BETAVET®
(Betamethasone Sodium Phosphate and Betamethasone Acetate Injepctable Suspension)

BETAVET® is a white or practically white, odorless powder, and is hygroscopic. It is freely soluble in methanol, but is practically insoluble in acetone and in chloroform.

Betamethasone 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 is soluble in acetone, and is soluble in alcohol and in chloroform.

Metabolism
Betamethasone sodium phosphate and betamethasone acetate are as follows:

\[
\text{Chemical structures for betamethasone sodium phosphate and betamethasone acetate.}
\]

BETAVET® is contraindicated for the control of pain and inflammation associated with osteoarthrosis in horses.

Dosage and Administration
Stake well immediately before use.

Use 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 4 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 facilitate premature parturition induced by dystocia, fetal death, retained placenta, and motts.

Additionally, corticosteroids administered to dogs, rabbits and rats during pregnancy have resulted in soft palate in offspring. Corticosteroids administered to dogs during pregnancy also have 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, can be 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 bacterial infection of the treated joint. One BETAVET treated horse developed bilateral laminitis lameness on Day 5, with snow packed in the shoes and poor coroner condition noted by the investigator. The horse was diagnosed with laminitis. Radiographs showed no abnormalities, and the horse was scored short on shoeing changes were implemented.

Table 1. Adverse Reactions

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>Number (%) of BETAVET-treated horses</th>
<th>Number (%) of saline-treated horses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute joint effusion</td>
<td>18 (15%)</td>
<td>16 (13%)</td>
</tr>
<tr>
<td>Acute moderate to severe exacerbation of pain</td>
<td>9 (7.7%)</td>
<td>8 (6.7%)</td>
</tr>
<tr>
<td>Inappetance</td>
<td>6 (5.3%)</td>
<td>4 (3.3%)</td>
</tr>
<tr>
<td>Agitation</td>
<td>5 (4.2%)</td>
<td>3 (2.5%)</td>
</tr>
<tr>
<td>Swelling (within 2 days after injection)</td>
<td>18 (15%)</td>
<td>16 (13%)</td>
</tr>
<tr>
<td>Increased swelling</td>
<td>7 (5.9%)</td>
<td>7 (5.8%)</td>
</tr>
<tr>
<td>Increased joint heat</td>
<td>3 (2.5%)</td>
<td>2 (1.6%)</td>
</tr>
<tr>
<td>Depression</td>
<td>8 (6.7%)</td>
<td>7 (5.8%)</td>
</tr>
<tr>
<td>Acute non-weight bearing lameness</td>
<td>7 (5.9%)</td>
<td>5 (4.1%)</td>
</tr>
<tr>
<td>Laminitis</td>
<td>4 (3.3%)</td>
<td>4 (3.3%)</td>
</tr>
<tr>
<td>Mucopurulent discharge</td>
<td>2 (1.7%)</td>
<td>2 (1.6%)</td>
</tr>
<tr>
<td>Erythema</td>
<td>1 (0.8%)</td>
<td>1 (0.8%)</td>
</tr>
<tr>
<td>Mucopurulent discharge</td>
<td>1 (0.8%)</td>
<td>1 (0.8%)</td>
</tr>
<tr>
<td>Mucopurulent discharge</td>
<td>1 (0.8%)</td>
<td>1 (0.8%)</td>
</tr>
</tbody>
</table>

ART / 2 DATE: 08/26/2021
CUSTOMER: AMERICAN REGENT

P/N: BETAVET, RQ1053-A, P
Lot: 437228
Size: 125.5 x 5.5 (L x W)
Fold: 1.125 x 5.5 (L x W)
Eye Marks: 16.34-50-D
DRING: 148100

CODE: Type / Encoding / Human Readable
128 / RQ1053A / RQ1053A

APPROVED
ArtPhi

Approved by ArtPhi and Accel Manager

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Clinical Volunteer: A potent glucocorticoid with anti-inflammatory and immunosuppressive properties. Depending upon their physico-chemical properties, drugs administered intra-articularly may enter the general circulation because the synovial cavity is in direct equilibrium with the surrounding blood supply. After the initial injection, administration of 5 mg BETAVET in 10 mL in horses, there were quantifiable concentrations of betamethasone (above 1.0 ng/mL) in the plasma. Maximum plasma concentrations (Cmax) and time to Cmax (Tmax) 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-competitive 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 were below the limit of quantification in plasma.

Effectiveness: A negative control, randomized, masked field study was conducted to evaluate the effectiveness of BETAVET administered at 1.0 mL, (9 mg betamethasone) once intra-articularly for the control of pain and inflammation associated with osteoarthritis in horses. A total of 151 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 and lameness score at 1.5 mL (9 mg betamethasone) once intra-articularly into the left middle carpal joint once every 5-days for 3 treatments.

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). The effective plasma terminal elimination half-life ranged from 4 to 8 hours. The non-competitive 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 were below the limit of quantification in plasma.