Approved Labels (2012)

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

IBR-BVD-Type 1 and 2-PI3-BRSV

Indications: For vaccination of healty 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; as an aid in the prevention of respiratory disease caused by IBR virus, BVD virus types 1 and 2, Bovine Respiratory Syncytial Virus (BRSV); and as an aid in the reduction of respiratory disease caused by Parainfluenza 3 (PI3) virus. 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.

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 vials contains IBR, BVD Type 1 (Singler 1a cytopathic) and Type 2 (CP-64 cytopathic), PI3, and BRSV modified live viruses. The plastic vial contains an adjuvant system. Contains neomycin and thimerosal as preservatives.

Directions and Dosage: See insert.

Available:
20 mL (10 doses)
100 mL (50 doses)

Boehringer Ingelheim

Boehringer Ingelheim Vetmedica, Inc.
St. Joseph, MO 64506
U.S. Vet. License No. 124
Code 126731

This package contains one 50 dose vial of MUX vaccine and one 100 mL vial of adjuvanted elixir.

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. Anaphylactic reactions may occur. Antidote: Epinephrine.
Bovine Rhinotracheitis-Virus
Diarrhea-Parainfluenza 3-
Respiratory Syncytial Virus Vaccine
Modified Live Virus

**Express FP 5**

**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; as an aid in the prevention of respiratory disease caused by Parainfluenza 3 (PI3) virus. A 12-month, modified live virus vaccine has been demonstrated against IBR-induced abortion and against disease, including persistently infected calves, caused by BVD types 1 and 2.

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 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, BVD Type 1 (Singer 1a cytopathic) and Type 2 (296 cytopathic), PI3, and BRV modified live viruses. The plastic vial contains an adjuvant system. Contains neomycin and thimerosal as preservatives.

**Directions and Dosage**
Shake the accompanying bottle of adjuvanted diluent, then rehydrate the modified live virus vaccine by aseptically adding the diluent to the vaccine vial. Shake the rehydrated vaccine and use immediately. Using aseptic technique, inject 2 mL subcutaneously or intramuscularly. If using subcutaneous route, inject in front of the shoulder and midway of the neck, away from the supracaudal lymph node. If initial vaccination, repeat with any Express’ vaccine containing BRSV 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, administer 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 store out of direct sunlight at 35-45°F (2-7°C). Avoid the past 12 months. See below for details. If initial vaccination provided they were vaccinated, according to label directions, with any Express® FP vaccine within 12 months prior to vaccination. Prevented fraction for abortion = 0.84 (84.0%) with exact 95% confidence limits of (0.54, 0.98).

**Summary of BVD Vaccine 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 and 70 were assigned to the BVDV Type 2 vaccine 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-VLS. The rest of the heifers were vaccinated with Citadel® VLS. 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 BJD 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-VLS administered one year prior to challenge provided fetal 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 vaccinated fraction = 1.0 (100%) with exact 95% confidence limits of 0.83,1.0); viremia BVDV Type 2 vaccinated fraction = 0.94 (94%) with exact 95% confidence limits of 0.72,1.0); leukopenia BVDV Type 1 vaccinated fraction = 0.80 (80%) with exact 95% confidence limits of 0.32,1.0); leukopenia BVDV Type 2 vaccinated fraction = 0.91 (91%) with exact 95% confidence limits of 0.58,1.0).

**Challenge**

<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>20/22 (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>

**Summary of IBR abortion Duration of Immunity Efficacy Studies**
Eighty-four heifers negative with IBR titers <1:2 were enrolled in this study to evaluate the efficacy and duration of immunity of the IBR modified live vaccine component in an IBR abortion challenge model. Twenty-five heifers were administered Express FP 5-VLS 12 months prior to challenge, 29 were administered Express FP 5-VLS 8 months prior to challenge and 27 heifers were administered Citadel VL5 for the challenge control group. Vaccines and controls were separated 25 days post-vaccination then re-commingled. All heifers were artificially inseminated on Day 193 and a clean up bull was put in with the heifers from Day 193 to Day 207. Heifers were then challenged on Day 386 with IBR Cooper strain, IV, via jugular venipuncture. Post-challenge all heifers were commingled for the duration of the study.

The proportion positive for abortion included 2/13 (15.4%) for heifers vaccinated 12 months prior to challenge (p=0.0001), 5/19 (26.3%) for heifers vaccinated 8 months prior to challenge (p=0.0001) and 18/19 (94.7%) for the control group. Fetal tissues tested negative for other potential causes of abortion, which supported that post-challenge abortions were IBR-related and that abortions were prevented in heifers challenged with IBR 12 months post-vaccination (prevented fraction for abortion = 0.84 (84.0%) with exact 95% confidence limits of (0.54, 0.98).

**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 bacterin. 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 close and kept 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 re-vaccinated 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-looking 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, unstrested 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.

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