

FLUNIXIN- flunixin meglumine injection, solution
BUTLER ANIMAL HEALTH SUPPLY, LLC dba COVETRUS NORTH AMERICA

covetrus®
Flunixin Injection
(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 Flunixin Injection contains 50 mg flunixin (equivalent to 83 mg flunixin meglumine), 0.1 mg edetate disodium, 2.5 mg sodium formaldehyde sulphoxylate, 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, non-steroidal, analgesic agent with anti-inflammatory and anti-pyretic 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/kg.^{2,5} Total body water is approximately equal to 570 ml/kg)⁶. In cattle, elimination occurs primarily through biliary excretion⁷. This may, at least in part, explain the presence of multiple peaks in the blood concentration/time profile following IV administration².

In healthy cattle, total body clearance has been reported to range from 90 to 151 mL/kg/hr²⁻⁵. 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_B). 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 concentration.^{4,9} These observations account for the counterclockwise hysteresis

concentration. These observations account for the counter-intuitive hyperalgesia 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: Flunixin 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: Flunixin Injection is indicated for the control of pyrexia associated with bovine respiratory disease, endotoxemia and acute bovine mastitis. Flunixin Injection is also indicated for the control of inflammation in endotoxemia.

DOSE AND ADMINISTRATION

Horse: The recommended dose for musculoskeletal disorders is 0.5 mg per pound (1 mL/100 lbs) of bodyweight once daily. Treatment may be given by intravenous or intramuscular injection and repeated for up to five 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 bodyweight. 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 the colic should be determined and treated with concomitant therapy.

Cattle: The recommended dose for control of pyrexia associated with bovine respiratory disease and endotoxemia and control of inflammation in endotoxemia is 1.1 to 2.2 mg/kg (0.5 to 1 mg/lb; 1 to 2 mL per 100 lbs) of bodyweight 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 bodyweight. Avoid rapid intravenous administration of the drug.

The recommended dose for acute bovine mastitis is 2.2 mg/kg (1.0 mg/lb; 2 mL per 100 lbs) of bodyweight given once by intravenous administration.

CONTRAINDICATIONS

Horse: There are no known contra-indications 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 initiation of parturition. The use of flunixin can delay parturition and prolong labor which

may increase the risk of stillbirth. Do not use Flunixin Injection (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. Intramuscular administration has resulted in violative residues 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 Flunixin Injection (flunixin meglumine injection) with other anti-inflammatory drugs, such as other NSAIDs and corticosteroids, should be avoided or closely monitored.

Horse: The effect of flunixin meglumine injection on pregnancy has not been determined. Studies to determine activity of flunixin meglumine injection 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 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 Flunixin Injection is used within 24 hours after parturition.

SAFETY

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

the 0.5mg/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 at 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 injection. 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 Covetrus® North America at (855) 724-3461. 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

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

Store between 2° and 30°C (36° and 86°F). Use within 60 days of first puncture. When using a draw-off spike or needle with a bore diameter larger than 16-gauge, discard any product remaining in the vial immediately after use.

REFERENCES

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- food-producing animals. *J Am Vet Med Assoc.* 1989;194:45-49
8. Wagner JG. Significance of ratios of different volumes of distribution in pharmacokinetics. *Biopharm & Drug Dispos.* 1983;4:263-270
 9. Lees P, Higgins AJ. Flunixin Inhibits prostaglandin E2 production in equine inflammation. *Res Vet Sci.* 1984;37: 347-349
 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.

Approved by FDA under ANADA # 200-308

Made in the UK

Questions?

(855) 724-3461

Distributed by:

Covetrus® North America

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Dublin, OH 43017

covetrus.com

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AH-FlunixinInjectionPI-01

REV: 1023

008845I01

Principal Display Panel - 250 mL Carton Label

covetrus®

NDC: 11695-7021-2

Flunixin Injection

(flunixin meglumine injection)

50 mg/mL

Sterile

Multiple-Dose Vial

Only for Intravenous Use in Beef and Dairy Cattle.

Not for Use in Dry Dairy Cows and Veal Calves.

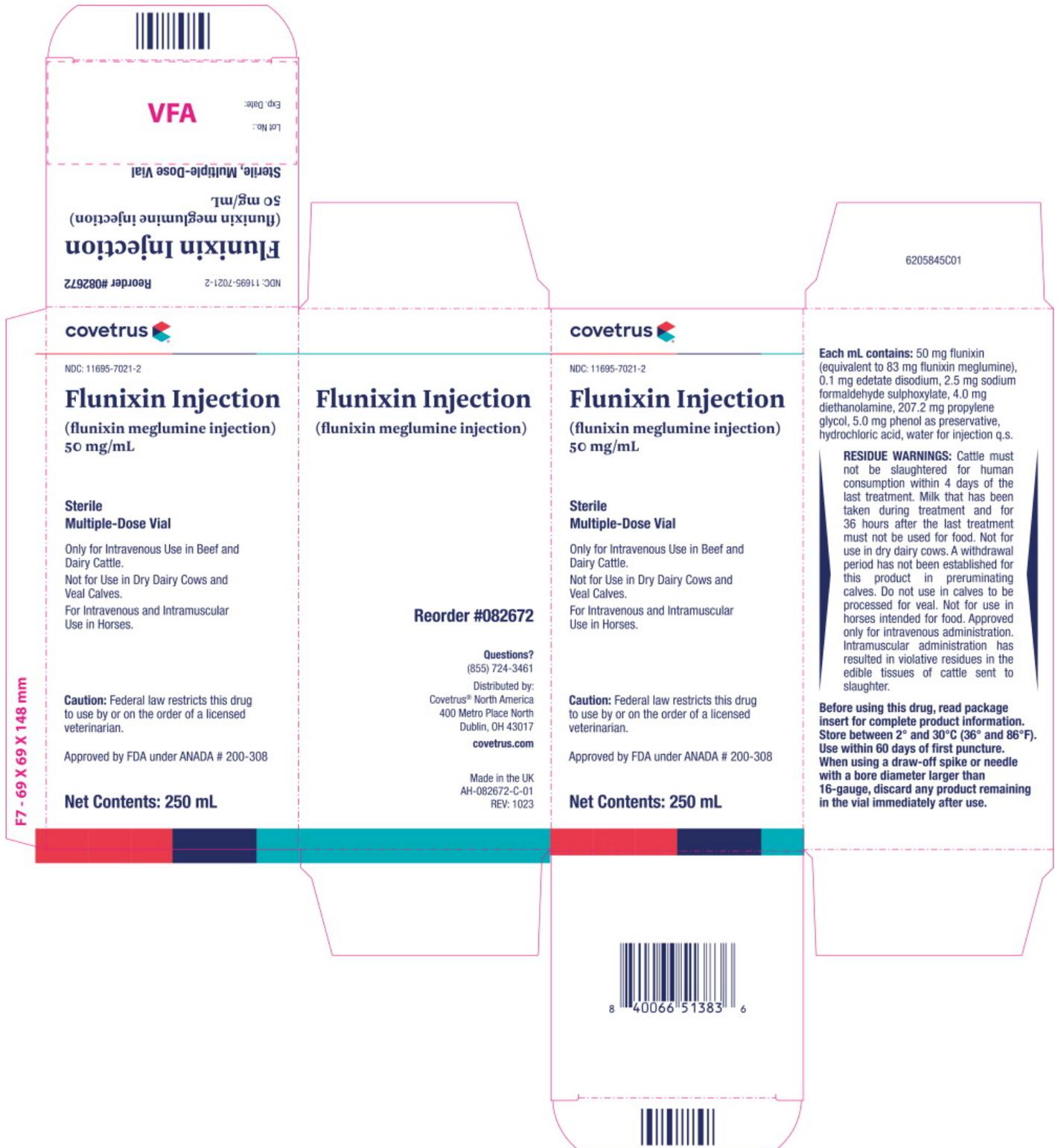
For Intravenous and Intramuscular

Use in Horses.

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

Approved by FDA under ANADA # 200-308

Net Contents: 250 mL



Principal Display Panel - 250 mL Bottle Label

covetrus®

NDC: 11695-7021-2

Flunixin Injection

(flunixin meglumine injection)

50 mg/mL

Sterile, Multiple-Dose Vial

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

Approved by FDA under ANADA # 200-308

Net Contents: 250 mL

| | | |
|---|--|---|
| <p>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. Intramuscular administration has resulted in violative residues in the edible tissues of cattle sent to slaughter.</p> <p>Store between 2° and 30°C (36° and 86°F). Use within 60 days of first puncture. When using a draw-off spike or needle with a bore diameter larger than 16-gauge, discard any product remaining in the vial immediately after use.</p> | <p>covetrus </p> <p>NDC: 11695-7021-2</p> <p>Flunixin Injection (flunixin meglumine injection) 50 mg/mL</p> <p>Sterile, Multiple-Dose Vial</p> <p>Caution: Federal law restricts this drug to use by or on the order of a licensed veterinarian.</p> <p>Approved by FDA under ANADA # 200-308</p> <p>Net Contents: 250 mL</p>  | <p>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.</p> <p>Before using this drug, read package insert for complete product information.</p> <p>Questions? (855) 724-3461</p> <p>Distributed by: Covetrus® North America 400 Metro Place North Dublin, OH 43017 covetrus.com</p> <p>Reorder #082672</p> <p>Made in the UK AH-082672-L-01 REV: 1023 009845L01</p> <p>Lot No.: Exp. Date:</p> <p>OVERPRINT AREA 20 x 25mm</p> |
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FLUNIXIN

flunixin meglumine injection, solution

Product Information

| | | | |
|--------------------------------|----------------------------|---------------------------|----------------|
| Product Type | PRESCRIPTION ANIMAL DRUG | Item Code (Source) | NDC:11695-7021 |
| Route of Administration | INTRAMUSCULAR, INTRAVENOUS | | |

Active Ingredient/Active Moiety

| Ingredient Name | Basis of Strength | Strength |
|--|--------------------|---------------|
| flunixin meglumine (UNII: 8Y3JK0JW3U) (flunixin - UNII:3561B1O400) | flunixin meglumine | 50 mg in 1 mL |

Inactive Ingredients

| Ingredient Name | Strength |
|---|------------------|
| sodium formaldehyde sulfoxylate (UNII: X4ZGP7K714) | 2.5 mg in 1 mL |
| edetate disodium (UNII: 7FLD91C86K) | 0.1 mg in 1 mL |
| diethanolamine (UNII: AZE05TDV2V) | 4.0 mg in 1 mL |
| propylene glycol (UNII: 6DC9Q167V3) | 207.2 mg in 1 mL |
| phenol (UNII: 339NCG44TV) | 5.0 mg in 1 mL |
| hydrochloric acid (UNII: QTT17582CB) | |
| water (UNII: 059QF0KO0R) | |

Packaging

| # | Item Code | Package Description | Marketing Start Date | Marketing End Date |
|---|------------------|---------------------------|----------------------|--------------------|
| 1 | NDC:11695-7021-1 | 1 in 1 CARTON | | |
| 1 | | 100 mL in 1 BOTTLE, GLASS | | |
| 2 | NDC:11695-7021-2 | 1 in 1 CARTON | | |
| 2 | | 250 mL in 1 BOTTLE, GLASS | | |

Marketing Information

| Marketing Category | Application Number or Monograph Citation | Marketing Start Date | Marketing End Date |
|--------------------|--|----------------------|--------------------|
| ANADA | ANADA200308 | 01/04/2024 | |

Labeler - BUTLER ANIMAL HEALTH SUPPLY, LLC dba COVETRUS NORTH AMERICA (603750329)

Registrant - Norbrook Laboratories Limited (214580029)

Establishment

| Name | Address | ID/FEI | Business Operations |
|-------------------------------|---------|-----------|------------------------------------|
| Norbrook Laboratories Limited | | 211218325 | MANUFACTURE, ANALYSIS, PACK, LABEL |

Revised: 12/2023

BUTLER ANIMAL HEALTH SUPPLY, LLC dba COVETRUS NORTH AMERICA