

117A-305

Date of Approval: AUG 2 1981

FREEDOM OF INFORMATION SUMMARY

ANADA 200-324

Dexamethasone Injection, 2 mg/mL
(2 mg dexamethasone)

Indications for use: For the treatment of primary bovine ketosis and as an anti-inflammatory agent in cattle and horses.

**Sponsored by:
Veterinary Laboratories, Inc.
Lenexa, KS 66215**

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FREEDOM OF INFORMATION SUMMARY

1. GENERAL INFORMATION:

- a. File Number: ANADA 200-324
- b. Sponsor: Veterinary Laboratories, Inc.
12340 Santa Fe Drive
Lenexa, KS 66215
Drug Labeler Code: 000857
- c. Established Name: Dexamethasone Injection
- d. Proprietary Name: Dexamethasone Injection 2 mg/mL
- e. Dosage Form: Injectable
- f. How Supplied: 100 mL multiple dose vial
- g. How Dispensed: Rx
- h. Amount of Active Ingredients: Each mL contains: 2 mg dexamethasone; 500 mg polyethylene glycol 400; 9 mg benzyl alcohol, 1.8 mg methylparaben, and 0.2 mg propylparaben as preservatives; 4.75% alcohol; HCl to adjust pH to approximately 4.9; water for injection qs.
- i. Route of Administration: Intravenously or intramuscularly
- j. Species/Class: Bovine and equine
- k. Recommended Dosage: Bovine-5 to 20 mg
Equine-2.5 to 5 mg

- l. Pharmacological Category: Anti-inflammatory.
- m. Indications: Treatment of primary bovine ketosis and as an anti-inflammatory agent in cattle and horses.
- n. Pioneer Product: Azium[®] manufactured by Schering-Plough Animal Health (NADA 12-559)

2. TARGET ANIMAL SAFETY AND DRUG EFFECTIVENESS:

Under the provisions of the Federal Food, Drug, and Cosmetic Act, as amended by the Generic Animal Drug and Patent Term Restoration Act (GADPTRA) of 1988, an Abbreviated New Animal Drug Application (ANADA) may be submitted for a generic version of an approved new animal drug (pioneer product). New target animal safety and drug effectiveness data and human food safety data (other than tissue residue data) are not required for approval of an ANADA.

Ordinarily the ANADA Sponsor shows the generic product is bioequivalent to the pioneer, which has been shown to be safe and effective. If bioequivalence is demonstrated through a clinical endpoint study, then a tissue residue study to establish the withdrawal time for the generic product should also be conducted. For certain dosage forms, the agency will grant a waiver from conducting an *in vivo* bioequivalence study (55 FR 24645, June 18, 1990; Fifth GADPTRA Policy Letter; Bioequivalence Guideline, October 2000).

Based upon the formulation characteristics of the generic product, Veterinary Laboratories, Inc. was granted a waiver from the requirement of an *in vivo* bioequivalence study for Dexamethasone Injection 2 mg/mL. The generic and the pioneer product (injectable solutions) contain the same active and inactive ingredients in the same concentration. The pioneer product, Azium[®], the subject of Schering-Plough Animal Health's NADA 12-559, was approved on March 29, 1961.

3. HUMAN SAFETY:

There is no tolerance or withdrawal period associated with this or the pioneer product. Therefore, no human safety data pertaining to residues in food were required.

4. AGENCY CONCLUSIONS:

This Abbreviated New Animal Drug Application (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 Dexamethasone Injection, when used under its proposed conditions of use, is safe and effective for its labeled indications.

5. ATTACHMENTS:

Labeling:

Pioneer Labeling for NADA 12-559:
Azium[®]-100 mL vial size and insert

Generic Labeling for ANADA 200-324

Dexamethasone Injection- 100 mL vial size and insert

For Intravenous or Intramuscular Injection

Usual Doses:
Bovine - 5 to 20 mg
Equine - 2.5 to 5 mg
Warning: A withdrawal period has not been established for this product in pre-ruminating calves. Do not use in calves to be processed for veal.
Each mL contains: 2 mg dexamethasone, 500 mg polyethylene glycol 400; 8 mg benzyl alcohol, 1.8 mg methylparaben, and 0.2 mg propylparaben as preservatives; 4.75% alcohol; HCl to adjust pH to approximately 4.9; water for injection q.s.
Store between 2° and 30°C (36° and 86°F).
Read accompanying directions carefully.

NDC 0061-0884-01

100 mL
Multiple Dose Vial
2 mg/mL

Sterile

Azium® Solution
(DEXAMETHASONE)
Veterinary

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

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Azium[®]
 (DEXAMETHASONE)
Solution
Veterinary

For intravenous
 or intramuscular
 injection.



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Azium[®]
 (DEXAMETHASONE)
Solution
Veterinary

Each mL contains: 2 mg dexamethasone;
 500 mg polyethylene glycol 400; 9 mg benzyl
 alcohol, 1.8 mg methylparaben, and 0.2 mg
 propylparaben as preservatives; 4.75%
 alcohol; HCl to adjust pH to approximately 4.9;
 water for injection q.s.

Usual Dose:
 Bovine - 5 to 20 mg
 Equine - 2.5 to 5 mg

Warning: A withdrawal period has not been
 established for this product in pre-ruminating
 calves. Do not use in calves to be processed for veal.

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

Read accompanying directions carefully.

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Schering-Plough Animal Health Corp.,
 Kenilworth, NJ 07033

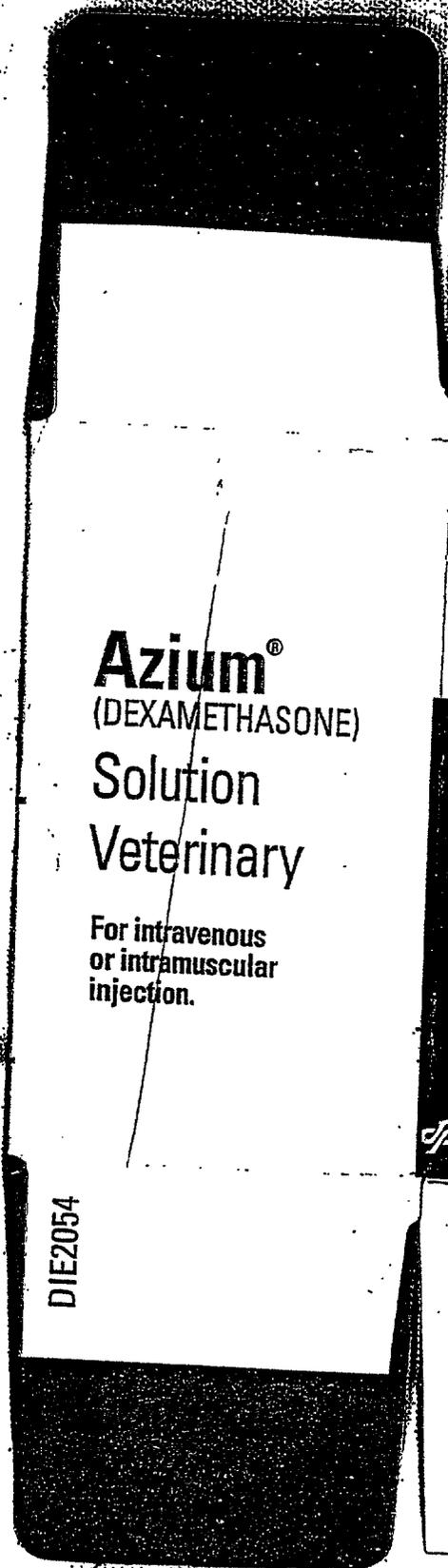
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Azium[®]
(DEXAMETHASONE)
Solution
Veterinary

For intravenous
or intramuscular
injection.

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100 mL
Multiple Dose Vial
2 mg/mL

Sterile

NDC 0061-0884-01.

Azium[®]
(DEXAMETHASONE)
Solution
Veterinary

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



Schering-Plough Animal Health





F-13406456

PRODUCT INFORMATION

**AZIUM®
(DEXAMETHASONE)
Solution - 2 mg/mL
for intravenous or
intramuscular injection**

Veterinary

CAUTION

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

DESCRIPTION

AZIUM (dexamethasone) Solution is a synthetic analogue of prednisolone, having similar but more potent anti-inflammatory therapeutic action and diversified hormonal and metabolic effects. Modification of the basic corticoid structure as achieved in AZIUM offers enhanced anti-inflammatory effect compared to older corticosteroids. The dosage of AZIUM required is markedly lower than that of prednisone and prednisolone.

AZIUM Solution is not species-specific; however, the veterinarian should read the sections on **INDICATIONS, DOSAGE, SIDE EFFECTS, CONTRAINDICATIONS, PRECAUTIONS, and WARNINGS** before this drug is used.

AZIUM Solution is intended for *intravenous* or *intramuscular* administration. Each mL contains 2 mg dexamethasone, 500 mg polyethylene glycol 400, 9 mg benzyl alcohol, 1.8 mg methylparaben and 0.2 mg propylparaben as preservatives, 4.75% alcohol, HCl to adjust pH to approximately 4.9, water for injection q.s.

EXPERIMENTAL STUDIES

Experimental animal studies on dexamethasone have revealed it possesses greater anti-inflammatory activity than many steroids. Veterinary clinical evidence indicates dexamethasone has approximately twenty times the anti-inflammatory activity of prednisolone and seventy to eighty times that of hydrocortisone. Thymus involution studies show dexamethasone possesses twenty-five times the activity of prednisolone. In reference to mineralocorticoid activity, dexamethasone does not cause significant sodium or water retention. Metabolic balance studies show that animals on controlled and limited protein intake will exhibit nitrogen losses on exceedingly high dosages.

INDICATIONS

AZIUM Solution is indicated for the treatment of primary bovine ketosis and as an anti-inflammatory agent in the bovine and equine.

As supportive therapy, AZIUM Solution may be used in the management of various rheumatic, allergic, dermatologic, and other diseases known to be responsive to anti-inflammatory corticosteroids. AZIUM Solution may be used

intravenously as supportive therapy when an immediate hormonal response is required.

Bovine Ketosis

AZIUM Solution is offered for the treatment of primary ketosis. The gluconeogenic effects of AZIUM, when administered intramuscularly, are generally noted within the first 6 to 12 hours. When AZIUM Solution is used intravenously, the effects may be noted sooner. Blood sugar levels rise to normal levels rapidly and generally rise to above normal levels within 12 to 24 hours. Acetone bodies are reduced to normal concentrations usually within 24 hours. The physical attitude of animals treated with AZIUM brightens and appetite improves, usually within 12 hours. Milk production, which is suppressed as a compensatory reaction in this condition, begins to increase. In some instances, it may even surpass previous peaks. The recovery process usually takes from 3 to 7 days.

Supportive Therapy

AZIUM Solution may be used as supportive therapy in mastitis, metritis, traumatic gastritis, and pyelonephritis, while appropriate primary therapy is administered. In these cases, the corticosteroid combats accompanying stress and enhances the feeling of general well-being.

AZIUM Solution may also be used as supportive therapy in inflammatory conditions, such as arthritic conditions, snake bite, acute mastitis, shipping fever, pneumonia, laminitis, and retained placenta.

Equine

AZIUM Solution is indicated for the treatment of acute musculoskeletal inflammations, such as bursitis, carpalitis, osselets, tendonitis, myositis, and sprains. If bony changes exist in any of these conditions, joints, or accessory structures, responses to AZIUM cannot be expected. In addition, AZIUM may be used as supportive therapy in fatigue, heat exhaustion, influenza, laminitis, and retained placenta provided that the primary cause is determined and corrected.

ADMINISTRATION AND DOSAGE

Therapy with AZIUM Solution, as with any other potent corticosteroid, should be individualized according to the severity of the condition being treated, anticipated duration of steroid therapy, and the animal's threshold or tolerance for steroid excess.

Treatment may be changed over to AZIUM Solution from any other glucocorticoid with proper reduction or adjustment of dosage.

Bovine—AZIUM Solution—5 to 20 mg intravenously or intramuscularly.

AZIUM Powder may be administered or the parenteral dose repeated as needed.

Equine—AZIUM Solution—2.5 to 5 mg intravenously or intramuscularly.

AZIUM Powder may be administered or the parenteral dose repeated as needed.

PRODUCT
INFORMATION**AZIUM®
(DEXAMETHASONE)**
Solution - 2 mg/mL
for intravenous or
intramuscular injection

Veterinary

CONTRAINDICATIONS

Except for emergency therapy, do not use in animals with chronic nephritis and hypercorticalism (Cushing's syndrome). Existence of congestive heart failure, diabetes, and osteoporosis are relative contraindications. Do not use in viral infections during the viremic stage.

PRECAUTIONS

Animals receiving AZIUM Solution should be under close observation. Because of the anti-inflammatory action of corticosteroids, signs of infection may be masked and it may be necessary to stop treatment until a further diagnosis is made. Overdosage of some glucocorticoids may result in sodium retention, fluid retention, potassium loss, and weight gain.

AZIUM Solution may be administered to animals with acute or chronic bacterial infections providing the infections are controlled with appropriate antibiotic or chemotherapeutic agents.

Doses greater than those recommended in horses may produce a transient drowsiness or lethargy in some horses. The lethargy usually abates in 24 hours.

Use of corticosteroids, depending on dose, duration, and specific steroid, may result in inhibition of endogenous steroid production following drug withdrawal. In patients presently receiving or recently withdrawn from systemic corticosteroid treatments, therapy with a rapidly acting corticosteroid should be considered in unusually stressful situations.

WARNINGS

Clinical and experimental data have demonstrated that corticosteroids administered orally or parenterally to animals may induce the first stage of parturition when administered during the last trimester of pregnancy and may precipitate parturition followed by dystocia, fetal death, retained placenta, and metritis.

Additionally, corticosteroids administered to dogs, rabbits, and rodents during pregnancy have produced cleft palate. Other congenital anomalies including deformed forelegs, phocomelia, and anasarca have been reported in offspring of dogs which received corticosteroids during pregnancy.

A withdrawal period has not been established for this product in pre-

ruminating calves. Do not use in calves to be processed for veal.

SIDE EFFECTS

Side effects, such as SAP and SGPT enzyme elevations; weight loss, anorexia, polydipsia, and polyuria have occurred following the use of synthetic corticosteroids in dogs. Vomiting and diarrhea (occasionally bloody) have been observed in dogs and cats.

Cushing's syndrome in dogs has been reported in association with prolonged or repeated steroid therapy.

Corticosteroids reportedly cause laminitis in horses.

HOW SUPPLIED

AZIUM Solution, 2 mg per mL, 100-mL multiple dose vial, box of 1.

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

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March 1994
Schering-Plough Animal Health Corp.
Kenilworth, NJ 07033

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<p>pregnancy and may precipitate parturition followed by dystocia, fetal death, retained placenta, and metritis.</p> <p>Additionally, corticosteroids administered to dogs, rabbits, and rodents during pregnancy have produced cleft palate. Other congenital anomalies including deformed forelegs, phocomelia, and anasarca have been reported in offspring of dogs which received corticosteroids during pregnancy.</p> <p>A withdrawal period has not been established for this product in pre-ruminating calves. Do not use in calves to be processed for veal.</p> <p>SIDE EFFECTS Side effects such as SAP and SGPT enzyme elevations, weight loss, anorexia, polydipsia, and polyuria have occurred following the use of synthetic corticosteroids in dogs. Vomiting and diarrhea (occasionally bloody) have been observed in dogs and cats.</p> <p>Cushing's syndrome in dogs has been reported in association with prolonged or repeated steroid therapy.</p> <p>Corticosteroids reportedly cause laminitis in horses.</p> <p style="text-align: center;">8</p>	<p>HOW SUPPLIED DEXAMETHASONE INJECTION 2 mg/mL, 100 mL multiple dose vial.</p> <p>Store between 2° and 30°C (36° and 86°F).</p> <p>D-2953-04 Rev. 6/03</p> <p>Distributed by Sparhawk Laboratories, Inc. Lenexa, KS 66215, USA Manufactured by Veterinary Laboratories, Inc. Lenexa, KS 66215, USA</p> <p>ANADA#: 200-324, Approved by FDA</p> <p style="text-align: center;">9</p>	<p>Each mL contains: 2 mg dexamethasone; 500 mg polyethylene glycol 400; 9 mg benzyl alcohol, 1.8 mg methylparaben, and 0.2 mg propylparaben as preservatives; 4.75% alcohol; HCl to adjust pH to approximately 4.8; water for injection q.s.</p> <p style="text-align: center;">TAKE TIME  OBSERVE LABEL DIRECTIONS</p> <p>Distributed by Sparhawk Laboratories, Inc. Lenexa, KS 66215, USA Manufactured by Veterinary Laboratories, Inc. Lenexa, KS 66215, USA</p> <p>Rev. 6/03 D-2953-04</p> <p style="text-align: center;">10</p>	<p>DEXAMETHASONE INJECTION 2 mg/mL Solution for intravenous or intramuscular injection Veterinary</p> <p>CAUTION Federal law restricts this drug to use by or on the order of a licensed veterinarian.</p> <p>DESCRIPTION DEXAMETHASONE INJECTION 2 mg/mL is a synthetic analogue of prednisolone, having similar but more potent anti-inflammatory therapeutic action and diversified hormonal and metabolic effects. Modification of the basic corticoid structure as achieved in DEXAMETHASONE INJECTION 2 mg/mL offers enhanced anti-inflammatory effect compared to older corticosteroids. The dosage of DEXAMETHASONE INJECTION 2 mg/mL required is markedly lower than that of prednisone and prednisolone.</p> <p style="text-align: center;">11</p>
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<p>cause significant sodium or water retention. Metabolic balance studies show that animals on controlled and limited protein intake will exhibit nitrogen losses on exceedingly high dosages.</p> <p>INDICATIONS DEXAMETHASONE INJECTION 2 mg/mL is indicated for the treatment of primary bovine ketosis and as an anti-inflammatory agent in the bovine and equine.</p> <p>As supportive therapy, DEXAMETHASONE INJECTION 2 mg/mL may be used in the management of various rheumatic, allergic, dermatologic, and other diseases known to be responsive to anti-inflammatory corticosteroids. DEXAMETHASONE INJECTION 2 mg/mL may be used intravenously as supportive therapy when an immediate hormonal response is required.</p> <p>Bovine Ketosis DEXAMETHASONE INJECTION 2 mg/mL is offered for the treatment of primary ketosis. The gluconeogenic effects of DEXAMETHASONE INJECTION 2 mg/mL, when administered intravenously, are generally noted within the first 6 to 12 hours. When DEXAMETHASONE INJECTION 2</p> <p style="text-align: center;">3</p>	<p>mg/mL is used intravenously, the effects may be noted sooner. Blood sugar levels rise to normal levels rapidly and generally rise to above normal levels within 12 to 24 hours. Acetone bodies are reduced to normal concentrations usually within 24 hours. The physical attitude of animals treated with DEXAMETHASONE INJECTION 2 mg/mL brightens and appetite improves, usually within 12 hours. Milk production, which is suppressed as a compensatory reaction in this condition, begins to increase. In some instances, it may even surpass previous peaks. The recovery process usually takes from 3 to 7 days.</p> <p>Supportive Therapy DEXAMETHASONE INJECTION 2 mg/mL may be used as supportive therapy in mastitis, metritis, traumatic gastritis, and pyelonephritis, while appropriate primary therapy is administered. In these cases, the corticosteroid combats accompanying stress and enhances the feeling of general well-being. DEXAMETHASONE INJECTION 2 mg/mL may also be used as supportive therapy in inflammatory conditions, such as arthritic conditions, snake bite, acute mastitis, shipping fever, pneumonia, laminitis, and retained placenta.</p> <p style="text-align: center;">4</p>	<p>Equine DEXAMETHASONE INJECTION 2 mg/mL is indicated for the treatment of acute musculoskeletal inflammations, such as bursitis, capsitis, osselets, tendonitis, myositis, and sprains. If bony changes exist in any of the conditions, joints, or accessory structures, response to DEXAMETHASONE INJECTION 2 mg/mL cannot be expected. In addition, DEXAMETHASONE INJECTION 2 mg/mL may be used as supportive therapy in fatigue, heat exhaustion, influenza, laminitis, and retained placenta provided that the primary cause is determined and corrected.</p> <p>ADMINISTRATION AND DOSAGE Therapy with DEXAMETHASONE INJECTION 2 mg/mL, as with any other potent corticosteroid, should be individualized according to the severity of the condition being treated, anticipated duration of steroid therapy, and the animal's threshold or tolerance for steroid excess.</p> <p>Treatment may be changed over to other glucocorticoid with proper reduction or adjustment of dosage.</p> <p style="text-align: center;">5</p>	<p>Bovine - DEXAMETHASONE INJECTION 2 mg/mL - 5 to 20 mg intravenously or intramuscularly. Dexamethasone Powder may be administered on the parenteral dose repeated as needed.</p> <p>Equine - DEXAMETHASONE INJECTION 2 mg/mL - 2.5 to 5 mg intravenously or intramuscularly. Dexamethasone Powder may be administered on the parenteral dose repeated as needed.</p> <p>CONTRAINDICATIONS Except for emergency therapy, do not use in animals with chronic nephritis and hypercorticism (Cushing's syndrome). Existence of congestive heart failure, diabetes, and osteoporosis are relative contraindications. Do not use in viral infections during the viremic stage.</p> <p>PRECAUTIONS Animals receiving DEXAMETHASONE INJECTION 2 mg/mL should be under close observation. Because of the anti-inflammatory action of corticosteroids, signs of infection may be masked and it may be necessary to stop treatment until a further diagnosis is made. Overdosage of some glucocorticoids may</p> <p style="text-align: center;">6</p>
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