



Dawn M. Cleaver, DVM
Associate Director, Regulatory Affairs
Zoetis, Inc.
333 Portage Street
Kalamazoo, MI 49007

RE: NADA 141-345
APOQUEL® (oclacitinib tablet)

Dear Dr. Cleaver,

The U.S. Food and Drug Administration (FDA), Center for Veterinary Medicine (CVM), Division of Surveillance has reviewed the website for APOQUEL (oclacitinib tablet),

<https://www.zoetisus.com/products/dogs/apoquel/index.aspx>.

This website makes false or misleading representations about the risks associated with APOQUEL. The website therefore misbrands APOQUEL within the meaning of the Federal Food, Drug, and Cosmetic Act (FD&C Act), and makes its distribution violative. 21 U.S.C. 352(a), (n); 321(n); 331(a).

Background

Below are the indication and summary of the most serious and most common risks associated with the use of APOQUEL.

According to the FDA-approved package insert (PI), APOQUEL is indicated for the control of pruritus associated with allergic dermatitis and control of atopic dermatitis in dogs at least 12 months of age.

The PI contains warnings and precautions including the following: (1) should not be used in dogs with serious infections; (2) may increase susceptibility to infection, including demodicosis, and exacerbate neoplastic conditions; (3) is not for use in breeding dogs, or pregnant or lactating bitches; (4) has not been evaluated in combination with glucocorticoids, cyclosporine, or other systemic immunosuppressive agents; and (5) dogs receiving APOQUEL should be monitored for the development of infections, including demodicosis, and neoplasia.

U.S. Food and Drug Administration
Center for Veterinary Medicine
7500 Standish Place
Rockville, MD 20855
www.fda.gov

False or Misleading Risk Presentation

Promotional materials misbrand a drug if they are false or misleading with respect to risk or benefits. The determination of whether promotional materials are misleading includes, among other things, not only representations made or suggested in promotional materials, but also failure to reveal facts material in light of the representations made or with respect to consequences that may result from the use of the drug as recommended or suggested in the materials.

The opening page on the APOQUEL website contains the following statements, with a link on the word “Safe:”

Safe:

- Without many of the side effects associated with steroids
- Can be used with many other drugs, including anti-infectives, parasiticides, antifungals, NSAIDs and allergen-specific immunotherapy

When clicking on “Safe”, another page opens that contains additional positive information regarding safety:

- Minimal side effects - Side effects of APOQUEL were similar to placebo without many of the side effects associated with the use of steroids
- Can be used concomitantly with many other medications - APOQUEL can be used with many common therapies including vaccines, NSAIDs, antibiotics and allergen-specific immunotherapy

These claims misleadingly suggest that APOQUEL is safer than steroids without providing comparative studies to support the claim. Moreover, they misleadingly minimize the risk associated with the use of APOQUEL by citing a short term study to support the claim that the side effects are minimal and were similar to placebo when a higher frequency of adverse reactions in Apoquel treated dogs was seen in a longer-term study.

The website cites a short-term study¹ (Cosgrove, 2013) to substantiate claims that the product is “safe,” and that the “side effects were similar to placebo without many of the side effects associated with the use of steroids.” The website also cites a long-term study² (Cosgrove, 2015) to substantiate claims that the product is “safe for long-term use” and that APOQUEL “can be used concomitantly with many other medications.” The Cosgrove 2015 reference contains the following statement regarding risks identified in this study: “The abnormal clinical signs reported most frequently (in ≥5% of the dogs) as a non-pre-existing finding were as follows: urinary tract infection/cystitis (11.3%),

1 Cosgrove SB, Wren JA, Cleaver DM, et al. Efficacy and safety of oclacitinib for the control of pruritus and associated skin lesions in dogs with canine allergic dermatitis. *Vet Dermatol.* 2013;24(5):479-e114. doi:10.1111/vde.12047.

2 Cosgrove SB, Cleaver DM, King VL, et al. Long-term compassionate use of oclacitinib in dogs with atopic and allergic skin disease: safety, efficacy and quality of life. *Vet Dermatol.* 2015;26(3):171-179. doi:10.1111/vde.12194.

vomiting (10.1%), otitis (9.3%), pyoderma (9.3%) and diarrhea (6.1%).” These findings contradict the reported findings of the Cosgrove 2013 study that the side effects of APOQUEL are similar to placebo. In addition, several of these findings are consistent with the Warnings statement “APOQUEL may increase susceptibility to infection...” contained in the FDA-approved product labeling.

In addition, these claims misleadingly suggest that APOQUEL can be safely used concomitantly with other products, but omit the following important information found on the approved labeling: “The use of APOQUEL has not been evaluated in combination with other systemic immunosuppressive agents.”

We acknowledge that the opening page on the APOQUEL website includes the following safety information:

- **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 cyclosporine. 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.

However, the website’s representation of APOQUEL as having “minimal side effects,” as being “similar to placebo without many of the side effects associated with the use of steroids,” and as “safe for use with many other drugs, including...allergen-specific immunotherapy” contradicts the important safety information and the risks associated with the use of APOQUEL.

Conclusion and Requested Action

For the reasons discussed above, the website misbrands APOQUEL within the meaning of the FD&C Act, and make its distribution violative. 21 U.S.C. 352(a), (n); 321(n); 331(a).

CVM requests that Zoetis, Inc. immediately cease the dissemination of the APOQUEL promotional items described above and any other materials that fail to accurately represent the risks associated with the use of APOQUEL.

Please submit a written response within thirty calendar days of receipt of this letter describing whether you intend to comply with this request, listing all promotional materials (with the Form FDA 2301 submission date) for APOQUEL that contain presentations such as those described above, and explaining your plan for discontinuing use of such materials, or, in the alternative, for ceasing distribution of

APOQUEL. Please direct your response to Dr. Neal Bataller at the Food and Drug Administration, Center for Veterinary Medicine, Division of Surveillance, HFV-210, 7519 Standish Place, Rockville, Maryland 20855.

The violations discussed in this letter do not necessarily constitute an exhaustive list. It is your responsibility to ensure that the promotional materials for APOQUEL, as well as other Zoetis, Inc. products, comply with the requirements of the FD&C Act and applicable FDA regulations.

If you have any questions, please contact Dr. Dorothy McAdams at the address above, or by phone at (240) 402-5763.

Sincerely,

Neal Bataller, ME, DVM
Director, Division of Surveillance
Office of Surveillance and Compliance
Center for Veterinary Medicine