

PREVAIL- flunixin meglumine solution
VetOne/MWI

Prevail™

(flunixin meglumine injection)

50 mg/mL

Only for Intravenous Use in Beef and Dairy Cattle. Not for Use in Dry Dairy Cows and Veal Calves. For Intravenous and Intramuscular Use in Horses.

CAUTION Federal law restricts this drug to use by or on the order of a licensed veterinarian.

DESCRIPTION Each milliliter of Prevail™ (flunixin meglumine injection) contains 50 mg flunixin (equivalent to 83 mg flunixin meglumine), 0.1 mg edetate disodium, 2.2 mg sodium formaldehyde sulfoxylate, 4.0 mg diethanolamine, 207.2 mg propylene glycol, 5.0 mg phenol as preservative, hydrochloric acid, water for injection q.s.

PHARMACOLOGY:

Flunixin meglumine is a potent, non-narcotic nonsteroidal, analgesic agent with anti-inflammatory and antipyretic activity. It is significantly more potent than pentazocine, meperidine, and codeine as an analgesic in the rat yeast paw test.

Horse: Flunixin is four times as potent on a mg-per-mg basis as phenylbutazone as measured by the reduction in lameness and swelling in the horse. Plasma half-life in horse serum is 1.6 hours following a single dose of 1.1 mg/kg. Measurable amounts are detectable in horse plasma at 8 hours post injection.

Cattle: Flunixin meglumine is a weak acid ($pK_a=5.82$)¹ which exhibits a high degree of plasma protein binding (approximately 99%)². However, free (unbound) drug appears to readily partition into body tissues (V_{SS} predictions range from 297 to 782 mL/kg²⁻⁵. Total body water is approximately equal to 570 mL/kg)⁶. In cattle, elimination occurs primarily through biliary excretion.⁷ This may, at least in part, explain the presence of multiple peaks in the blood concentration/time profile following IV administration.²

In healthy cattle, total body clearance has been reported to range from 90 to 151 mL/kg/hr.²⁻⁵ These studies also report a large discrepancy between the volume of distribution at steady state (V_{SS}) and the volume of distribution associated with the terminal elimination phase (V_{β}). This discrepancy appears to be attributable to extended drug elimination from a deep compartment.⁸ The terminal half-life has been shown to vary from 3.14 to 8.12 hours.²⁻⁵

Flunixin persists in inflammatory tissues⁹ and is associated with anti-inflammatory properties which extend well beyond the period associated with detectable plasma drug concentrations.⁴⁻⁹ These observations account for the counterclockwise hysteresis associated with flunixin's pharmacokinetic/pharmacodynamic relationships.¹⁰ Therefore, prediction of drug concentrations based upon the estimated plasma terminal elimination half-life will likely underestimate both the duration of drug action and the concentration of drug remaining at the site of activity.

INDICATIONS

Horse: Prevail™ (flunixin meglumine injection) is recommended for the alleviation of inflammation and pain associated with musculoskeletal disorders in the horse. It is also recommended for the alleviation of visceral pain associated with colic in the horse.

Cattle: Prevail™ (flunixin meglumine injection) is indicated for the control of pyrexia associated with bovine respiratory disease, endotoxemia and acute bovine mastitis. Prevail™ is also indicated for the control of inflammation in endotoxemia.

DOSE AND ADMINISTRATION

100 mL: Use within 28 days of first puncture and puncture a maximum of 19 times. If using a needle larger than 16 gauge, discard any product remaining in the vial immediately after use.

250 mL: Use within 28 days of first puncture and puncture a maximum of 30 times. If more than 30 punctures are anticipated, the use of multi-dosing equipment is recommended. Puncture a maximum of 5 times with a dosage delivery device no larger than 4 gauge. Any product remaining beyond these parameters should be discarded.

Horse: The recommended dose for musculoskeletal disorders is 0.5 mg per pound (1 mL/100 lbs) of body weight once daily. Treatment may be given by intravenous or intramuscular injection and repeated for up to 5 days. Studies show onset of activity is within 2 hours. Peak response occurs between 12 and 16 hours and duration of activity is 24-36 hours.

The recommended dose for the alleviation of pain associated with equine colic is 0.5 mg per pound of body weight. Intravenous administration is recommended for prompt relief. Clinical studies show pain is alleviated in less than 15 minutes in many cases. Treatment may be repeated when signs of colic recur. During clinical studies approximately 10% of the horses required one or two additional treatments. The cause of colic should be determined and treated with concomitant therapy.

Cattle: The recommended dose for control of pyrexia associated with bovine respiratory disease and endotoxemia is 1.1 to 2.2 mg/kg (0.5 to 1.0 mg/lb; 1 to 2 mL per 100 lbs) of body weight given by slow intravenous administration either once a day as a single dose or divided into two doses administered at 12-hour intervals for up to 3 days. The total daily dose should not exceed 2.2 mg/kg (1.0 mg/lb) of body weight. Avoid rapid intravenous administration of the drug.

The recommended dose for acute bovine mastitis is 2.2 mg/kg (1 mg/lb; 2 mL per 100 lbs) of body weight given once by intravenous administration.

CONTRAINDICATIONS

Horse: There are no known contraindications to this drug when used as directed. Intra-arterial injection should be avoided. Horses inadvertently injected intra-arterially can show adverse reactions. Signs can be ataxia, incoordination, hyperventilation, hysteria, and muscle weakness. Signs are transient and disappear without antidotal medication within a few minutes. Do not use in horses showing hypersensitivity to flunixin meglumine.

Cattle: NSAIDs inhibit production of prostaglandins which are important in signaling the inhibition of parturition. The use of flunixin can delay parturition and prolong labor which may increase the risk of stillbirth. Do not use Prevail™ (flunixin meglumine injection) within 48 hours of expected parturition. Do not use in animals showing hypersensitivity

to flunixin meglumine. Use judiciously when renal impairment or gastric ulceration are suspected.

RESIDUE WARNINGS: Cattle must not be slaughtered for human consumption within 4 days of the last treatment. Milk that has been taken during treatment and for 36 hours after the last treatment must not be used for food. Not for use in dry dairy cows. A withdrawal period has not been established for this product in preruminating calves. Do not use in calves to be processed for veal. Not for use in horses intended for food. Approved only for intravenous administration in cattle. Intramuscular administration has result in violative residue in the edible tissues of cattle sent to slaughter.

PRECAUTIONS:

As a class, cyclo-oxygenase inhibitory NSAIDs may be associated with gastrointestinal and renal toxicity. Sensitivity to drug-associated adverse effects varies with the individual patient. Patients at greatest risk for renal toxicity are those that are dehydrated, on concomitant diuretic therapy, or those with renal, cardiovascular, and/or hepatic dysfunction. Since many NSAIDs possess the potential to induce gastrointestinal ulceration, concomitant use of Prevail™ (flunixin meglumine injection) with other anti-inflammatory drugs, such as other NSAIDs and corticosteroids, should be avoided or closely monitored.

Horse: The effect of Prevail™ (flunixin meglumine injection) on pregnancy has not been determined. Studies to determine activity of Prevail™ when administered concomitantly with other drugs have not been conducted. Drug compatibility should be monitored closely in patients requiring adjunctive therapy.

Cattle: Do not use in bulls intended for breeding, as reproductive effects of Prevail™ (flunixin meglumine injection) in these classes of cattle have not been investigated. NSAIDs are known to have potential effects on both parturition (See Contraindications) and the estrous cycle. There may be a delay in the onset of estrus if flunixin is administered during the prostaglandin phase of the estrous cycle. NSAIDs are known to have the potential to delay parturition through a tocolytic effect. The use of NSAIDs in the immediate post-partum period may interfere with uterine involution and expulsion of fetal membranes. Cows should be monitored carefully for placental retention and metritis if Prevail™ is used within 24 hours after parturition.

SAFETY

Horse: A 3-fold intramuscular dose of 1.5 mg/lb of body weight daily for 10 consecutive days was safe. No changes were observed in hematology, serum chemistry, or urinalysis values. Intravenous dosages of 0.5 mg/lb daily for 15 days; 1.5 mg/lb daily for 10 days; and 2.5 mg/lb daily for 5 days produced no changes in blood or urine parameters. No injection site irritation was observed following intramuscular injection of the 0.5 mg/lb recommended dose. Some irritation was observed following a 3-fold dose administered intramuscularly.

Cattle: No flunixin-related changes (adverse reactions) were noted in cattle administered a 1X (2.2 mg/kg; 1.0 mg/lb) dose for 9 days (three times the maximum clinical duration). Minimal toxicity manifested itself at moderately elevated doses (3X and 5X) when flunixin was administered daily for 9 days, with occasional findings of blood in the feces and/or urine. Discontinue use if hematuria or fecal blood are observed.

ADVERSE REACTIONS:

In horses, isolated reports of local reactions following intramuscular injection, particularly in the neck, have been received. These include localized swelling, sweating, induration, and stiffness. In rare instances in horses, fatal or nonfatal clostridial infections or other infections have been reported in association with intramuscular use of flunixin meglumine. In horses and cattle, rare instances of anaphylactic-like reactions, some of which have been fatal, have been reported, primarily following intravenous use.

To report suspected adverse drug events, for technical assistance or to obtain a copy of the Safety Data Sheet (SDS), contact Bimeda, Inc. at 1-888-524-6332. For additional information about adverse drug experience reporting for animal drugs, contact FDA at 1-888-FDA-VETS or online at www.fda.gov/reportanimalae.

HOW SUPPLIED:

Prevail™ (flunixin meglumine injection) , 50 mg/mL, is available in 100 mL and 250 mL multi-dose vials.

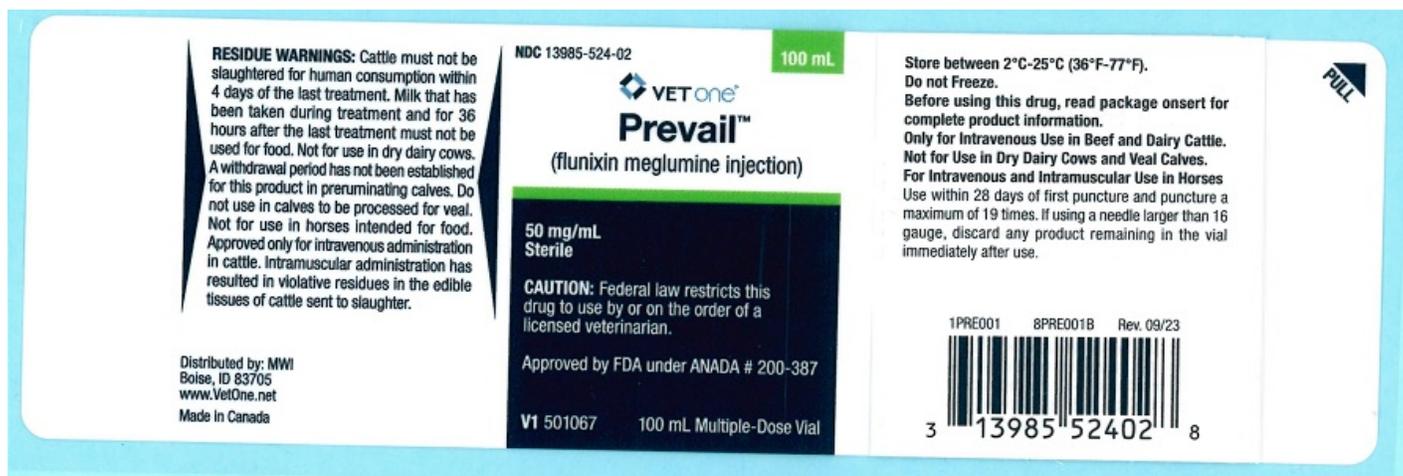
Store between 2°C and 25°C (36°F and 77°F). Do not Freeze.

See the in-use directions provided in the DOSE AND ADMINISTRATION section.

Approved by FDA under ANADA # 200-387

REFERENCES

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3. Anderson KL, Neff-Davis CA, Davis LE, Bass VD. Pharmacokinetics of flunixin meglumine in lactating cattle after single and multiple intramuscular and intravenous administrations. *Am J Vet Res.* 1990;51:1464-1467.
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7. Kopcha M, Ahl AS. Experimental uses of flunixin meglumine and phenylbutazone in food-producing animals. *J Am Vet Med Assoc.* 1989;194:445-49.
8. Wagner JG. Significance of ratios of different volumes of distribution in pharmacokinetics. *Biopharma and Drug Dispos.* 1983;4:263-270.
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10. Landoni MF, Cunningham FM, Lees P. Determination of pharmacokinetics and pharmacodynamics of flunixin in calves by use of pharmacokinetic/pharmacodynamic modeling. *Am J Vet Res.* 1995;56:786-794.



PREVAIL

flunixin meglumine solution

Product Information

Product Type	PRESCRIPTION ANIMAL DRUG	Item Code (Source)	NDC:13985-524
Route of Administration	INTRAVENOUS, INTRAMUSCULAR		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
FLUNIXIN MEGLUMINE (UNII: 8Y3JK0JW3U) (FLUNIXIN - UNII:356IB1O400)	FLUNIXIN MEGLUMINE	50 mg in 1 mL

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:13985-524-02	100 mL in 1 VIAL, MULTI-DOSE		
2	NDC:13985-524-04	250 mL in 1 VIAL, MULTI-DOSE		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANADA	ANADA200387	03/12/2012	

Labeler - VetOne/MWI (019926120)

Registrant - Bimeda Inc., Division of Cross Vetpharm Group (060492923)

Establishment

Name	Address	ID/FEI	Business Operations
Bimeda-MTC Division of Cross Vetpharm Group		256232216	manufacture

