

TECHNICAL BULLETIN



BetaVet® (Betamethasone sodium phosphate and betamethasone acetate) Use in Equine Athletes

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In the equine athlete, single or repetitive episodes of trauma to the synovial membrane and fibrous joint capsule commonly result in inflammatory synovitis and capsulitis. Inflammatory mediators resulting from synovitis can cause biochemical damage that leads to degradation of articular cartilage, resulting in osteoarthritis (OA).¹ OA is defined as the progressive deterioration of articular cartilage accompanied by changes in bone and soft tissue.¹ The ongoing pain and inflammation associated with development of OA can be career-limiting for athletic horses required to perform at a high level. In the medical management of OA by equine practitioners, intra-articular corticosteroids are considered a cornerstone of therapy to reduce inflammation.

The equine sports industry has fallen under scrutiny in recent years due to horses suffering catastrophic injury during high-profile events.² Use of intra-articular corticosteroids close to competition has become a concern due to their ability not only to decrease inflammation and pain, and reduce potential overloading of other limbs, but also for their ability to mask pain resulting from ongoing joint deterioration or injury that would otherwise prohibit a horse from competing.^{2,3} Indiscriminate use of medication in equine sports has led to significant oversight and monitoring with the ultimate goal of assuring the health and welfare of both animal and human participants. In an effort to promote national uniformity with respect to medication regulations, the Association of Racing Commissioners International (ARCI) and Racing Medication and Testing Consortium (RMTC), as well as the Federation Equestre Internationale (FEI) and United States Equestrian Federation (USEF), have established regulatory thresholds and withdrawal time guidance for a limited number of therapeutic medications, including intra-articular corticosteroids.³

However, racetrack and sport horse veterinarians face the unique challenge of administering appropriate treatment at therapeutic levels, while adhering to withdrawal time guidelines. The potential for positive tests in serum or plasma creates added pressure and responsibility as veterinarians make medical decisions. Practitioners who need to treat more than one joint, or large joints, are faced with the knowledge that using increased doses of drug and/or combination therapy for a therapeutic purpose may lead to withdrawal violations.³ In 2015, BetaVet®, a combination of betamethasone sodium phosphate and betamethasone acetate, gained FDA approval for intra-articular use in horses for control of pain and inflammation associated with osteoarthritis.⁴ The following information is presented to assist practitioners in the use of BetaVet® within a regulated equine sports environment.

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INDICATIONS

BetaVet® 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.



FDA approved BetaVet® is indicated for the control of pain and inflammation associated with osteoarthritis in horses. BetaVet® is supplied as a 5 ml vial (6 mg/ml) containing 30 mg betamethasone. One ml of BetaVet® contains:

- 3.15 mg betamethasone sodium phosphate
- 2.85 mg betamethasone acetate

BetaVet® recommended Dosage and Administration:⁴

- 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 (18 mg total body dose)⁴

Clinical Pharmacology:

- Drugs administered intra-articularly may enter the general circulation because the synovial joint cavity is in direct equilibrium with the surrounding blood supply⁴
- Pharmacokinetic data generated for BetaVet® approval demonstrated a time to peak plasma concentration (T_{max}) achieved in 4.5-8 hours, with a terminal half-life ($T_{1/2}$) from 4 to 8 hours⁴
- Betamethasone was found to be systemically available in plasma following intra-articular administration of 9 mg BetaVet®⁵

Current Regulatory Guidelines for Betamethasone in Equine Athletic Competition:³

- At the time of this writing, for betamethasone ARCI recommends a 7-day withdrawal guidance for 9 mg in a single joint space, with a threshold concentration of 10 pg/ml³
- Results of a 2016 study examining corticosteroid clearance following intra-articular administration in racehorses suggest that intra-articular doses of betamethasone* "less than 30 mg should not result in excess of the regulatory threshold, when following the ARCI recommended withdrawal time guidance"^{†3}
- FEI and USEF currently recommend a 7-day withdrawal time for betamethasone at 30 mg total body dose administered in up to two joints⁶

* American Regent, Inc. Shirley, New York, USA.

† The study examined corticosteroid serum levels only and did not assess urine levels thus extrapolation of withdrawal time guidance to jurisdictions where corticosteroids are regulated in urine is not appropriate.

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 and 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.



Additional Factors Potentially Affecting Withdrawal Time:

- Higher doses and non-intra-articular routes of administration of corticosteroids may require a prolonged withdrawal time³
- Extravasation into subcutaneous tissues or inadvertent extra-articular injection during an intended intra-articular corticosteroid injection may necessitate a prolonged withdrawal time³
- Use of an intra-articular medical device concurrently with betamethasone* may extend the withdrawal time, based on a 2016 study³

Note: The labeled dosage of BetaVet® is 1.5 ml (9 mg total betamethasone) per joint administered by intra-articular injection. BetaVet® may be administered concurrently in up to 2 joints per horse (18 mg total body dose).⁴ BetaVet® has not been studied with, and is neither approved nor indicated for concurrent use with other products.

Please see included Important Safety Information.

AAEP Position on Use of Intra-Articular Corticosteroids in Performance Horses:

The American Association of Equine Practitioners (AAEP) has issued the following statement regarding the use of intra-articular medications in non-racing performance horses:

"The AAEP recognizes that the judicious use of intra-articular medications with a valid veterinarian-patient relationship is appropriate treatment and can benefit a horse's health and well-being. The AAEP defines this relationship to be a clinical or lameness examination with appropriate diagnostic tests prior to initiation of a therapeutic plan. Clinicians treating performance horses in the competitive environment are encouraged to develop treatment regimens, particularly with reference to use of IA corticosteroids, which allow adequate evaluation of the horse's response to treatment prior to competition."⁷

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) 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.

DOSAGE AND ADMINISTRATION: Shake well immediately before use. Use immediately after opening, then discard any remaining contents.

RX ONLY

Please see Full Prescribing Information in pocket.



References:

1. McIlwraith CW, Frisbie DD, Kawcak CE, van Weeren PR. Traumatic arthritis and posttraumatic osteoarthritis in the horse. In: *Joint Disease in the Horse*. St. Louis, MO: Elsevier, 2016; 33.
2. McIlwraith CW, Frisbie DD, Kawcak CE, van Weeren PR. Intraarticular corticosteroids. In: *Joint Disease in the Horse*. St. Louis, MO: Elsevier, 2016; 202.
3. Knych HK, Blea JA, Arthur RM, Overly LR, McIlwraith CW. Clearance of corticosteroids following intra-articular administration of clinical doses to racehorses. *Equine Vet Edu*. 2016; 28(3): 140-144.
4. BetaVet® [package insert]. Shirley, NY: Luitpold Animal Health; 2014.
5. Freedom of Information Summary, BetaVet NADA 141-418.
<http://www.fda.gov/downloads/animalveterinary/products/approvedanimaldrugproducts/foiadrugsummaries/ucm433794.pdf>. Accessed July 21, 2015.
6. http://www.fei.org/system/files/FEI_detection_times_lab_2015_1.pdf. Accessed June 02, 2016.
7. <http://rmtcnet.com/wp-content/uploads/2015/07/RMTC-Position-Paper-on-Corticosteroids.pdf> as referenced within. AAEP American Association of Equine Practitioners, *Clinical guidelines for veterinarians treating the non-racing performance horse*. 2011.

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