

~Dairy Details~

Produced by Northern Valley Dairy Production Medicine Center

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New Product Introduction: Imrestor™

By now most of you have probably heard of Imrestor, Elanco's new product. This exciting new product is labeled for reduction of clinical mastitis in the first 30 days of lactation. The actual name of the ingredient is pegbovigrastim, and it belongs to a class of compounds called cytokines. Cytokines are substances, typically proteins, secreted by cells of the immune system that have effects on other cells.

Pegbovigrastim is a synthetic version that has been modified to have extended activity in the animal. Pegbovigrastim acts on specific white blood cells called neutrophils. That is a mouthful; let us back up and look at just what neutrophils are.



Neutrophils are produced by cells in bone marrow, and are dumped into the blood stream. They circulate through the arteries, veins and smaller blood vessels in the body. Neutrophils roll along the walls of smaller arterioles, and respond to signals from other immune cells. Those signals inform the neutrophils of potential pathogenic invaders in body tissues, outside of the blood vessels. Neutrophils respond by slowing down, penetrating the wall of the blood vessels to enter the surrounding tissues and then engulfing the invading bacteria. After engulfing, which is technically called phagocytosis, the neutrophils secrete compounds such as hydrogen peroxide and bleach to kill the engulfed bacteria. The neutrophil then undergoes apoptosis, which is a version of cell death where the neutrophil begins to break apart but is then ingested by another immune cell, called a macrophage. Thus, in a normally functioning immune system, the neutrophil needs to do at least three things well. First, it needs to get to the site of infection quickly. If this does not happen quickly enough, disease can occur. This is what often happens in severe coliform mastitis; neutrophils may be slow to respond and enter the tissues of the mammary several hours later than needed. Second, it needs to phagocytose and kill the bacterium. In some cases of immune suppression, neutrophils have reduced ability to accomplish this. In fact, it has been known for several decades that stress in lactating dairy cows can reduce neutrophil phagocytosis in milk. Third, neutrophils need to undergo apoptosis. If neutrophils die too quickly various substances can be released into the surrounding tissue, which can damage the tissue and cause significant inflammation. This may be one of the mechanisms for mammary tissue damage in severe coliform mastitis, for example.

Around calving, normal cows undergo suppression of the immune system. This suppression is due to effects of estrogen, progesterone, endorphins, cortisol, negative energy and protein balance, and specific genetic susceptibility of the cow. Regarding neutrophils, two things happen. First, levels of circulating neutrophils drop. Second, neutrophils become less effective at destroying bacteria. They are less effective because they lose their ability to roll along the walls of the blood vessels, and thus take longer to arrive at the site of infection, and because they lose some of their ability to phagocytose and kill bacteria. In short, there are fewer neutrophils and those that are available are less effective. Pegbovigrastim stimulates the bone marrow

cells to produce more neutrophils and helps restore the function of neutrophils. These extra neutrophils are sort of a reserve that is available if needed. The net result is a faster response time and more effective killing. Pegbovigrastim is not likely to enhance immunity in non-suppressed cows because those cows already have enough neutrophils, and enlarging the reserve will not necessarily improve immunity. Also, normal cows have normal neutrophil function, and pegbovigrastim will not necessarily improve neutrophil function beyond what is normal.

Around calving cows are particularly susceptible to mastitis and metritis. Immune suppression may mean that more cows develop infection, that subclinical disease becomes clinical disease, or clinical disease becomes more severe. Imrestor is only approved for reduction of clinical mastitis, and Elanco does not have data to present regarding reduction of new subclinical infections. Nor do they have any data regarding reduction of metritis incidence or severity. In New Zealand, however, the product is approved for restoration of immune function, and is not linked to any particular disease.

Imrestor is not a hormone; nor is it an antibiotic, so there are no milk or slaughter withholding requirements. It has been shown to be viewed favorably by consumers of dairy product in exploratory testing. The product is labeled to be administered seven to ten days prior to expected calving, and then again within 24 hours of calving. Imrestor will come in single dose syringes, with needles attached, and Elanco will provide a sharps disposal service as they do with Posilac.

The human form of this product is typically given to patients experiencing profound immune suppression following chemotherapy. It has been available as a short acting product for about 25 years and as a long acting product for about 15 years, so the compound itself and the use for restoration of immune function is not new, and is well proven. Its use in cattle has been studied by USDA researchers since at least 1981, but Imrestor is the first approved product for use in food animals. Imrestor is an exciting new product that may prove to be very useful in preventing periparturient disease in dairy cattle. We expect it to be available before July 2016. Call us for more information.

Save the Date for 2016 June Dairy Days!

This year's June Dairy Days will be held at our clinic on Wednesday, June 8 from 11:00 AM – 1:30 PM. Everyone is welcome to join us for lunch, door prizes, and socializing! Hope to see you there



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