DEAR EDITOR:

We read with interest the peer-reviewed article on oclacitinib (December 2015 issue, page 30). It provides a nice summary of several aspects of oclacitinib that are important for clinicians to know. However, some of the information in the Contraindications section may be inaccurate and misleading. The first sentence reads “As an immunomodulatory agent, oclacitinib is contraindicated in dogs with a history of neoplasia, generalized demodicosis, and concurrent serious infection.” In our view:

It is not clear that the statement that “oclacitinib is contraindicated in dogs with a history of neoplasia or demodicosis” is the authors’ opinion. The Food and Drug Administration (FDA)-approved prescribing information states that oclacitinib may increase susceptibility to demodicosis and may exacerbate neoplastic conditions, and that patients treated with oclacitinib should be monitored for development of demodicosis or neoplasia.¹ The FDA did not mandate that current demodicosis or a history of demodicosis or neoplasia should be considered as contraindications for oclacitinib administration.

There are no contraindications of use on the Apoquel (Zoetis, apoquel.com) label. We accept that the authors are entitled to their personal opinions, but it should be clear to readers that this statement reflects an opinion. We recognize that the use of Apoquel in dogs with serious infections is a part of the warning on the label and that part of the statement is correct.

The 2 references for this statement do not support the information, and neither reference discusses demodicosis in dogs treated with oclacitinib.

It is also stated that “Oclacitinib is not labeled to be used in dogs younger than 1 year of age, as a few dogs in this age range developed adverse events (eg, pneumonia, demodicosis) in original field studies.”

Although it is correct that Apoquel is indicated for use in dogs 12 months of age or older, the only published data indicating development of demodicosis in dogs <1 year of age is a margin of safety study involving laboratory animals. This is quite different and distinct from field studies. The statement is not technically correct, as the label contains no contraindications.

Specifically, the margin of safety study was in 6-month-old laboratory dogs, some of which developed demodicosis after 4 months of high doses (3× and 5× the label dose administered twice a day) of oclacitinib, leading to discontinuation of the study. This did not occur in a similar margin of safety study in 12-month-old laboratory dogs. As a consequence, a margin of safety was established in 12-month-old dogs but not in juvenile dogs, and thus the label indicates that oclacitinib should only be administered in dogs at least 12 months of age. This information can be found on the Apoquel product label, which is referenced for this statement. In another laboratory study cited on the label, eight 16-week-old vaccine-naïve puppies administered oclacitinib maleate at 1.8 mg/kg oclacitinib (3× the maximum exposure dose) twice a day for 84 days showed no demodicosis.

We hope that future manuscripts concerning this product are correctly referenced, with clear indications whether data and statements are derived from published manuscripts or official documents (eg, product inserts) or from the opinion of the author(s). Clinician’s Brief is a popular vehicle for practicing clinicians to
receive clinically-relevant information, and we would like to think that the information conveyed is always accurate. Of additional concern is that potentially misleading statements, once published in peer-reviewed articles such as this, act as a reference for later articles concerning oclacinib, thus possibly perpetuating opinions as fact.
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— Andy Hillier, BVSc, MANZCVS (Canine Medicine), DACVD, Senior Veterinary Dermatologist, Zoetis
— Michele Rosenbaum, VMD, DACVD, Senior Veterinary Dermatologist, Zoetis
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AUTHORS RESPOND:

We appreciate the comments, which add very useful information to our article. We agree that the recommendation to avoid oclacinib in dogs with a history of generalized demodicosis represents only our opinion and is not expressly stated on the product label. We apologize if this created any confusion.

Our responsibility as veterinarians is to minimize the risk for adverse effects of any prescribed treatment. This principle becomes particularly relevant when prescribing long-term use of new medications with a short history of pharmacovigilance. In the specific case of oclacinib, we thought it best to be restrictive when prescribing the drug to patients with a history of generalized demodicosis based on the following evidence:

- Immunological data from research on immunosuppressed mice developing demodicosis, which suggests that IL-4 and IL-13 pathways are of key importance in the control of cutaneous Demodex spp populations. These 2 cytokines work through the signaling pathway of Janus kinase 1, an enzyme that is inhibited by oclacinib.  
  
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- Data from the safety studies referenced on the label and mentioned in the above letter indicating that some 6-month-old dogs developed demodicosis after 4 months of high doses (3x and 5x the label dose administered twice a day).
- Personal observation of 2 cases in which dogs with a history of generalized demodicosis developed demodicosis when being treated with oclacinib.

After reading the letter of our colleagues, who have an intimate knowledge of the drug, it may be possible that we have been over-restrictive when prescribing oclacinib to some patients with a history of demodicosis. However, we did this with the sole aim of avoiding any risk to our patients.
— Lluís Ferrer, DVM, DECVD, PhD
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References