Herd Health Practices

Jake's mastitis prevention practices prior to using Imrestor include J5 mastitis vaccine, dry cow tubes, and an internal teat sealant.

With the robotic milking system, the cows have to go through a sort gate to get milked again, or sorted out if they were milked recently, to get more feed. Additionally, the robots help Jake determine which cows might be infected with clinical mastitis.

"The robots have a quarter level daily mastitis detection report, and it tags cows based on expected yield. So, if they don't meet their expected yield, if their conductivity tests higher than normal, or if blood is detected, it flags them as [having] mastitis."

Cows with clinical mastitis are treated with antibiotics for 5 days with a 72-hour milk discard time.

"…we pull them right away, and a toxic cow would usually get treated with Spectramast® in the quarter along with other supportive therapies prescribed by our veterinarian."

Unfortunately, this process typically results in 8 days worth of lost production, and sick cows can affect farm morale.

Elanco Imrestor® (pegbovigrastim injection)

Talk to Your Veterinarian About Imrestor Today

Imrestor is FDA-approved for the reduction in the incidence of clinical mastitis in the first 30 days of lactation in periparturient dairy cows and periparturient replacement dairy heifers.

Imrestor helps…

RESTORE the function and increase the number of neutrophils when periparturient immune suppression leaves her vulnerable to infection

REDUCE the incidence of clinical mastitis around calving by 28%

PROTECT her potential and the well-being of the entire dairy, as well as minimize the frustration of treating mastitis, with a product that is proven safe and effective for your herd

Imrestor had a positive effect on JTP Farms, and Jake has a new perspective to share with dairy producers who've never used it:

"I feel really good when I go through my pens twice a day and look at my heifers and cows, knowing that I'm helping to protect my herd."

TO HELP PROTECT THE WHOLE HERD WITH IMRESTOR AS PART OF AN ONGOING HERD HEALTH MANAGEMENT PROGRAM, CONTACT YOUR VETERINARIAN OR ELANCO REPRESENTATIVE.

IMPORTANT SAFETY INFORMATION

Available only by veterinary prescription. Do not use Imrestor to treat cows with clinical mastitis because effectiveness has not been demonstrated for this use.

DEDICATED *to the* DEDICATED™

Elanco

Elanco Imrestor® (pegbovigrastim injection)

The Imrestor® Effect

SUCCESS STORIES ON DAIRIES

JTP Farms | Dorchester, WI

Elanco

JTP Farms

After graduating from University of Wisconsin-River Falls with an agricultural education degree and gaining over 10 years of dairy experience off the farm, Jake decided to come home to the family dairy business. In January 2012, JTP Farms was founded in Dorchester, Wisconsin as the next generation of his family's dairy legacy. It was designed from scratch as a state-of-the-art robotic milking dairy.

"We milk with four DeLaval robots with 60-65 cows per pen. Because each robot has its own separate pen of cows to milk, we also utilize the guidance system versus the free cow traffic."

ABOUT JTP FARMS

- Sand-bedded free stalls
- 285 cows
- Pregnancy rate of 30%
- 94 lbs of milk per day
- 2 full-time employees, 4 part-time
- 4 DeLaval robots

Adding Another Innovation with Imrestor® (pegbovigrastim injection)

During a conversation with his nutritionist, Jake became interested in Imrestor. Consequently, Jake consulted with his veterinarian to discuss how to implement Imrestor on his dairy.

Jake expected Imrestor to reduce early lactation clinical mastitis, which helps protect the potential of cows to reach their peak milk production. This could also help Jake save time treating sick cows and improve farm morale.

JTP Farms
Results with Imrestor

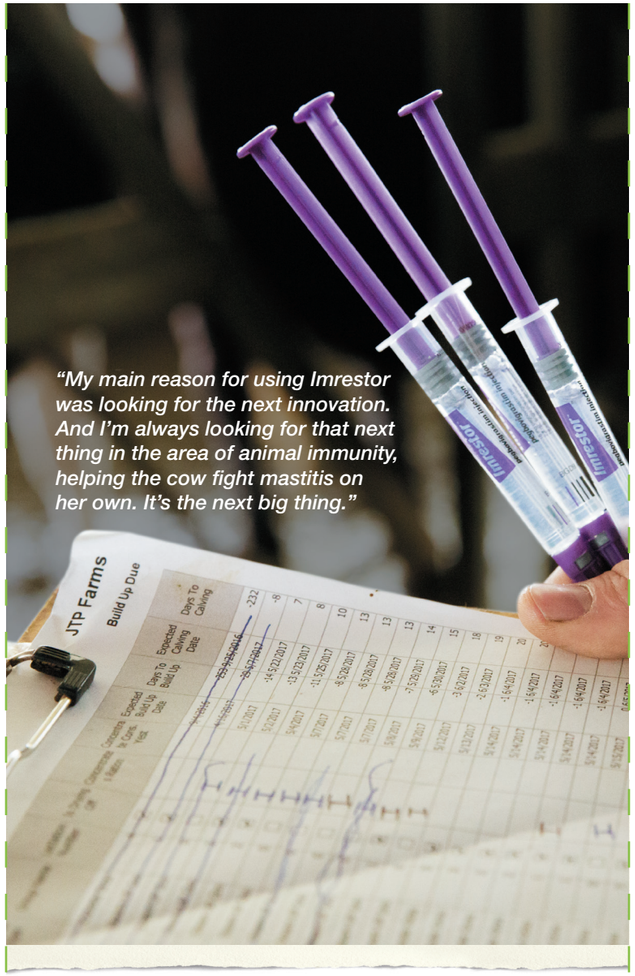
Jake began using Imrestor and noticed the benefits almost immediately.

- Reduction in mastitis
- Easy to administer
- Treating fewer cows
- Reduction in antibiotic use

"We used to buy Spectramast® by the case. Now I just buy it by the box."

IMPORTANT SAFETY INFORMATION

In case of accidental self-injection, wash the site of injection thoroughly with clean running water. Foreign proteins such as pegbovigrastim have the potential to cause anaphylactic-type reactions. No withdrawal period or milk discard time is required when used according to the labeling.



IMPORTANT SAFETY INFORMATION

Some cases of hypersensitivity-type reactions have been observed in studies outside the United States within five minutes to two hours, occurring most often after the first administration of Imrestor. Clinical signs may include elevated respiratory rate, dyspnea, urticaria, sweating, dependent edema, swollen mucous membranes, and/or hypersalivation, and, rarely, death. These reactions resolve within hours of onset with or without therapeutic intervention and have not been shown to reoccur with subsequent injections of Imrestor. Abomasal ulcerations/erosions were observed in the Margin of Safety studies; it was concluded that these findings were not clinically relevant. For complete safety information see product label on adjacent panels.

Elanco™ AH0955

Imrestor™
pegbovigrastim injection

15 mg pegbovigrastim per 2.7 mL single dose syringe
For subcutaneous injection in periparturient dairy cows and periparturient replacement dairy heifers.

CAUTION: Federal (USA) law restricts this drug to use by or on the order of a licensed veterinarian.

DESCRIPTION: Imrestor is a sterile injectable formulation of pegbovigrastim (an immunomodulator, bovine granulocyte stimulating factor) in single-dose syringes. Each syringe of Imrestor contains pegbovigrastim (15 mg), L-arginine hydrochloride (94 mg), L-arginine (40 mg), and citric acid monohydrate (17 mg).

INDICATIONS FOR USE: For the reduction in the incidence of clinical mastitis in the first 30 days of lactation in periparturient dairy cows and periparturient replacement dairy heifers.

DOSAGE AND ADMINISTRATION: This is a two-dose regimen. The same dose is used regardless of cow/heifer body weight. Remove surface dirt from the injection site area before injecting. Inject the entire contents of the syringe subcutaneously. Do not reuse the syringe.

Administer the first dose (syringe) 7 days prior to the cow's or heifer's anticipated calving date. If necessary, the first dose may be administered within a range of 4 to 10 days prior to the anticipated calving date to accommodate management schedules. Administer the second dose (syringe) within 24 hours after calving.

Animals that calve either less than or more than7 days after the first dose should receive the second dose within 24 hours after calving.

Prior to administration, Imrestor should be visually inspected for particulate matter and discoloration. Imrestor is a clear, colorless solution and may contain a few small, translucent or white particles. Imrestor should not be used if it is discolored or cloudy, or if other particulate matter is present. Do not shake or tap the syringe prior to use.

WARNINGS:

RESIDUE WARNING: No withdrawal period or milk discard time is required when used according to the labeling.

HUMAN WARNINGS: Not for use in humans. Keep out of reach of children.

USER SAFETY WARNINGS: In case of accidental self-injection, wash the site of injection thoroughly with clean running water. Foreign proteins such as pegbovigrastim have the potential to cause anaphylactic-type reactions. If you experience swelling or redness at the site of exposure, or more severe reactions such as shortness of breath, seek medical attention immediately and take the package insert with you. Report the event to Elanco Animal Health at 1-800-428-4441. To obtain a Safety Data Sheet, contact Elanco Animal Health at 1-800-428-4441.

PRECAUTIONS: Do not use Imrestor to treat cows with clinical mastitis because effectiveness has not been demonstrated for this use.

ADVERSE REACTIONS: Some cases of hypersensitivity-type reactions have been observed in studies outside the United States within five minutes to two hours, occurring most often after the first administration of Imrestor. Clinical signs may include elevated respiratory rate, dyspnea, urticaria, sweating, dependent edema, swollen mucous membranes, and/or hypersalivation, and, rarely death. These reactions resolve within hours of onset with or without therapeutic intervention and have not been shown to reoccur with subsequent injections of Imrestor. Abomasal ulcerations/erosions were observed in the Margin of Safety studies. (See Target Animal Safety section).

To report a suspected adverse drug event, contact Elanco Animal Health at 1-800-428-4441.

For additional information about adverse drug experience reporting for animal drugs, contact FDA at 1-888-FDA-VETS or http://www.fda.gov/AnimalVeterinary/SafetyHealth.

CLINICAL PHARMACOLOGY: Endogenous granulocyte colony stimulating factor is a protein (cytokine) which induces increased production of mature neutrophils from bone marrow stem cells and activation of the functional capabilities of mature circulating neutrophils. Pegbovigrastim is a modified form of bovine granulocyte colony stimulating factor conjugated to polyethylene glycol (PEG). This PEGylation technology enables sustained biological activity of the protein. In one study, cows treated with 20 µg/kg pegbovigrastim displayed statistically significant increased absolute neutrophil counts relative to the untreated control group beginning 5 hours post-dosing. Absolute neutrophil counts peaked 36 hours post-dosing and remained elevated up to 12 days post-dosing.

EFFECTIVENESS: The effectiveness of Imrestor for the reduction in the incidence of clinical mastitis was demonstrated in a multi-site natural infection field study conducted at four sites in the U.S. and one site in France. A total of 801 healthy periparturient commercial dairy heifers and cows were enrolled and treated with Imrestor or saline by subcutaneous injection in the neck when they were identified as being approximately 7 days before their anticipated calving date (Day -7), and again within 24 hoursafter calving (Day 0). Each quarter of each enrolled animal was evaluated at each milking from Days 3 to 30 to monitor the development of clinical mastitis. Animals developing clinical mastitis (using quarter health, milk quality, and California Mastitis Test [CMT] evaluations) through Day 30 were classified as treatment failures. Administration of Imrestor resulted in a statistically significant difference ($p = 0.025$) in the incidence of clinical mastitis (treatment failure rate) across all five sites with a difference in favor of the Imrestor-treated group (failure rate: 60/331 = 18.13%) compared to the saline-treated group (failure rate: 85/338 = 25.15%).

TARGET ANIMAL SAFETY:

Margin of Safety: In the first study, forty primiparous and multiparous Jersey cows were assigned to one of four treatments: saline control, 1X, 2X, or 3X the intended dose of Imrestor administered at Days -7 and -3 prior to anticipated calving date and within 24 hours after calving. Cows and heifers were monitored daily until 4 days postpartum. Calves were monitored daily for 14 days after birth. Measurements on cows included bodyweights, feed consumption, milk production, somatic cell counts, physical examinations, and clinical pathology. A complete postmortem examination was conducted on each adult animal. Measurements in calves included physical examinations, bodyweights, and hematology. There were no test article related findings associated with abnormal clinical observations, feed consumption, milk production, physical examinations, or urinalysis in adult animals. A mature neutrophilia was seen in all treated animals, regardless of dose group. This was considered a test article related change and consistent with the mechanism of action of Imrestor. No test article related hematology changes were observed in the calves. Observations of mastitis, metritis, and abomasal ulcers were documented, with more animals in the treated groups affected compared to the controls. Two animals (one each from 1X and 3X groups) had perforated abomasal ulcers found at necropsy.

A second study evaluated the margin of safety of pegbovigrastim in multiparous Holstein dairy cows. Forty-five multiparous Holstein dairy cows were assigned to one of five treatments: saline control, 1X, 2X, 2.5X, or 3X the recommended dose of one syringe of pegbovigrastim administered subcutaneously on Day -7 relative to the anticipated calving date and within 24 hours after calving. Cows were monitored daily until 14 days postpartum. Measurements included bodyweights, feed consumption, milk production, somatic cell counts, physical examinations, and clinical pathology, including reticulocyte counts and fecal occult blood.

A postmortem examination that focused on the gastrointestinal tract, uterus, and mammary tissue was conducted on each cow. Calves were not evaluated in this study. There were no test article related findings associated with abnormal clinical observations, feed consumption, milk production, or physical examinations.

A mature neutrophilia was observed in all treated animals which was consistent with the Imrestor mechanism of action and was similar to what was observed in the first margin of safety study. Treated animals had a greater number of mild gastrointestinal erosions and small areas of reddened or thinned mucosa along various portions of the gastrointestinal tract as compared to the control animals. No abomasal ulcers were seen on necropsy.

It was concluded from these studies that abomasal ulcerations/erosions could be test article related. However, given the lack of clinical signs associated with such gastrointestinal pathology in conjunction with the mild nature of the erosions in the second study, it was concluded that these findings were not clinically relevant.

Injection Site Safety: Injection site safety was evaluated following the injection of Imrestor into healthy periparturient dairy cows. Results of the injection site toleration study showed that subcutaneous injections of pegbovigrastim administered 14 days prior to slaughter in 6 cows had no gross lesions and would require no carcass trim at slaughter. Additionally, subcutaneous injections of pegbovigrastim administered approximately 12 hours prior to slaughter in 6 cows caused minimal acute local tissue reactions generally characterized by focal hemorrhage and edema and would be removed along with the hide at the time of slaughter and would not result in any carcass trim.

Reproductive Safety: Animals in the effectiveness study were also evaluated for reproductive safety. This study included 801 animals: 401 control animals and 400 treated animals. Variables measured included daily health observations on cows and calves, mortality, gestation length, percent live births, and first service conception rates following treatment. There were no statistically significant differences between treated and control animals for these reproductive variables.

STORAGE INFORMATION: Store under refrigeration (2° to 8°C; 36° to 46°F). DO NOT FREEZE. Avoid prolonged exposure to sunlight. Excursions of up to 24 hours at room temperature (15° to 30°C; 59° to 86°F) are allowed after receipt.

DISPOSAL: Dispose of used syringes in a leak-resistant, puncture-resistant container in accordance with applicable Federal, state and local regulations.

HOW SUPPLIED: 10, 50 or 100 single-dose syringe packages with each syringe containing 15 mg of pegbovigrastim.

NADA 141-392. Approved by FDA.

Manufactured for Elanco Animal Health, a Division of Eli Lilly and Company, Indianapolis, IN 46285.

For technical assistance or to report suspected adverse drug events, contact Elanco Animal Health at 1-800-428-4441.

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