Rapid onset and long-acting relief of pain and inflammation.[1]

The only **dual-action** injectable corticosteroid approved by the FDA for use in horses.

BetaVet®
betamethasone
sodium phosphate and
betamethasone acetate
injectable suspension

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

reasons

The only dual-action betamethasone product proven safe and effective in horses.

- BetaVet® is a sterile aqueous suspension of betamethasone acetate in betamethasone sodium phosphate injection.
- Intra-articular (IA) corticosteroid injections, when used appropriately, are considered **a cornerstone of therapy** to reduce inflammation.
- Target animal safety (TAS) study[2] supported the FDA approval of BetaVet® when administered IA to horses in a maximum of 2 joints at a one-time dosing of 9 mg per joint.

For complete details of the BetaVet® Target Animal Safety Study, visit betavetequine.com.

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

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. **Please see accompanying Full Prescribing Information or at *betavetequine.com*. For additional Important Safety Information, please see next page.**

proven

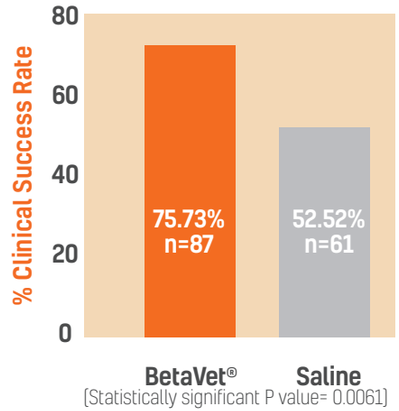
A unique formula backed by science.

- **Controls pain and inflammation** associated with equine osteoarthritis
- **Unique equine formula with 2 active ingredients:**
  - Betamethasone sodium phosphate (3.15 mg[2]), a highly soluble betamethasone ester with a rapid onset of action[1]
  - Betamethasone acetate (2.85 mg[2]), a less soluble betamethasone ester with prolonged action
- Time to peak plasma (Tmax) concentrations achieved in as little as 4.5 to 8 hours*

*Clinical significance of these results is unknown.

Pivotal field studies show over 75% efficacy.[2]

- **BetaVet® clinical success rate of 75.73%** (n=87) compared to Saline (Control) clinical success rate of 52.52% (n=61)
- **Field efficacy study** based on a negative control, randomized masked trial of 239 horses — BetaVet® n=114; Saline (Control) n=115
- **Clinical success defined** as improvement in one lameness grade according to the AAEP lameness scoring system, Day 5 after treatment



[Statistically significant P value= 0.0061]

The most common adverse events included local swelling, mild increases in lameness, loose stool, increased heat in the treated joint, depression, anxiety and inappetence.

advantages

The advantages of an FDA-approved product.

As you choose and use products for your equine patients, your clients may want to know why you recommend one option over another.

When you choose BetaVet,® you can be sure you're administering an FDA-approved product that has undergone rigorous clinical testing for both efficacy and safety in horses.

What sets BetaVet® apart?

FIRST FDA-approved betamethasone for equine use[2]

FDA-approved product benefits	BetaVet®	Other IA corticosteroids
ONLY dual-action equine corticosteroid with two active ingredients[2]	✓	✗
Fastest time to maximum measured plasma concentration post-IA injection[3]	✓	✗
No deleterious effects shown on equine articular cartilage[4]	✓	✗
Wider therapeutic index for betamethasone anecdotally reported for laminitis risk[5]	✓	✗
Meets ARCI, RMTC, USEF requirements for shortest withdrawal time (7 days)[6,7,8]	✓	✓*

*See triamcinolone reference #8.

dosing

Dosing and administration

- **Shake well immediately before use.**
- **Using strict aseptic technique**, administer BetaVet® 1.5 mL (9 mg total betamethasone) per joint by intra-articular injection.
- **May be administered concurrently** in up to 2 joints per horse.
- **Use immediately** after opening; discard any remaining contents.

PRECAUTIONS: Corticosteroids, including BetaVet,® administered intra-articularly are systemically absorbed. Do not use in horses with acute infections.

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

From the manufacturer of Adequan® i.m. (polysulfated glycosaminoglycan), trusted by veterinarians for more than 30 years.

Want to learn more or place an order?

- **Contact** your American Regent, Inc., Sales Representative
- **Call 1-800-458-0163**
- **Visit betavetequine.com**

1. Trotter GW. Intra-articular corticosteroids. In: McIlwraith CW, Trotter GW, eds. *Joint Disease in the Horse*. Philadelphia, PA; W.B. Saunders, 1996; 237-256.
2. BetaVet® (betamethasone sodium phosphate and betamethasone acetate injectable suspension), Package Insert. American Regent, Inc.
3. Knych HK, Stanley SD, Harrison LM and McKemie DS. Pharmacokinetics of Betamethasone in Plasma, Urine and Synovial Fluid Following Intra-Articular Administration to Exercised Thoroughbred Horses. *Drug Test Anal*. 2017 Sep;9(9):1385-1391.
4. Foland JW, McIlwraith CW, Trotter GW, Powers BE, and Lamar CH. Effect of Betamethasone and Exercise on Equine Carpal Joints with Fragments. *Vet Surg*. 1994;23:369-376.
5. Frisbie D. New Research and Regulatory Issue Associated with Corticosteroids. *AAEP Proceedings*; November 26-29, 2000; San Antonio, TX.
6. ARCI Controlled Therapeutic Medication Schedule for Horses; V4.0 (Rev. April 20, 2017)
7. RMTC Approved Controlled Therapeutic Medications. 2 Feb 2016.
8. FEI List of Detection Times, Fédération Equestre Internationale (FEI), 13 Jul 2018.

PP-BV-US-0045 (v2.0)

Please see accompanying Full Prescribing Information or at *betavetequine.com*.

AMERICAN REGENT® ANIMAL HEALTH

BetaVet®
betamethasone
sodium phosphate and
betamethasone acetate
injectable suspension

BETAVET®

(Betamethasone Sodium Phosphate and
Betamethasone Acetate Injectable Suspension)

RQ1053A

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.

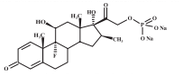
DESCRIPTION

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.

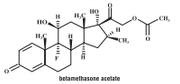
The formula for betamethasone sodium phosphate is $C_{22}H_{28}FNa_2O_8P$ and it has a molecular weight of 516.41. Chemically, it is 9-Fluoro-11β, 17,21-trihydroxy-16β-methylpregna-1,4-diene-3,20-dione 21-(disodium phosphate).

The formula for betamethasone acetate is $C_{24}H_{31}FO_6$ and it has a molecular weight of 434.50. Chemically, it is 9-Fluoro-11β,17,21-trihydroxy-16β-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



betamethasone acetate

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%)
Inappetance	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_{LOQ}) 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)

Rev. 8/2021

RQ1053A