

Cytopoint™ (formerly known as Canine Atopic Dermatitis Immunotherapeutic or CAD11) is the brand name of lokivetmab, a monoclonal anti-canine IL-31 antibody produced by Zoetis that reduces pruritus in atopic dogs¹. In a placebo-controlled trial of 211 client-owned dogs, owners reported a reduction in pruritus in as little as 1 day after Cytopoint™ was administered². Veterinarian assessment of treated and placebo-control groups (using CADESI-03 scoring³) showed that lesional skin began healing within 7 days after a single dose of lokivetmab². Treatment success at day 28 (judged by a 50% reduction of CADESI-03 score) was reported in 46% of dogs given a single dose of Cytopoint™ at 2 mg/kg on day 0, compared with 9% for placebo².

IL-31 is one of a dozen or more cytokines known to induce itch in dogs⁴. Produced by activated T_H2 cells, IL-31 has been shown to induce pruritus in humans, mice and dogs 5-7. Circulating IL-31 is found in just over half (57%) of dogs with naturally-occurring atopic dermatitis⁸. IL-31 receptors are found on a wide variety of cell types and are abundant in dorsal ganglion root neurons, enabling IL-31 to directly link T cell-mediated allergenic signals to sensory nerves responsible for the sensation of itch^{7,9}.

Cytopoint™ is a therapeutic monoclonal antibody (mAb), acting to neutralize canine IL-31 in the same way as naturally occurring antibodies would do; it is a biotherapeutic agent, not a drug¹⁰. Monoclonal antibodies (mAbs) are secreted by hybridomas, made in vitro by fusing immortalized tumor (mouse myeloma) cells and antigen-primed mouse B lymphocytes¹¹. Each cloned hybridoma cell line secretes one unique murine antibody, recognizing a single, specific amino acid sequence (epitope) on the target protein. Mouse antibodies are large proteins that would be rapidly cleared by protective immune responses in a foreign host such as the dog, reducing therapeutic efficacy. To solve this problem, recombinant DNA techniques were utilized to genetically engineer or “caninize” Cytopoint™, replacing mouse antibody protein sequences with canine sequences. Genetically engineered Cytopoint™ is 90% canine immunoglobulin, thereby rendering it stable when injected into dogs¹⁰. Therapeutic mAbs have relatively low clearance rates from the body, with half-lives of up to 4 weeks¹², during which time they are metabolized into small peptides and amino acids, which are then naturally excreted. Cytopoint™ has a biological half-life of 16 days².

Unlike Apoquel®, which indirectly blocks IL-31 by selectively targeting co-activator JAK1/3 cytokine signaling¹³, Cytopoint™ directly binds to circulating canine IL-31, blocking it from binding to its receptor at the cell surface¹⁴. Without receptor binding, the brain does not receive neuroimmune itch signals from peripheral sensory nerve cells in the skin, and IL-31 induced pruritus does not occur^{7,9}.

Cytopoint™ was approved for use in dogs only by the U.S. Department of Agriculture (USDA) in January 2017. It is recommended for use only in dogs with a clinical diagnosis of atopic dermatitis. Zoetis reports that it is safe for dogs of any age, and is not contraindicated in dogs with concomitant diseases¹⁵. Cytopoint™ has not been evaluated in pregnant, breeding or lactating dogs¹.

Cytopoint™ is administered by subcutaneous injection, and is packaged in single-use 1.0 mL vials, available in four concentrations (dosage sizes): 10, 20, 30 and 40 mg/mL. Recommended dosage is 2 mg/kg, given at 4 to 8 week intervals as needed¹⁶. It is reported to be well tolerated, with no serious adverse effects associated with use of the product. In a field study of 245 dogs conducted by Zoetis, immediate reactions of discomfort at administration were equally distributed between dogs receiving either placebo or lokivetmab¹.

Cytopoint™ is a biotherapeutic antibody for managing pruritus in atopic dogs. Like its predecessor Apoquel®, Cytopoint™ acts upon canine IL-31 to prevent neuroimmune itch signals from entering the brain. While currently available data suggest that lokivetmab is a useful tool for short term management of acute flare ups, this product is very new to veterinary practice. Use of this biologic for extended periods to treat chronic atopic dermatitis in dogs should be accompanied by an awareness of the numerous ways that IL-31 affects atopy and innate immune responses. IL-31 affects regulation of the physical skin barrier in multiple ways that are incompletely understood¹⁷. It also stimulates the expression of anti-microbial peptides, which support innate immune responses in preventing bacterial growth on the skin¹⁷. Firmer consensus on overall effectiveness of Cytopoint™ awaits further pharmacovigilance studies.

Allergen-specific immunotherapy remains the safest and most well-characterized option for the core treatment of atopy¹⁸. It is the only allergy treatment that improves symptoms by altering IgE-mediated immune responses to allergens, rather than immunosuppressing the immune system or blunting clinical symptoms¹⁹. Cytopoint™ is an excellent adjunctive treatment method for managing pruritus in the initial stages of immunotherapy, during the 6-9 months before therapeutic immune system changes result in significant improvement in an affected dog's symptoms.

References

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