CYTOPOINT

Media Backgrounder

CYTOPOINT™, Canine Atopic Dermatitis and Monoclonal Antibodies

About canine atopic dermatitis

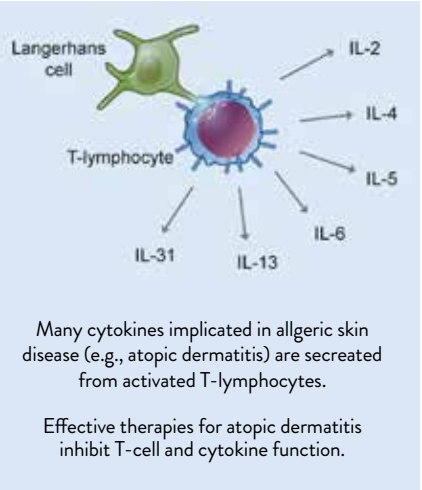
Canine atopic dermatitis is a genetically predisposed inflammatory and itchy (pruritic) allergic skin disease associated with exposure (or hypersensitivity or excessive reactivity) to environmental allergens such as pollen, mites and mold spores.[1] One of every six dogs is treated by a veterinarian for itch, and 15 to 20 percent of those dogs are diagnosed with atopic dermatitis.[2]

Zoetis now offers two targeted treatment options for canine patients with atopic dermatitis: CYTOPOINT™ and APOQUEL® (oclacitinib tablet). Other treatment options include steroids and cyclosporine.

The role of cytokines in atopic dermatitis

Research over the past decade has produced breakthroughs in understanding the pathophysiology of allergic skin disease—in particular, atopic dermatitis. Scientists now know that cytokines (small protein messengers that have an effect on communications or interactions between cells), such as interleukins, play an important role in orchestrating the cycle of itch and inflammation (see Figure 1).[3] Zoetis has focused its research on the pruritogenic cytokine interleukin (IL)-31.

Figure 1: Cytokines involved in canine atopic dermatitis.



Many cytokines implicated in allgeric skin disease (e.g., atopic dermatitis) are secreated from activated T-lymphocytes.

Effective therapies for atopic dermatitis inhibit T-cell and cytokine function.

A key function of IL-31 is to stimulate the neuronal itch pathway by activating peripheral sensory nerves. IL-31 can be identified in the serum of dogs with atopic dermatitis, but not in healthy dogs; additionally, when IL-31 is injected into laboratory dogs, pruritic behaviors are induced.[4] Through this research, Zoetis discovered and developed an anti-canine IL-31 monoclonal antibody (mAb). Now branded as CYTOPOINT, it specifically targets and neutralizes only cytokine IL-31 to help provide fast, effective and long-lasting relief of clinical signs associated with atopic dermatitis in dogs of any age.

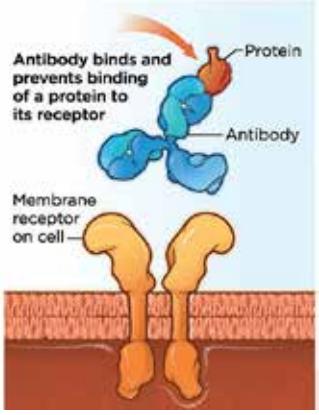
Monoclonal antibodies: A new frontier for veterinary medicine

All mammals produce antibodies to protect against foreign proteins or antigens introduced into the body. Used in human medicine for many years, mAbs are produced in a laboratory from a single cell line and, when administered to patients, target and neutralize specific antigens (see Figure 2).

Some biologic products, such as vaccines, provoke active immune responses to help provide protection from disease, whereas mAbs are passive and are not designed to stimulate the immune system. mAbs have three main advantages:

1. mAbs have high target specificity—they have no effect on any molecule or cell other than their target.
2. mAbs do not have intracellular activity—as a result, there are few anticipated side effects and reactions.
3. mAbs are not metabolized by the kidney or liver, but are catabolized (degraded) within the cells, resulting in amino acids that are recycled within the body. This is the same process by which natural antibodies are catabolized in the body.

Figure 2: How antibodies work.



CYTOPOINT specifically targets and neutralizes IL-31 before it can bind to its receptor on a nerve cell.

About CYTOPOINT

The U.S. Department of Agriculture (USDA) has granted Zoetis a full license for CYTOPOINT, the first mAb therapy to be licensed for the treatment of canine atopic dermatitis. This novel mAb therapy was designed specifically to target canine IL-31. Administered by a veterinarian, CYTOPOINT begins working within one day and delivers four to eight weeks of relief. This allows damaged skin a chance to heal and helps improve the long-term quality of life for atopic dogs and their owners.

More treatment options for veterinarians

With the licensing of CYTOPOINT, veterinarians now have two innovative therapeutic options to customize treatment for dogs with atopic dermatitis. CYTOPOINT is designed to provide long-lasting relief with a single subcutaneous injection for dogs diagnosed with atopic dermatitis. APOQUEL is the first Janus kinase inhibitor approved by the U.S. Food and Drug Administration for veterinary use to provide fast and safe itch relief for dogs at least 12 months of age that have symptoms associated with allergic dermatitis triggered by food, fleas or contact allergens, as well as control of atopic dermatitis.

More information is available at www.cytopoint.com.

IMPORTANT SAFETY INFORMATION:

Do not use APOQUEL in dogs less than 12 months of age or those with serious infections. APOQUEL may increase the chances of developing serious infections, and may cause existing parasitic skin infestations or pre-existing cancers to get worse. APOQUEL has not been tested in dogs receiving some medications including some commonly used to treat skin conditions such as corticosteroids and cyclosporines. Do not use in breeding, pregnant, or lactating dogs. Most common side effects are vomiting and diarrhea. APOQUEL has been used safely with many common medications including parasiticides, antibiotics and vaccines.
See full Prescribing Information.

[1] Halliwell R. Revised nomenclature for veterinary allergy. *Vet Immunol Immunopathol.* 2006;114(3-4):207-208.

[2] Data on file, IL-31 Positioning Research. IPSOS 2014. IL-31 Pricing Research. SKP. 2015, Zoetis LLC.

[3] Marsella R, Sousa CA, Gonzales AJ, Fadok VA. Current understanding of pathophysiologic mechanisms of canine atopic dermatitis. *J Am Vet Med Assoc*. 2012;241(2):194-207.

[4] Gonzales AJ, Fleck TJ, Humphrey WR, et. al. IL-31-induced pruritus in dogs: a novel experimental model to evaluate anti-pruritic effects of canine therapeutics. *Vet Dermatol*. 2016;27(1):34-e10.

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