

Date of Approval: JUL 29 2004

FREEDOM OF INFORMATION SUMMARY

Supplemental Abbreviated New Animal Drug Application

ANADA 200-061

Flunixin Meglumine Solution 50 mg/mL
(flunixin meglumine)

Injectable Solution for use in Horses, Beef Cattle, and Nonlactating
Dairy Cattle

This supplement provides for the addition of a claim for
intravenous use in beef cattle and nonlactating dairy cattle.

Sponsor:

Agri Laboratories, Ltd.

FREEDOM OF INFORMATION SUMMARY

1. GENERAL INFORMATION:

- a. File Number: ANADA 200-061
- b. Sponsor: Agri Laboratories, Ltd.
P.O. Box 3103
St. Joseph, MO 64503
- Drug Labeler Code: 057561
- c. Established Names: Flunixin meglumine
- d. Proprietary Name: Flunixin Meglumine Solution
- e. Dosage Form: Sterile solution
- f. How Supplied: 50 mL, 100 mL, and 250 mL multi-dose vials
- g. How Dispensed: Rx
- h. Amount of Active Ingredients: 50 mg/mL flunixin meglumine
- i. Route of Administration: For intravenous or intramuscular injection in horses and for intravenous injection in beef cattle and nonlactating dairy cattle
- j. Species/Class: Horses; beef cattle; nonlactating dairy cattle
- k. Recommended Dosage: Horse: The recommended dose for musculoskeletal disorders is 0.5 mg per pound (1mL/100 lbs) of body weight once daily. Treatment may be given by intravenous or intramuscular injection and repeated for up to 5 days.
- 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 Treatment may be repeated when signs of colic recur.

Cattle: The recommended dose for cattle is 1.1 to 2.2 mg/kg (0.5 to 1 mg/lb; 1 to 2 mL per 100 lbs.) 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.

l. Pharmacological Category:

Anti-inflammatory; Analgesic

m. Indications:

Horse: Flunixin Meglumine 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 Meglumine is indicated for the control of pyrexia associated with bovine respiratory disease and endotoxemia. Flunixin Meglumine is also indicated for the control of inflammation in endotoxemia.

n. Pioneer Product:

BANAMINE Injectable Solution; flunixin meglumine; NADA 101-479; Schering-Plough Animal Health Corp.

o. Effect of Supplement:

This supplement provides for the addition of a claim for intravenous use in beef cattle and nonlactating dairy cattle to the labeling of the approved product Flunixin Meglumine Solution. The exclusivity period protecting this claim for the pioneer product expired on May 6, 2001.

2. TARGET ANIMAL SAFETY AND DRUG EFFECTIVENESS:

This approval does not affect this section of the summary. Refer to the Freedom of Information Summary of the original ANADA 200-061 E-0004 dated September 11, 1996, for more detail.

3. **HUMAN SAFETY:**

- **Tolerance:**

The tolerance established for the pioneer product applies to the generic product. A tolerance is established for residues of parent flunixin free acid of 0.125 part per million (ppm) in cattle liver (target tissue) and 0.025 ppm in cattle muscle under 21 CFR 556.286. The acceptable daily intake for total residues of flunixin is 0.72 micrograms per kilogram of body weight per day (21 CFR 556.286).

- **Withdrawal Time:**

Because a waiver of the *in vivo* bioequivalence study was granted, the withdrawal times are those previously assigned to the pioneer product. For this reason, a withdrawal period of 4 days has been established for Flunixin Meglumine Solution (flunixin meglumine) in beef cattle and nonlactating dairy cattle (21 CFR 522.970).

- **Regulatory Method for Residues:**

The determinative procedure for the determination of flunixin residues in bovine liver is a high performance liquid chromatography (HPLC) method. The confirmatory procedure for the determination of flunixin residues in bovine liver utilizes liquid chromatography/ mass spectrometry/mass spectrometry (LC/MS/MS) methodology.

The validated methods are on file at the Center for Veterinary Medicine, 7500 Standish Place, Rockville, MD 20855.

4. **AGENCY CONCLUSIONS:**

This ANADA submitted under section 512(b) of the Federal Food, Drug, and Cosmetic Act satisfies the requirements of section 512(n) of the act and demonstrates that Flunixin Meglumine Solution for use in horses, beef cattle, and non-lactating dairy cattle, when used under the proposed conditions of use, is safe and effective for its labeled indications.

5. **ATTACHMENTS:**

Facsimile generic labeling and currently approved pioneer labeling are attached as indicated below:

Generic Labeling: Flunixin Meglumine Solution (ANADA 200-061)
Labels for 50 mL, 100 mL, and 250 mL multi-dose vials
Package Insert

Pioneer Labeling: BANAMINE Injectable Solution (NADA 101-479)
Labels for 50 mL, 100 mL, and 250 mL multi-dose vials
Package Insert

For intravenous or intramuscular use in horses and for intravenous use in beef and nonlactating dairy cattle only. Not for use in lactating or dry dairy cows. Not for use in veal calves.

Read accompanying directions carefully.

Store between 2° and 30° C (36° and 86° F)

Rev 0201



MFD. FOR AGRI LABORATORIES, LTD.
St. Joseph, MO 64503

FLUNIXIN MEGLUMINE
SOLUTION 50 mg/mL
Sterile Multiple Dose Vial
Caution: Federal law restricts this drug to use by or on the order of a licensed veterinarian.
ANADA 200-061, Approved by FDA
NET CONTENTS: 50 mL
AgriLabs®

RESIDUE WARNINGS: Cattle must not be slaughtered for human consumption within 4 days of the last treatment. Not for use in lactating or dry dairy cows. A withdrawal period has not been established for this product in preparturient calves. Do not use in calves to be processed for veal. Not for use in horses intended for food.

FOR USE IN ANIMALS ONLY.

Lot No.:
Exp. Date:

For intravenous or intramuscular use in horses and for intravenous use in beef and nonlactating dairy cattle only. Not for use in lactating or dry dairy cows. Not for use in veal calves.

Read accompanying directions carefully.

Store between 2° and 30°C (36° and 86° F).

Rev. 0601



MFD. FOR AGRI LABORATORIES, LTD.
St. Joseph, MO 64503



**FLUNIXIN MEGLUMINE
SOLUTION 50 mg/mL**

Sterile Multiple Dose Vial

Caution: Federal law restricts this drug to use by or on the order of a licensed veterinarian.
ANADA 200-061, Approved by FDA

NET CONTENTS: 100 mL



RESIDUE WARNINGS: Cattle must not be slaughtered for human consumption within 4 days of the last treatment. Not for use in lactating or dry dairy cows. A withdrawal period has not been established for this product in preweaning calves. Do not use in calves to be processed for veal. Not for use in horses intended for food.

FOR USE IN ANIMALS ONLY.

Lot No.:

Exp. Date:

For intravenous or intramuscular use in horses and for intravenous use in beef and nonlactating dairy cattle only. Not for use in lactating or dry dairy cows. Not for use in veal calves.

Read accompanying directions carefully.

Store between 2° and 30°C (36° and 86° F).

Rev. 0601



MFD. FOR AGRI LABORATORIES, LTD.
St. Joseph, MO 64503



**FLUNIXIN MEGLUMINE
SOLUTION 50 mg/mL**

Sterile Multiple Dose Vial

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

ANADA 200-061, Approved by FDA

NET CONTENTS: 250 mL



RESIDUE WARNINGS: Cattle must not be slaughtered for human consumption within 4 days of the last treatment. Not for use in lactating or dry dairy cows. A withdrawal period has not been established for this product in prurminating calves. Do not use in calves to be processed for veal. Not for use in horses intended for food.

FOR USE IN ANIMALS ONLY

Lot No.

Exp. Date

Package Insert - Generic
Front

ANADA 200-061, Approved by FDA

FLUNIXIN-MEGLUMINE

Solution—50 mg/mL

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

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

DESCRIPTION: Each milliliter contains flunixin meglumine equivalent to 50 mg flunixin, 0.1 mg edetate disodium, 2.5 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, non-steroidal, 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 ($pK_a=5.82$) which exhibits a high degree of plasma protein binding (approximately 99%).² However, free (unbound) drug appears to readily partition into body tissues (V_d 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 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_d). 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:* Flunixin Meglumine 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 Meglumine is indicated for the control of pyrexia associated with bovine respiratory disease and endotoxemia. Flunixin Meglumine 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 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 cattle is 1.1 to 2.2 mg/kg (0.5 to 1 mg/lb; 1 to 2 mL per 100 lbs) 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.

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: There are no known contraindications to this drug in cattle when used as directed. 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. Not for use in lactating or 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.

Package Insert - Generic Back

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 Meglumine with other anti-inflammatory drugs, such as other NSAIDs and corticosteroids, should be avoided or closely monitored.

Horse: The effect of Flunixin Meglumine on pregnancy has not been determined. Studies to determine activity of Flunixin Meglumine 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 in these classes of cattle have not been investigated. NSAIDs are known to have potential effects on both parturition 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. The effects of flunixin on imminent parturition have not been evaluated in a controlled study. NSAIDs are known to have the potential to delay parturition through a tocolytic effect. Do not exceed the recommended dose.

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.

HOW SUPPLIED Flunixin Meglumine Solution 50 mg/mL, is available in 50-mL, 100-mL and 250-mL multi-dose vials.

Store between 2° and 30° C (36° and 86°F).

FOR USE IN ANIMALS ONLY

REFERENCES

1. Johansson M, Anler EI Gas chromatographic analysis of flunixin in equine urine after extractive methylation. *J Chromatogr.* 1988;427:55-66.
2. Odensvik K, Johansson M. High-performance liquid chromatography method for determination of flunixin in bovine plasma and pharmacokinetics after single and repeated doses of the drug. *Am J Vet Res.* 1995;56:489-495.
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.
4. Odensvik K. Pharmacokinetics of flunixin and its effect on prostaglandin $F_{2\alpha}$ metabolite concentrations after oral and intravenous administration in heifers. *J Vet Pharmacol Ther.* 1995;18:254-259.
5. Hardee GE, Smith JA, Harris SJ. Pharmacokinetics of flunixin meglumine in the cow. *Res Vet Sci.* 1985;39:110-112.
6. Ruckebusch Y, Phaneuf LP, Dunlop R. Physiology of Small and Large Animals. Chapter 2: "Body Fluid Compartments." Philadelphia, Pa: B.C. Decker, 1991:8-18.
7. Kopcha M, Ahl AS. Experimental uses of flunixin meglumine and phenylbutazone in 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, Higgings AJ. Flunixin inhibits prostaglandin E_2 production in equine inflammation. *Res Vet Sci.* 1984;37:347-349.
10. Ladoni 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.

JUNE 2001

Agri Laboratories Ltd.
St. Joseph, MO 64503

RESIDUE WARNINGS: Cattle must not be slaughtered for human consumption within 4 days of the last treatment. Not for use in lactating or dry dairy cows. A withdrawal period has not been established for this product in preparturient calves. Do not use in calves to be processed for veal. Not for use in horses intended for food.

Store between 2° and 30°C (36° and 86°F).

LOT
EXP

 **Banamine**[®]
(FLUNIXIN MEGLUMINE)
Injectable Solution
Veterinary

NDC 008-0851-02

50 mL
Multiple-Dose Vial
50 mg/mL
Sterile

Caution: Federal law restricts this drug to use by or on the order of a licensed veterinarian.
NADA 141-473. Approved by FDA.
Schering-Plough Animal Health

For intravenous or intramuscular use in horses and for intravenous use in beef and nonlactating dairy cattle only. Not for use in lactating or dry dairy cows. Not for use in veal calves.
Read accompanying directions carefully.
Copyright © 1985, 1996, 1998, Schering-Plough Animal Health Corp., Union, NJ 07093.
All rights reserved. 12334076 Rev 6/97

RESIDUE WARNINGS: Cattle must not be slaughtered for human consumption within 4 days of the last treatment. Not for use in lactating or dry dairy cows. A withdrawal period has not been established for this product in pre-ruminating calves. Do not use in calves to be processed for veal. Not for use in horses intended for food.

Store between 2° and 30° C (36° and 86° F).

LOT
EXP



Banamine[®]
(FLUNixin MEGlumine)
Injectable Solution
Veterinary
Caution: Federal law restricts this drug to use by or on the order of a licensed veterinarian.
NADA #101-419, Approved by FDA.
Schering-Plough Animal Health

NDC 0081-
0851-03

100 mL
Multiple-Dose Vial
50 mg/mL
Sterile

For intravenous or intramuscular use in horses and for intravenous use in beef and nonlactating dairy cattle only. Not for use in lactating or dry dairy cows. Not for use in veal calves.

Read accompanying directions carefully.
Copyright © 1985, 1996, 1998, Schering-Plough Animal Health Corp., Union, NJ 07083. All rights reserved. 13059179 Rev 5/97

For intravenous or intramuscular use in horses and for intravenous use in beef and nonlactating dairy cattle only. Not for use in lactating or dry dairy cows. Not for use in veal calves. Store between 2° and 30° C (36° and 86° F). Read accompanying directions carefully.

RESIDUE WARNINGS: Cattle must not be slaughtered for human consumption within 4 days of the last treatment. Not for use in lactating or dry dairy cows. A withdrawal period has not been established for this product in pre-ruminating calves. Do not use in calves to be processed for veal. Not for use in horses intended for food.



NDC 0061-0851-04

Sterile

250 mL
Multiple-Dose Vial
50 mg/mL

Banamine®

(FLUNIXIN MEGLUMINE)

Injectable Solution

Veterinary

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

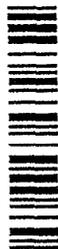
NADA #101-479, Approved by FDA.
Schering-Plough Animal Health

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LOT

EXP

FRONT



F-13502676

NADA #101-479, Approved by FDA.

PRODUCT
INFORMATION

13502676
Banamine[®]
(FLUNIXIN MEGLUMINE)

Injectable Solution
50 mg/mL
Veterinary

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

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

DESCRIPTION Each milliliter of BANAMINE Injectable Solution contains flunixin meglumine equivalent to 50 mg flunixin, 0.1 mg edetate disodium, 2.5 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 postinjection.

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.^{2,3} Total body water is approximately equal to 570 mL/kg.⁴ 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.^{1,5} 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_d). 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.^{2,1}

Flunixin persists in inflammatory tissues⁹ and is associated with anti-inflammatory properties which extend well beyond the period associated with detectable plasma drug concentrations.¹⁰ 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:** BANAMINE Injectable Solution 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: BANAMINE Injectable Solution is indicated for the control of pyrexia associated with bovine respiratory disease and endotoxemia. BANAMINE Injectable Solution 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 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 cattle is 1.1 to 2.2 mg/kg (0.5 to 1 mg/lb; 1 to 2 mL per 100 lbs) 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.

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: There are no known contraindications to this drug in cattle when used as directed. Do not use in animals showing hypersensitivity to flunixin meglu-

BACK

mine. 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. Not for use in lactating or 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.

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 BANAMINE Injectable Solution with other anti-inflammatory drugs, such as other NSAIDs and corticosteroids, should be avoided or closely monitored.

Horse: The effect of BANAMINE Injectable Solution on pregnancy has not been determined. Studies to determine activity of BANAMINE Injectable Solution 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 BANAMINE Injectable Solution in these classes of cattle have not been investigated. NSAIDs are known to have potential effects on both parturition 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. The effects of flunixin on imminent parturition have not been evaluated in a controlled study. NSAIDs are known to have the potential to delay parturition through a tocolytic effect. Do not exceed the recommended dose.

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 BANAMINE Injectable Solution. In horses and cattle, rare instances of anaphylactic-like reactions, some of which have been fatal, have been reported, primarily following intravenous use.

HOW SUPPLIED BANAMINE Injectable Solution, 50 mg/mL, is available in 50-mL (NDC 0061-0851-02), 100-mL (NDC 0061-0851-03), and 250-mL (NDC 0061-0851-04) multi-dose vials.

Store between 2° and 30°C (36° and 86°F).

REFERENCES

- Johansson M, Anler EL. Gas chromatographic analysis of flunixin in equine urine after extractive methylation. *J Chromatogr*. 1988;427:55-66.
- Odensvik K, Johansson M. High-performance liquid chromatography method for determination of flunixin in bovine plasma and pharmacokinetics after single and repeated doses of the drug. *Am J Vet Res*. 1995;56:489-495.
- 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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APRIL 1998

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