatic, or renal compromise may be increased)^(R-1; 3; 16)

Dehydration^(R-1; 3)

(dehydration could increase the risk of renal toxicity with NSAID administration)

Side/Adverse Effects

The following side/adverse effects have been selected on the basis of their potential clinical significance (possible signs in parentheses where appropriate)—not necessarily inclusive:

Those indicating need for medical attention

Incidence unknown

Cattle

Hematochezia, hematuria

Note: *Hematochezia* and *hematuria* were reported when cattle were treated with three to five times the recommended dose.^(R-1)

Dogs

Ulceration, gastric^(R-8)

Horses

Anorexia;^(R-32) **depression; local tissue reactions** (induration, swelling, stiffness, sweating)—with intramuscular administration in some horses, particularly if given in the neck;^(R-1) **oral and gastric ulceration**—with very high doses or long-term use

Note: In rare cases, infections, sometimes clostridial, have been associated with the *local tissue reactions* seen with intramuscular administration.^(R-1)

Oral or gastric ulcerations are unlikely to occur when flunixin is administered at the recommended dose for 2 weeks.^(R-13)

Pigs

Local tissue reactions^(R-3)

Incidence rare

Cattle and horses

Anaphylactic-like reactions—primarily with intravenous administration^(R-1)

Overdose

For information in cases of overdose or unintentional ingestion, contact the American Society for the Prevention of Cruelty to Animals (ASPCA) National Animal Poison Control Center (888-426-4435 or 900-443-0000; a fee may be required for consultation) and/or the drug manufacturer.

Oral Dosage Forms

Note: The text between ^{ELUS} and ^{EL} describes uses not included in U.S. product labeling. Text between ^{ELCAN} and ^{EL} describes uses that are not included in Canadian product labeling.

The ^{ELUS} or ^{ELCAN} designation can signify a lack of product availability in the country indicated. See also the *Strength(s) usually available* section for each dosage form.

FLUNIXIN MEGLUMINE GRANULES USP

Usual dose: ^{ELUS} *Horses* ^{EL}—

Inflammation, musculoskeletal; or

Pain, musculoskeletal: Oral, 1.1 mg per kg of body weight, administered once a day for up to five days.^(R-25)

Strength(s) usually available:^(R-5; 25)

U.S.—

Veterinary-labeled product(s):
Not commercially available.
Canada—

Veterinary-labeled product(s):
25 mg per gram of granules (Rx) [*Banamine*].

Packaging and storage: Store between 2 and 30 °C (36 and 86 °F), unless otherwise specified by the manufacturer.

USP requirements: Preserve in well-closed containers. Label Granules to indicate that they are for veterinary use only. Contain an amount of flunixin meglumine equivalent to the labeled amount of flunixin, within ±10%. Meet the requirements for Identification, Dissolution (75% in 30 minutes in 0.1 N hydrochloric acid in Apparatus 2 at 50 rpm), and Uniformity of dosage units.^(R-20)

FLUNIXIN MEGLUMINE PASTE USP

Usual dose: ^{EL,CAN}Horses^{EL}—
Inflammation, musculoskeletal; or
Pain, musculoskeletal: Oral, 1.1 mg per kg of body weight, administered once a day for up to five days.^(R-2)

Strength(s) usually available:^(R-2; 5)
U.S.—
Veterinary-labeled product(s):
1.5 gram per 30-gram tube (Rx) [*Banamine*].
Canada—
Veterinary-labeled product(s):
Not commercially available.

Packaging and storage: Store between 2 and 30 °C (36 and 86 °F), unless otherwise specified by the manufacturer.^(R-2) Protect from freezing.

USP requirements: Preserve in a well-closed container. Label the Paste to indicate that it is for veterinary use only. Contains an amount of flunixin meglumine equivalent to the labeled amount of flunixin, within ±10%. Meets the requirements for Identification and Microbial limits.^(R-20)

Parenteral Dosage Forms

Note: The text between ^{EL,US} and ^{EL} describes uses not included in U.S. product labeling. Text between ^{EL,CAN} and ^{EL} describes uses that are not included in Canadian product labeling.
The ^{EL,US} or ^{EL,CAN} designation can signify a lack of product availability in the country indicated. See also the *Strength(s) usually available* section for each dosage form.

FLUNIXIN MEGLUMINE INJECTION USP

Usual dose:
Cattle—
Fever, associated with bovine respiratory disease, endotoxemia, and acute bovine mastitis;^(R-1; 24)
Inflammation, endotoxemia-associated;^(R-1; 24) or
^{EL,US,CAN}Sepsis (treatment adjunct)^{EL}: Intravenous, administered slowly, 2.2 mg per kg of body weight every twenty-four hours, or 1.1 mg per kg of body weight every twelve hours, for up to three days.^(R-1)
Withdrawal times: US—Meat: 4 days, Milk: 36 hours.^(R-1)
Canada—Meat: 6 days, Milk: 36 hours.^(R-24) Products in both the US and Canada are not labeled for use in dry dairy cows or calves to be processed for veal.^(R-1; 24)
Note: ^{EL,US,CAN}Emphysema, acute bovine pulmonary—
Although the efficacy has not been established, a study that showed some potential for reduction of pulmonary effects in an experimental model of the disorder in calves used an intravenous dose of 2.2 mg per kg of

body weight a day for three days^{EL}.^(R-27; 33)

Note: In cattle, intramuscular injection is not recommended.^(R-1; 24) local tissue reactions may result. Repeated intramuscular injections result in prolonged half-life, potentially lengthening residue withdrawal periods, and should be avoided.

Caution is advised when *dehydration* or other factors increasing the risk of nephrotoxicity are present (see also the *Medical considerations/Contraindications* section of this monograph).^(R-1)

Horses—

Inflammation, musculoskeletal;^(R-1)
Pain, colic-associated;^(R-1)
Pain, musculoskeletal;^(R-1)
^{EL,US,CAN}Fever^{EL};
^{EL,US,CAN}Inflammation, endotoxemia-associated^{EL},^(R-36-41) or
^{EL,US,CAN}Sepsis (treatment adjunct)^{EL}: Intramuscular or intravenous, 1.1 mg per kg of body weight once a day for up to five days.^(R-1)

Withdrawal times: US and Canada—Product labeling states that flunixin injection is not for use in horses intended to be slaughtered for use in food.^(R-1; 24)

Note: For *colic-associated pain*, intravenous administration is recommended; in a few animals, one or two additional doses may be necessary if signs of colic return while underlying causes are determined and treated.^(R-1)

^{EL,US,CAN}For treatment of *endotoxemia* or *sepsis* in horses, an intravenous dosage regimen similar to that for colic-associated pain might be used, with additional doses every six to twelve hours after the initial one, dependent on the clinical course. The dose recommendation is based on studies performed with experimentally induced models of endotoxemia in horses.^(R-37; 39; 41)

Other studies using models of endotoxemia in horses have shown that 0.25 mg of flunixin per kg of body weight every eight hours will provide dose-dependent suppression of eicosanoid synthesis, while not relieving all clinical signs; the level of pain relief provided by this dose was not assessed.^{EL}^(R-26; 36; 38; 40)

Note: Intramuscular administration of flunixin meglumine injection has been reported to cause *local tissue reactions* (including induration, swelling, stiffness, and sweating) in some horses, especially if administered in the neck.^(R-1) Infections, sometimes clostridial, have been associated with intramuscular administration in rare cases.^(R-1)

Intra-arterial injection should be avoided.^(R-1)

^{EL,CAN}Pigs^{EL}—Fever: Intramuscular, 2.2 mg per kg of body weight, administered as a single dose in the neck musculature.^(R-3)

Withdrawal times: US—Meat: 12 days.^(R-3) In some animals, local tissue irritation from intramuscular injection does not resolve by 28 days after injection; some trim loss may occur at slaughter.^(R-3)

^{EL,US,CAN}Dogs^{EL}—

Fever;
Inflammation, endotoxemia-associated; or
Sepsis (treatment adjunct): Intramuscular or intravenous, 0.5 to 1 mg per kg of body weight as a single dose, or, if necessary, once a day for no more than three days.^(R-19)

Note: Because dogs are sensitive to the toxic effects of other nonsteroidal anti-inflammatory analgesics, one reference suggests administering only a single dose of flunixin, and another suggests daily treatment for no more than 3 days.^(R-17-19)

The dose listed above is based on studies performed with experimentally induced models of endotoxemia or sepsis in dogs.^(R-21; 34; 35; 47)

Strength(s) usually available:^(R-1; 5)

U.S.—

Veterinary-labeled product(s):

50 mg per mL (Rx) [*Banamine*; *Banamine-S* [pigs]; *Flumeglumine*; *Flu-nix*; *Flunixamine*; *Suppressor* [horses only]; *Suppressor-Dairy*; *Vedagesic*; GENERIC].

Canada—

Veterinary-labeled product(s):

50 mg per mL (Rx) [*Banamine* [cattle and horses]; *Cronyxin*; *Flunazine*; *Suppressor*; GENERIC].

Note: Many U.S. products are labeled for both horses and cattle; in Canada, the majority are labeled for horses only.

Packaging and storage: Store between 2 and 30 °C (36 and 86 °F), unless otherwise specified by the manufacturer.^(R-1; 3; 24) Protect from freezing.

USP requirements: Preserve in multiple-dose containers at controlled room temperature. A sterile solution of Flunixin Meglumine in Water for Injection. Label Injection to indicate that it is for veterinary use only. Contains an amount of flunixin meglumine equivalent to the labeled amount of flunixin, within ±10%. Meets the requirements for Identification, Bacterial endotoxins, Sterility, and pH (7.8–9.0).^(R-20)

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