



Veterinary Medical Affairs, American Regent, Inc.

## FDA-Approved Drugs vs. Compounded Products and Veterinary Medical Devices.

Equine veterinarians are increasingly challenged to provide sound medical care while operating within economic restrictions. In efforts to maintain client goodwill and minimize treatment costs, veterinarians may consider non-Food and Drug Administration (FDA) approved product alternatives, such as compounded drugs and veterinary medical devices. When veterinarians choose to administer products that have not undergone equivalent clinical testing for safety and efficacy in the horse, unforeseen risks may arise. Therefore, it is important for veterinarians to understand and, if appropriate, communicate the importance of using FDA approved drugs, such as Adequan® i.m. [polysulfated glycosaminoglycan] and BetaVet® [betamethasone sodium phosphate and betamethasone acetate injectable suspension].



**Adequan® i.m.** [polysulfated glycosaminoglycan]

### INDICATIONS

Adequan® i.m. is recommended for the intramuscular treatment of non-infectious degenerative and/or traumatic joint dysfunction and associated lameness of the carpal and hock joints in horses.

### IMPORTANT SAFETY INFORMATION

There are no known contraindications to the use of intramuscular Polysulfated Glycosaminoglycan [PSGAG]. Studies have not been conducted to establish safety in breeding horses. **WARNING:** Do not use in horses intended for human consumption. Not for use in humans. Keep this and all medications out of the reach of children. **CAUTION:** Federal law restricts this drug to use by or on the order of a licensed veterinarian. For additional safety information, please see full prescribing information at [adequan.com](http://adequan.com).





# Adequan® i.m. and BetaVet® are FDA-Approved Pioneer Drugs.

### FDA Pioneer Drugs:<sup>1</sup>

- A drug that has undergone the scrutiny of blinded controlled studies to demonstrate safety and efficacy in accordance with Good Laboratory Procedures (GLPs)
- The product is manufactured under FDA mandated Good Manufacturing Practices (GMPs) in regularly inspected plants
- Therapeutic consistency, product quality, accurate shelf life, and scientifically substantiated labeling are FDA mandated
- Stringent standards for drug potency and purity must be established and stability data generated to determine expiration dating
- Detailed records of each batch of drug produced are maintained and retained for future testing
- The manufacturer conducts ongoing surveillance for adverse events involving lack of safety or efficacy and must regularly provide reporting data to the FDA
- **How to identify**
  - All FDA-approved veterinary pharmaceutical pioneer products carry a six-digit New Animal Drug Application (NADA) number. The drug label must include the following statement: Approved by FDA under NADA # XXX-XXX<sup>2</sup>



There is NO generic Adequan<sup>®</sup> i.m. (polysulfated glycosaminoglycan) or BetaVet<sup>®</sup> (betamethasone sodium phosphate and betamethasone acetate injectable suspension).

### Generic Drugs:<sup>3</sup>

- A generic drug is bioequivalent to a pioneer drug in dosage form, efficacy, safety and strength, route of administration, quality, and intended use
- Generic drug approvals are only considered after the pioneer drug's patent has expired
- Generic drugs are manufactured under the same GMP requirements as pioneer drugs
- Use of a human drug in an animal constitutes off-label use<sup>4</sup>
- **How to identify:**
  - Generic drug labels display an Abbreviated New Animal Drug Application [ANADA] number signifying FDA approval of a generic animal drug. They must include the following statement: Approved by FDA under ANADA # XXX-XXX<sup>2</sup>



## What About Compounded Veterinary Drugs?

### Compounded Drugs:<sup>5</sup>

- Any drug manipulated to produce a dosage form (other than that provided for in the directions for use on labeling of the approved drug product)
- Compounded drugs are not 'generic' drugs
- Neither cost nor convenience is a justification for using compounded preparations. Compounding provides a customized formulation for the special needs of a particular patient, when no approved presentation is available, within the context of a Veterinarian-Client-Patient Relationship (VCPR)
- FDA-approved medications should be used to formulate compounded medications
- Some state pharmacy boards require compounded drugs to be dispensed at cost
- Every compounded drug must have a beyond-use date which should not exceed 180 days from preparation<sup>6</sup>
- The prescribing veterinarian assumes responsibility when using compounded preparations
- **How to identify**
  - The primary label of a compounded medication should include a statement notifying the client that the medication has been compounded. When a branded drug product has been used as a source of the drug, the generic name of the drug product, not the proprietary name, should be placed on the label<sup>7</sup>
  - State regulations differ in label requirements

## Are Veterinary Medical Devices Equivalent to FDA-Approved Drugs?

### Veterinary Medical Devices:<sup>8</sup>

- Medical devices as defined by the FDA in the Food Drug and Cosmetic Act, Section 210(h): “an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, . . . which does not achieve any of its principal intended purposes through chemical action . . . and is not dependent upon being metabolized for the achievement of any of its principal intended purposes”
- Although under FDA oversight for promotion and marketing, devices manufactured solely for use in veterinary medicine are not required to undergo a pre-marketing approval process
- The manufacturing process of veterinary devices is not required to meet uniform standards, i.e. no set standards to assure quality control for purity, potency, stability and sterility; no mandatory requirements for reporting adverse events. It is the responsibility of the manufacturer and/or distributor of these articles to assure that these animal devices are safe, effective, and properly labeled
- “Off-label” drug use does not apply to veterinary medical devices. These devices have not undergone clinical testing for safety or efficacy as a drug, hence no approved label Indication, Dosing, or Contraindication information
  - A 2016 study evaluated the efficacy of IV administration of a combination product containing hyaluronan, sodium chondroitin sulfate, and N-acetyl-D-glucosamine for prevention or treatment of osteoarthritis in 32 healthy 2- to 5- year old horses<sup>9</sup>
  - The study concluded that caution should be used when administering the product IV to horses, particularly when administering it prophylactically, as it may have no benefit or may even cause harm<sup>9</sup>
- Veterinary device labeling and ingredients may appear very similar to FDA approved drugs
  - For example, some products contain only monosulfated chondroitin sulfate, which is not chemically equivalent to polysulfated glycosaminoglycan (PSGAG) in Adequan<sup>®</sup> i.m. Adequan<sup>®</sup> i.m. contains 3-4 sulfate esters per disaccharide molecule, differs in structure and function, and no bioequivalent product exists<sup>10,11</sup>
- **How to identify:**
  - The labeling of medical devices used within veterinary medicine may not contain language identifying the product as a device. If the practitioner has questions regarding the status of a product, he or she should contact the manufacturer

**In summary**, the significance of FDA approval is essential for both veterinarians and clients to understand. For a new animal drug to satisfy each stage of the FDA approval process often takes years, and veterinarians should consider the benefits of using these drugs over non-approved alternatives. Stringent FDA approval requirements provide the benchmark for veterinary drug safety and efficacy, and allow practitioners to provide optimal care to the horse.



## **BetaVet® (betamethasone sodium phosphate and betamethasone acetate injectable suspension)**

### **For Intra-articular (I.A.) use in Horses.**

**INDICATION:** BetaVet® (betamethasone sodium phosphate and betamethasone acetate injectable suspension) is indicated for the control of pain and inflammation associated with osteoarthritis in horses.

## **IMPORTANT SAFETY INFORMATION**

**CONTRAINDICATIONS:** BetaVet® is contraindicated in horses with hypersensitivity to betamethasone. Intra-articular injection of corticosteroids for local effect is contraindicated in the presence of septic arthritis.

**WARNINGS:** Do not use in horses intended for human consumption. 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 premature parturition followed by dystocia, fetal death, retained placenta, and metritis. Additionally, corticosteroids administered to dogs, rabbits and rodents during pregnancy have resulted in congenital anomalies. Before use of corticosteroids in pregnant animals, the possible benefits should be weighed against potential hazards. **Human Warnings:** Not for use in humans. Keep this and all medications out of the reach of children.

**PRECAUTIONS:** Corticosteroids, including BetaVet®, administered intra-articularly are systemically absorbed. Do not use in horses with acute infections. Acute moderate to severe exacerbation of pain, further loss of joint motion, fever, or malaise within several days following intra-articular injection may indicate a septic process. Because of the anti-inflammatory action of corticosteroids, signs of infection in the treated joint may be masked. Due to the potential for exacerbation of clinical signs of laminitis, glucocorticoids should be used with caution in horses with a history of laminitis, or horses otherwise at a higher risk for laminitis. Use with caution in horses with chronic nephritis, equine pituitary pars intermedia dysfunction (PPID), and congestive heart failure. Concurrent use of other anti-inflammatory drugs should be approached with caution. Consider appropriate wash out times prior to administering additional NSAIDs or corticosteroids.

**ADVERSE REACTIONS:** Adverse reactions reported during a field study of 239 horses of various breeds which had been administered either BetaVet® (n=119) or a saline control (n=120) at five percent (5%) and above were: acute joint effusion and/or local injection site swelling (within 2 days of injection), 15% BetaVet® and 13% saline control; increased lameness (within the first 5 days), 6.7% BetaVet® and 8.3% saline control; loose stool, 5.9% BetaVet® and 8.3% saline control; increased heat in joint, 2.5% BetaVet® and 5% saline control; and depression, 5.9% BetaVet® and 1.6% saline control.

**SHAKE WELL IMMEDIATELY BEFORE USE.** For additional safety information, please see full prescribing information.

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

# American Regent Animal Health is proud to provide the equine industry with the following Food and Drug Administration (FDA) approved products:



## To report an adverse event for any American Regent Animal Health product:

- **Contact American Regent Animal Health**
  - Toll-free: 1-888-354-4857
  - Email: [pv@americanregent.com](mailto:pv@americanregent.com)
- **Contact the Center for Veterinary Medicine**
  - Call: 1-888-463-6332
  - Email: [AskCVM@fda.hhs.gov](mailto:AskCVM@fda.hhs.gov)

## References:

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2. "Approved by FDA" Labeling Statement for Approved New Animal Drugs U.S. Food and Drug Administration. <https://www.fda.gov/animal-veterinary/resources-you/approved-fda-labeling-statement-approved-new-animal-drugs#:~:text=Also%20note%20that%2C%20on%20Blue%20Bird%20labeling%20for,use%20in%20the%20combination.%20Please%20do%20the%20following%3A>. Accessed February 23, 2023.
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**Please see accompanying Full Prescribing Information**



**SINGLE DOSE**  
Solution 500 mg/5 mL  
For Intramuscular Use In Horses



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

**DESCRIPTION:** Each 5 milliliters of Adequan® i.m. contains 500 mg of Polysulfated Glycosaminoglycan (PSGAG) and Water for Injection q.s. Sodium Hydroxide and/or Hydrochloric Acid added when necessary to adjust pH. Sodium Chloride may be added to adjust tonicity.

**PHARMACOLOGY:** Polysulfated Glycosaminoglycan is chemically similar to the glycosaminoglycans in articular cartilage matrix. PSGAG is a potent proteolytic enzyme inhibitor and diminishes or reverses the pathologic processes of traumatic or degenerative joint disease which result in a net loss of cartilage matrix components. PSGAG improves joint function by reducing synovial fluid protein levels and increasing synovial fluid hyaluronic acid concentration in traumatized equine carpal and hock joints.

**INDICATIONS:** Adequan® i.m. is recommended for the intramuscular treatment of non-infectious degenerative and/or traumatic joint dysfunction and associated lameness of the carpal and hock joints in horses.

**DOSAGE AND ADMINISTRATION:** The recommended dose of Adequan® i.m. in horses is 500 mg every 4 days for 28 days intramuscularly. The injection site must be thoroughly cleansed prior to injection. Do not mix Adequan® i.m. with other drugs or solvents.

**CONTRAINDICATIONS:** There are no known contraindications to the use of intramuscular Polysulfated Glycosaminoglycan.

**WARNINGS:** Do not use in horses intended for human consumption. Not for use in humans. Keep this and all medications out of the reach of children.

**PRECAUTIONS:** The safe use of Adequan® i.m. in horses used for breeding purposes, during pregnancy, or in lactating mares has not been evaluated.

**ANIMAL SAFETY:** Toxicity studies were conducted in horses. Doses as high as 2,500 mg were administered intramuscularly to 6 horses twice a week for 12 weeks. This dosage is 5 times the recommended dosage and 3 times the recommended therapeutic regimen. Clinical observations revealed no soreness or swelling at the injection site or in the affected joint. No animal had any clinical or laboratory evidence of toxicity.

**STORAGE CONDITIONS:** Store at 20°-25°C (68°-77°F); (See USP Controlled Room Temperature). Discard unused portion.

Dispose of spent needles in accordance with all federal, state and local environmental laws.

**HOW SUPPLIED:** Adequan® i.m. solution, 500 mg/5 mL (100 mg/mL) in a 5 mL single dose glass vial.

NDC 10797-995-70      5 mL Single Dose Vials      Packaged 7 vials per box

AMERICAN REGENT, INC.  
ANIMAL HEALTH  
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Made in U.S.A.  
IN99501  
Rev. 9/2021  
MG #44455

Approved by FDA under NADA # 140-901



**MULTI-DOSE**  
Solution 100 mg/mL in a 50 mL Preserved Multi-Dose Vial  
For Intramuscular Use In Horses Only. Not for Intra-Articular Use.



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

**DESCRIPTION:** Each mL contains Polysulfated Glycosaminoglycan (PSGAG) 100 mg, Benzyl Alcohol 0.9% v/v as a preservative, and Water for Injection q.s. Sodium Hydroxide and/or Hydrochloric Acid added when necessary to adjust pH. The solution is clear, colorless to slightly yellow.

**PHARMACOLOGY:** Polysulfated Glycosaminoglycan is chemically similar to the glycosaminoglycans in articular cartilage matrix. PSGAG is a potent proteolytic enzyme inhibitor and diminishes or reverses the pathologic processes of traumatic or degenerative joint disease which result in a net loss of cartilage matrix components. PSGAG improves joint function by reducing synovial fluid protein levels and increasing synovial fluid hyaluronic acid concentration in traumatized equine carpal and hock joints.

**INDICATIONS:** Adequan® i.m. Multi-Dose is recommended for the intramuscular treatment of non-infectious degenerative and/or traumatic joint dysfunction and associated lameness of the carpal and hock joints in horses.

**DOSAGE AND ADMINISTRATION:** Practice aseptic techniques in withdrawing each dose to decrease the possibility of post-injection bacterial infections. Adequately clean and disinfect the stopper prior to entry with a sterile needle and syringe. Use only sterile needles, and use each needle only once.

The vial stopper may be punctured a maximum of 10 times.

The recommended dose of Adequan® i.m. Multi-Dose in horses is 500 mg every 4 days for 28 days intramuscularly. The injection site must be thoroughly cleansed prior to injection. Do not mix Adequan® i.m. Multi-Dose with other drugs or solvents.

**CONTRAINDICATIONS:** There are no known contraindications to the use of intramuscular Polysulfated Glycosaminoglycan.

**WARNINGS:** Do not use in horses intended for human consumption. Not for use in humans. Keep this and all medications out of the reach of children.

**PRECAUTIONS:** The safe use of Adequan® i.m. Multi-Dose in horses used for breeding purposes, during pregnancy, or in lactating mares has not been evaluated.

**SAFETY AND EFFICACY:** Safety and efficacy studies utilizing Adequan® i.m. Multi-Dose were not performed. Adequan® i.m. Multi-Dose was approved based on the conclusion that the safety and effectiveness of Adequan® i.m. Multi-Dose will not differ from that demonstrated for the original formulation of Adequan® i.m.

**ANIMAL SAFETY:** Animal Safety studies utilizing Adequan® i.m. Multi-Dose were not performed. Safety studies were conducted in horses using the single dose formulation. Doses as high as 2,500 mg were administered intramuscularly to 6 horses twice a week for 12 weeks. This dosage is 5 times the recommended dosage and 3 times the recommended therapeutic regimen. Clinical observations revealed no soreness or swelling at the injection site or in the affected joint. No animal had any clinical or laboratory evidence of toxicity.

**STORAGE CONDITIONS:** Store at 20°-25°C (68°-77°F); excursions permitted to 15°-30°C (59°-86°F) (See USP Controlled Room Temperature). Avoid prolonged exposure to temperatures ≥ 40°C (104°F).

Use within 28 days of first puncture and puncture a maximum of 10 times. Dispose of spent needles in accordance with all federal, state and local environmental laws.

**HOW SUPPLIED:** Adequan® i.m. Multi-Dose solution, 5,000 mg/50 mL (100 mg/mL) in 50 mL multi-dose glass vials.

NDC 10797-959-01      50 mL Multi-Dose Vials      Packaged 1 vial per box

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Made in U.S.A.  
IN959  
Rev. 9/2021  
MG #44455

Approved by FDA under NADA # 140-901



## BETAVET®

(Betamethasone Sodium Phosphate and Betamethasone Acetate Injectable Suspension)



### BETAVET®

(Betamethasone Sodium Phosphate and Betamethasone Acetate Injectable Suspension)

6 mg betamethasone per mL  
For Intra-Articular (I.A.) Use in Horses

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

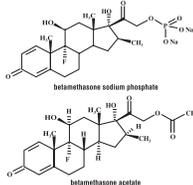
#### DESCRIPTION

BETAVET® is a sterile aqueous suspension of betamethasone acetate in betamethasone sodium phosphate injection. The combined betamethasone content of the suspension is 6 mg/mL where each mL contains 3.15 mg betamethasone (as betamethasone sodium phosphate); 2.85 mg betamethasone (as betamethasone acetate); 7.1 mg dibasic sodium phosphate; 3.4 mg monobasic sodium phosphate; 0.1 mg edetate disodium; and 0.2 mg benzalkonium chloride, as a preservative in water for injection. The pH is adjusted to between 6.8 and 7.2.

The formula for betamethasone sodium phosphate is  $C_{21}H_{35}FNa_3O_8P$  and it has a molecular weight of 516.41. Chemically, it is 9-Fluoro-11 $\beta$ , 17,21-trihydroxy-16 $\beta$ -methylpregna-1,4-diene-3,20-dione (disodium phosphate).

The formula for betamethasone acetate is  $C_{27}H_{41}FO_6$  and it has a molecular weight of 434.50. Chemically, it is 9-Fluoro-11 $\beta$ , 17,21-trihydroxy-16 $\beta$ -methylpregna-1,4-diene-3,20-dione 21-acetate.

The chemical structures for betamethasone sodium phosphate and betamethasone acetate are as follows:



Betamethasone sodium phosphate is a white to practically white, odorless powder, and is hygroscopic. It is freely soluble in water and in methanol, but is practically insoluble in acetone and in chloroform.

Betamethasone acetate is a white to creamy white, odorless powder that sinters and resolidifies at about 165°C, and remelts at about 200°C-220°C with decomposition. It is practically insoluble in water, but freely soluble in acetone, and is soluble in alcohol and in chloroform.

#### INDICATION

BETAVET is indicated for the control of pain and inflammation associated with osteoarthritis in horses.

#### DOSAGE AND ADMINISTRATION

**Shake well immediately before use.**

Using strict aseptic technique, administer 1.5 mL BETAVET (9 mg total betamethasone) per joint by intra-articular injection. BETAVET may be administered concurrently in up to 2 joints per horse.

Use immediately after opening, then discard any remaining contents.

#### CONTRAINDICATIONS

BETAVET is contraindicated in horses with hypersensitivity to betamethasone.

Intra-articular injection of corticosteroids for local effect is contraindicated in the presence of septic arthritis.

#### WARNINGS

**Do not use in horses intended for human consumption.**

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 premature parturition followed by dystocia, fetal death, retained placenta, and metritis.

Additionally, corticosteroids administered to dogs, rabbits and rodents during pregnancy have resulted in cleft palate in offspring. Corticosteroids administered to dogs during pregnancy have also resulted in other congenital anomalies including deformed forelegs, phocomelia and anasarca. Therefore, before use of corticosteroids in pregnant

animals, the possible benefits to the pregnant animal should be weighed against potential hazards to its developing embryo or fetus.

**Human Warnings:** Not for use in humans. For use in animals only. Keep this and all medications out of the reach of children. Consult a physician in the case of accidental human exposure.

#### PRECAUTIONS

Corticosteroids, including BETAVET, administered intra-articularly are systemically absorbed. Do not use in horses with acute infections.

Acute moderate to severe exacerbation of pain, further loss of joint motion, fever, or malaise within several days following intra-articular injection may indicate a septic process. Because of the anti-inflammatory action of corticosteroids, signs of infection in the treated joint may be masked. Appropriate examination of joint fluid is necessary to exclude a septic process. If a bacterial infection is present, appropriate antibacterial therapy should be instituted immediately. Additional doses of corticosteroids should not be administered until joint sepsis has been definitively ruled out.

Due to the potential for exacerbation of clinical signs of laminitis, glucocorticoids should be used with caution in horses with a history of laminitis, or horses otherwise at a higher risk for laminitis.

Use with caution in horses with chronic nephritis, equine pituitary pars intermedia dysfunction (PPID), and congestive heart failure.

Concurrent use of other anti-inflammatory drugs, such as NSAIDs or other corticosteroids, should be approached with caution. Due to the potential for systemic exposure, concomitant use of NSAIDs and corticosteroids may increase the risk of gastrointestinal, renal, and other toxicity. Consider appropriate wash out times prior to administering additional NSAIDs or corticosteroids.

#### ADVERSE REACTIONS

Adverse reactions reported during a field study of 239 horses of various breeds which had been administered either BETAVET (n=119) or a saline control (n=120) are summarized in Table 1. One BETAVET treated horse was removed from the study for onset of acute non-weight bearing lameness on Day 4. Treatment for presumed joint sepsis was instituted immediately, but the horse was eventually euthanized several weeks later due to a thromboembolic event associated with prolonged intravenous catheter placement. One BETAVET treated horse developed bilateral forelimb lameness on Day 8, with snow packed in the shoes and poor hoof conformation noted by the investigator. The horse was diagnosed with laminitis. Radiographs showed no abnormalities, and the horse was sound shortly after shoeing changes were implemented.

Table 1. Adverse Reactions

Adverse Reaction	Number (%) of BETAVET treated horses	Number (%) of saline treated horses
Acute joint effusion and/or local injection site swelling (within 2 days of injection)	18 (15%)	16 (13%)
Increased lameness (within the first 5 days)	8 (6.7%)	10 (8.3%)
Loose stool	7 (5.9%)	10 (8.3%)
Increased heat in joint	3 (2.5%)	6 (5%)
Depression	7 (5.9%)	2 (1.6%)
Agitation/anxiety	5 (4.2%)	3 (2.5%)
Delayed swelling of treated joint (5 or more days after injection)	3 (2.5%)	4 (3.3%)
Inappetence	4 (3.4%)	3 (2.5%)
Dry stool	2 (1.7%)	0 (0%)
Excessive sweating	1 (0.8%)	0 (0%)
Acute non-weight bearing lameness	1 (0.8%)	0 (0%)
Laminitis	1 (0.8%)	0 (0%)

#### CLINICAL PHARMACOLOGY

Betamethasone is a potent glucocorticoid steroid with anti-inflammatory and immunosuppressive properties. Depending upon their physico-chemical properties, drugs administered intra-articularly may enter the general circulation because the synovial joint cavity is in direct equilibrium with the surrounding blood supply. After the intra-articular administration of 9 mg BETAVET in horses, there were quantifiable concentrations of betamethasone (above 1.0 ng/mL) in the plasma. Maximum plasma concentrations ( $C_{max}$ ) and time to  $C_{max}$  ( $T_{max}$ ) values ranged from 2.70 to 3.88 ng/mL and 4.5 to 8 hours, respectively. The effective plasma terminal elimination half-life ranged from 4 to 8 hours. The non-compartmental area-under-the-curve to the limit of quantification ( $AUC_{(0-8)}$ ) ranged from 29.24 to 42.96 hr\*ng/mL. In contrast, most of the betamethasone disodium phosphate concentrations and all of the betamethasone acetate concentrations were below the limit of quantification in plasma.

#### EFFECTIVENESS

A negative control, randomized, masked field study provided data to evaluate the effectiveness of BETAVET administered at 1.5 mL (9 mg betamethasone) once intra-articularly for the control of pain and inflammation associated with osteoarthritis in horses. A total of 119 horses received BETAVET and 120 horses received saline. 229 horses were included in the final effectiveness analysis. Clinical success was defined as improvement in one lameness grade according to the AAEP lameness scoring system on Day 5 following treatment. Table 2 summarizes the clinical success and failure in each treatment group on Day 5. The success rate for horses in the BETAVET group was statistically significantly different ( $p=0.0061$ ) than that in the saline group, with success rates of 75.73% and 52.52%, respectively (back-transformed from the logistic regression).

Table 2. Clinical Effectiveness Results

	BETAVET (n=114)	Saline (n=115)
Number of Successes	87	61
Number of Failures	27	54

#### ANIMAL SAFETY

A 3-week target animal safety (TAS) study was conducted to evaluate the safety of BETAVET in mature, healthy horses. The study was designed with 4 treatment groups of 8 horses in each group. Treatment groups included a control (isotonic saline at a volume equivalent to the 4x group); 1X (0.0225 mg betamethasone per pound bodyweight; BETAVET); 2X (0.045 mg betamethasone per pound bodyweight; BETAVET) and 4X (0.09 mg betamethasone per pound bodyweight; BETAVET). Treatments were administered by intra-articular injection into the left middle carpal joint once every 5-days for 3 treatments.

Injection site reactions were the most common observations in all treatment groups. Injection site reactions were observed within 1 hour of dosing and included swelling at the injection site, lameness/stiffness of the left front limb, and flexing the left front knee at rest (see table 3).

Table 3. Incidence of Injection Site Reactions

Group	Total Swelling Observations	Excessive/obvious swelling	Pain at injection site	Knee flexed at rest	Lame or stiff
0x	14	1	0	0	0
1x	6	1	0	0	0
2x	11	2	0	0	0
4x	18	10	3	3	2

The injection site reactions ranged from slight swelling (in many horses on multiple days in all treatment groups) to excessive fluid with swelling, pain, and lameness (4x group only). Injection site reactions were observed most commonly on treatment days, and generally decreased in number and severity over subsequent days. The incidence of injection site reactions increased after the second and third injection (number of abnormalities noted on day 10 > day 5 > day 0). In the BETAVET treated groups the number and severity of the injection site reactions were dose dependent. The 4X BETAVET group had the highest overall incidence of and severity of injection site reactions, which included heat, swelling, pain, bleeding, and holding the limb up at rest. The control group and 4X group (which received similar injection volumes) had a similar incidence of injection site reactions; however, the severity of reactions was greater in the 4X group.

Absolute neutrophils were statistically significantly higher in the BETAVET treated groups as compared to the control group. Trends toward a decrease in lymphocytes and eosinophils, and an increase in monocytes were identified in the BETAVET treated groups after the initial dose of BETAVET. Individual animal values for white blood cells generally remained within the reference range. BETAVET treated horses also had a trend toward increased blood glucose after the initial dose. Some individual animals showed mild increases in blood glucose above the reference range.

#### STORAGE CONDITIONS

Store at 20° to 25°C (68° to 77°F) (See USP Controlled Room Temperature). **Protect from light.** Use carton to protect contents from light until used.

#### HOW SUPPLIED

BETAVET, containing 30 mg betamethasone/5 mL (6 mg betamethasone/mL) in 5 mL vials.

NDC 10797-720-01 5 mL Vials Packaged in boxes of 1

#### SHAKE WELL BEFORE USING

Approved by FDA under NADA # 141-418

AMERICAN REGENT, INC.

ANIMAL HEALTH  
Shirley, NY 11967

(1-888-354-4857)

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