Bovine Rhinotracheitis-Virus Diarrhea-Parainfluenza 3-Respiratory Syncytial Virus Vaccine, Modified Live Virus

Leptospira Canicola-Grippotyphosa-Hardjo-Icterohaemorrhagiae-Pomona Bacterin

**Indications**

For vaccination of healthy cows and heifers prior to breeding for prevention of persistently infected calves caused by Bovine Virus Diarrhea (BVDV) virus types 1 and 2; as an aid in the prevention of abortion due to Infectious Bovine Rhinotrachitis (IBR) virus; for the prevention of urinary shedding of *L. borgpetersenii* serovar *hardjo* (type *hardjo-bovis*); as an aid in the prevention of respiratory disease caused by IBR virus, BVDV virus types 1 and 2, Bovine Respiratory Syncytial Virus (BRSV); as an aid in the reduction of respiratory disease caused by Parainfluenza 3 (PI3) virus; and as an aid in reduction of leptospirosis caused by 5 serovars of Leptospira (*L. canicola, L. grippotyphosa, L. hardjo, L. icterohaemorrhagiae, L. pomona*).

A 12-month duration of immunity has been demonstrated against IBR-induced abortion and against disease, including persistently infected calves, caused by BVDV types 1 and 2. In addition, vaccinated animals subsequently exposed to *L. borgpetersenii* serovar *hardjo* (type *hardjo-bovis*) have been shown to clear renal infections within 8 weeks of exposure.

This vaccine may be administered to pregnant cattle provided they were vaccinated, according to label directions, with any Express® FP vaccine within the past 12 months. May also be administered to calves nursing pregnant cows provided their dams were vaccinated within the past 12 months with Express FP products. See below for details.

**Composition**

The product in the amber glass vial contains IBR, BVDV Type 1 (Singer 1a cytopathic) and Type 2 (296 cytopathic), PI3, and BRSV modified live viruses. The plastic vial contains the *Leptospira* organisms listed above, in an adjuvant system. Contains neomycin and thimerosal as preservatives.

**Directions and Dosage**

Shake the accompanying bottle of bacterin diluent, then rehydrate the modified live virus vaccine by aseptically adding the diluent to the modified live virus (MLV) in 14-28 days. Calves vaccinated before 6 months of age should be revaccinated at 6 months. A 2 mL booster dose is recommended annually. Cows and Heifers: Using aseptic technique, annually inject a single 2 mL dose subcutaneously or intramuscularly at or about 4 weeks prior to breeding. Pregnant cows and nursing calves may be vaccinated provided they were vaccinated, according to label directions, with any Express FP vaccine within the past 12 months. See below for details. If initial vaccination, see above.

**Precautions**

Store out of direct sunlight at 35-45°F (2-7°C). Avoid freezing. Use entire contents when first opened. Do not vaccinate within 21 days before slaughter. Stressed cattle should not be vaccinated. Burn containers and all unused contents. Injection site swelling may occur. Antidote: Epinephrine.

**Summary of BVD Type 1 and 2 Efficacy Studies**

Four non-cytopathic BVD challenge viruses were used in five different challenge studies to determine the efficacy of this product in preventing persistently infected calves due to BVD Types 1 and 2. The challenge viruses included two BVD Type 1b and two BVD Type 2 strains. The efficacy provided against challenge ranged from 91% to 100% prevention of persistent infection. The table below gives a summary of these studies.

<table>
<thead>
<tr>
<th>Challenge Virus</th>
<th>Treatment Group</th>
<th># Positive/ Total</th>
<th>Percent Protected</th>
</tr>
</thead>
<tbody>
<tr>
<td>BVDV Type 1</td>
<td>Vaccinates</td>
<td>1/29</td>
<td>96%</td>
</tr>
<tr>
<td>(2 Studies)</td>
<td>Controls</td>
<td>18/18</td>
<td>0%</td>
</tr>
<tr>
<td>BVDV Type 2</td>
<td>Vaccinates</td>
<td>2/46</td>
<td>96%</td>
</tr>
<tr>
<td>(3 Studies)</td>
<td>Controls</td>
<td>29/29</td>
<td>0%</td>
</tr>
</tbody>
</table>

**Summary of BVD Type 1 and 2 Duration of Immunity Efficacy Studies**

One hundred thirty-six seronegative heifers were enrolled in this study. Sixty-six were assigned to the BVDV Type 1 study and 70 were assigned to the BVDV Type 2 study. Thirty-two animals in the BVDV Type 1 study and 35 animals in the BVDV Type 2 study were vaccinated on Day 0 with Express® FP 5-VL5. The rest of the heifers were vaccinated with Citadel® VL5. All heifers in the BVDV Type 1 study were bred on Day 285 and the heifers in the BVDV Type 2 study were bred on Day 284. Heifers in the Type 1 study were challenged with virulent BVDV Type 1b strain BJ on Day 368 and the heifers in the Type 2 study were challenged on Day 374 with BVDV Type 2 strain PA 131. Temperatures, clinical observations, and blood samples were collected on multiple study days. Fetal tissues were collected on Day 440 for the Type 1 study and Day 439 for the Type 2 study. All control heifers remained seronegative to BVDV Type 1 and 2 prior to challenge.

The following table summarizes the results of the duration of immunity studies. These results indicate that a single dose of Express FP 5-VL5 administered one year prior to challenge provided feral protection against BVDV Type 1 and 2, preventing persistently infected calves: Type 1 [prevented fraction = 0.95 (95%) with exact 95% confidence limits of (0.75, 1.0)] and Type 2 [prevented fraction = 1.0 (100%) with exact 95% confidence limits of (0.81, 1.0)]. Vaccination also provided protection against viremia and leukopenia: Viremia BVDV Type 1 prevented fraction = 1.0 (100%) with exact 95% confidence limits of (0.83, 1.0); viremia BVDV Type 2 prevented fraction = 0.94 (94%) with exact 95% confidence limits of (0.72, 1.0); leukopenia BVDV Type 1 prevented fraction = 0.60 (60%) with exact 95% confidence limits of (0.32, 0.80); leukopenia BVDV Type 2 prevented fraction = 0.91 (91%) with exact 95% confidence limits of (0.58, 1.0).

<table>
<thead>
<tr>
<th>Challenge Virus</th>
<th>Treatment Group</th>
<th>PI Positive</th>
</tr>
</thead>
<tbody>
<tr>
<td>BVDV Type 1</td>
<td>Vaccinates</td>
<td>1/22 (4.5%)</td>
</tr>
<tr>
<td></td>
<td>Controls</td>
<td>20/23 (87.0%)</td>
</tr>
<tr>
<td>BVDV Type 2</td>
<td>Vaccinates</td>
<td>0/18 (0%)</td>
</tr>
<tr>
<td></td>
<td>Controls</td>
<td>21/22 (95.5%)</td>
</tr>
</tbody>
</table>
Culture results from weekly urine samples starting at 1 week post-challenge confirmed that vaccination prevented urinary shedding of the challenge organism. Kidney culture results confirmed that the vaccinated heifers were negative for kidney infection at 8 weeks post-challenge.

Summary of Pregnant Cow Safety Study
Safety in pregnant cows and heifers was demonstrated in a field study that utilized more than 1600 cattle from three separate herds, as well as a serological study from a fourth herd. All cows and heifers enrolled in the study were vaccinated prior to breeding with Express® FP 10, a modified live virus (MLV) vaccine containing Infectious Bovine Rhinotracheitis (IBR), Bovine Virus Diarrhea (BVD) Type 1, BVD Type 2, Parainfluenza 3 (PI3), and Bovine Respiratory Syncytial Virus (BRSV), as well as Leptospira canicola, L. grippotyphosa, L. hardjo, L.icterohaemorrhagiae, L. pomona bacteria. Approximately one-third of the enrolled cattle were assigned to each one of the three trimesters. After confirmation of pregnancy status, a second vaccination was administered during the assigned trimester. Half of each trimester group was given Express® FP 10 and the remaining half was given the Lepto 5 bacterin. All of the enrolled cattle were observed closely through calving. Any fetal losses were recorded and fetuses were subjected to a full necropsy. Fetal losses were similar in both treatment groups.

Overall fetal losses were 1.6% (13 of 810) in the test vaccination group and 1.9% (15 of 776) in the control group. There were no abortions or fetal losses diagnosed as due to IBR or BVD. The health of the calves from the enrolled cattle was monitored for 30 days after birth. There were no differences noted in the health status of calves between the two treatment groups.

In addition, a separate newborn calf serology study was conducted. A total of 120 calves from dams revaccinated in the second or third trimester were negative for pre-colostal antibodies to Bovine Virus Diarrhea Types 1 and 2 and Infectious Bovine Rhinotracheitis, further demonstrating that the Express® MLV products do not cause fetal infection when administered during pregnancy to previously vaccinated cows or heifers.

Fetal health risks associated with vaccination of pregnant animals with modified live vaccines cannot be unequivocally determined by clinical trials conducted for licensure. Management strategies based on vaccination of pregnant animals with modified live vaccines should be discussed with a veterinarian.

No vaccine can be expected to have 100% efficacy under all conditions. A small number of calves persistently infected with BVDV may have a devastating effect on herd health.

Note
It is possible that healthy-appearing cattle can be persistently infected with or incubating virulent BVD virus at the time of vaccination. In view of these findings and suggested causes, BVD vaccine is contraindicated in persistently infected cattle and use should be limited only to healthy, immunocompetent, unstressed cattle.

Caution
Animal inoculation only. Accidental injection into humans can cause serious local reactions. Contact a physician immediately if accidental injection occurs.

© 2012 Boehringer Ingelheim Vetmedica, Inc. All Rights Reserved.
Indications: For vaccination of healthy cows and heifers prior to breeding for prevention of persistently infected calves caused by Bovine Virus Diarrhea (BVD) virus types 1 and 2, as an aid in the prevention of abortion due to Infectious Bovine Rhinotracheitis (IBR) virus; for the prevention of urinary shedding of L. borgpetersenii serovar hardjo (type hardjo-bovis); as an aid in the prevention of respiratory disease caused by IBR virus, BVD virus types 1 and 2, Bovine Respiratory Syncytial Virus (BRSV); as an aid in the reduction of respiratory disease caused by Parainfluenza 3 (PI3) virus; and as an aid in reduction of leptospirosis caused by 5 serovars of Leptospira (L. canicola, L. grippotyphosa, L. hardjo, L. icterohaemorrhagiae, and L. pomona).

A 12-month duration of immunity has been demonstrated against IBR-induced abortion and against disease, including persistently infected calves, caused by BVD types 1 and 2. In addition, vaccinated animals subsequently exposed to L. borgpetersenii serovar hardjo (type hardjo-bovis) have been shown to clear renal infections within 8 weeks of exposure.

This vaccine may be administered to pregnant cattle provided they were vaccinated, according to label directions, with any Express® FP vaccine within the past 12 months. May also be administered to calves nursing pregnant cows provided their dams were vaccinated within the past 12 months with Express FP products. See insert for details.

Composition: The product in the amber glass vial contains IBR, BVD Type 1 (Singer 1a cytopathic) and Type 2 (296 cytopathic), PI3, and BRSV modified live viruses. The plastic vial contains the Leptospira organisms listed above, in an adjuvant system. Contains neomycin and thimerosal as preservatives.

Directions and Dosage: See insert.

This package contains one 10 dose vial of MLV vaccine and one 20 mL vial of bacterin diluent.

Precautions: Store out of direct sunlight at 35-45°F (2-7°C). Avoid freezing. Use entire contents when first opened. Do not vaccinate within 21 days before slaughter. Stressed cattle should not be vaccinated. Burn vaccine container and all unused contents. Injection site swelling may occur. Anaphylactoid reactions may occur. Antidote: Epinephrine.