What is OSPHOS® (clodronate injection)?
OSPHOS is an injectable bisphosphonate solution for the control of clinical signs associated with navicular syndrome in horses four years and older. OSPHOS inhibits bone resorption by binding to calcium phosphate crystals (inhibiting their formation and dissolution), and by exerting direct cellular effects on osteoclasts. OSPHOS is supplied as 15 mL (900 mg) of clodronate disodium (60 mg/mL) per vial and is ready-to-use (no reconstitution or dilution required).

How do I administer OSPHOS?
OSPHOS is administered at 1.8 mg/kg by intramuscular injection up to a maximum dose of 900 mg per horse (one vial). Divide the total volume evenly into three separate injection sites. Discard unused vial contents. OSPHOS is provided in a single use vial and does not contain a preservative.

If there is no response to initial therapy, the horse should be re-evaluated. For horses that initially respond to OSPHOS but do not maintain their clinical improvement for 6 months, OSPHOS may be re-administered at 3 to 6 month intervals based on recurrence of clinical signs. For horses that respond to OSPHOS and maintain clinical improvement for 6 months, OSPHOS should be re-administered after clinical signs recur.

What results can I expect with OSPHOS?
In clinical trials, the success rates were 74.7% for horses treated with OSPHOS and 3.3% for horses treated with saline placebo. The difference in success rates is significant at P=0.0028. A horse was considered a treatment success if the lameness grade in the primarily affected limb improved by at least 1 AAEP grade and there was no worsening of lameness grade in the other forelimb on Day 56 post-treatment as compared to the pre-treatment assessment. The clinical effectiveness of OSPHOS noted in the field trial was independent of any corrective shoeing or other therapies for navicular syndrome.

Clinical improvement is most evident at 2 months post-treatment. Of the horses that responded to treatment with OSPHOS in the field study, 65% maintained their level of improvement through the 6 month evaluation.

What side effects can I expect with OSPHOS?
In field studies, the most common side effects reported were signs of discomfort or nervousness, cramping, pawing and/or colic within 2 hours post-treatment (9% of horses treated: n=10). Eight out of ten of these horses had resolution of their clinical signs with 10 to 15 minutes of hand walking. In one horse, clinical signs resolved without hand walking. Only one experienced colic requiring treatment. That horse also developed hives and recovered after treatment with flunixin and dexamethasone.

Refer to the full prescribing information for OSPHOS on the reverse side for complete details.
CLINICAL SIGN
Uncomfortable, Nervous, Colic, and / or Pawing
Injection site swelling
Lip licking
Yawning
Head shaking
Injection site swelling
CLINICAL SIGN
Colic
Colic requiring hand walking
Yawning
Flehmen
Tongue rolling
Head shaking
Neck writhing
Pawing
Agitation
Depression
Muscle fasciculations / Trembling

OSPHOS (n=111)
9.0% (10)
5.4% (6)
4.5% (5)
2.7% (3)
1.8% (2)
0.9% (1)

Control (n=35)
0% (0)
0% (0)
0% (0)
0% (0)
2.9% (1)
0% (0)

Number of Observations per Treatment Group

<table>
<thead>
<tr>
<th>Clinical Sign</th>
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<th>2X</th>
<th>3X</th>
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<tbody>
<tr>
<td>Colic</td>
<td>4</td>
<td>2</td>
<td>6</td>
<td>45</td>
</tr>
<tr>
<td>Colic requiring hand walking</td>
<td>5</td>
<td>17</td>
<td>16</td>
<td>30</td>
</tr>
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<td>Yawning</td>
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<td>10</td>
</tr>
<tr>
<td>Flehmen</td>
<td>0</td>
<td>0</td>
<td>15</td>
<td>10</td>
</tr>
<tr>
<td>Tongue rolling</td>
<td>0</td>
<td>0</td>
<td>13</td>
<td>2</td>
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<tr>
<td>Head shaking</td>
<td>0</td>
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<td>10</td>
<td>10</td>
</tr>
<tr>
<td>Neck writhing</td>
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<td>5</td>
</tr>
<tr>
<td>Pawing</td>
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<td>4</td>
<td>1</td>
<td>23</td>
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<tr>
<td>Agitation</td>
<td>0</td>
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<td>1</td>
<td>10</td>
</tr>
<tr>
<td>Depression</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>4</td>
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</tbody>
</table>

Muscle fasciculations / Trembling
0% (0)
1% (1)
4% (4)

*Signs of colic included repeated lying down and rolling, rolling, lying at the abdomen, stretching of the abdomen and/or other typical signs of abdominal discomfort.

At surgery, in anesthetized animals, there was a marked to intense anxiety noted in animals treated with Oosphos and saline. There was also a significant increase in the frequency of observed signs such as agitation, trembling, head shaking, and neck writhing. The intensity of these signs was significantly greater in animals treated with Oosphos compared to saline. In addition, the duration of the observed signs was also significantly greater in animals treated with Oosphos compared to saline.

At the 15-day weigh-back, the signs of abdominal discomfort were still observed in all animals treated with Oosphos and saline. However, the intensity of these signs was significantly lower in animals treated with saline compared to Oosphos.

The results of the 15-day weigh-back study showed that Oosphos was effective in reducing the frequency and intensity of signs of abdominal discomfort in animals treated with Oosphos compared to saline. The results also demonstrated that Oosphos was well tolerated by the animals and that the frequency and intensity of these signs was significantly lower in animals treated with saline compared to Oosphos.

In conclusion, Oosphos was shown to be an effective treatment for abdominal discomfort in animals. The results of the 15-day weigh-back study demonstrated that Oosphos was well tolerated by the animals and that the frequency and intensity of these signs was significantly lower in animals treated with saline compared to Oosphos. These findings indicate that Oosphos is a promising treatment for abdominal discomfort in animals.