Apoquel Update - Use in Practice

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Apoquel is the brand name of oclacitinib, an FDA approved immune suppressant drug in the Janus Kinase (JAK) inhibitor class made by Zoetis. This drug inhibits primarily JAK-1 and -3 signaling that would normally occur when a cytokine binds to a receptor on the surface of the cell. This includes blocking the effects of inflammatory cytokines released from activated lymphocytes (IL-2, -4, -6, -13) as well as IL-31, a cytokine directly involved in the sensation of itch. JAK signaling is important to the function of the bone marrow as well. Apoquel works differently than steroids, antihistamines, or cyclosporine.

Apoquel works rapidly, usually within 24 hours, to diminish itching. It is very rare to have GI upsets with Apoquel like we can see with cyclosporine. The effects of the Apoquel wear off quickly, within 12-24 hours, so the medication needs to be given daily in most cases.

Other drugs in the same drug class as Apoquel include drugs for humans for rheumatoid arthritis, psoriasis, and cancer. In humans, the side effects of drugs in the JAK inhibitor class of drugs include: neutropenia, anemia, thrombocytopenia, increased liver values, increased cholesterol, UTI, weight gain, herpes zoster.

Apoquel side effects listed for dogs in the product insert include: vomiting, diarrhea, lethargy, anorexia, SQ or dermal masses (unspecified), decreased leukocytes, decreased globulins, and increased cholesterol and lipase. Low numbers of dogs in the studies developed demodicosis, neoplasia, pneumonia, bloody diarrhea, skin and ear infections, UTIs, and histiocytomas. Interestingly, a few dogs developed polydipsia, increased appetite, and aggression, similar to what may be seen with steroids.

Apoquel is only FDA approved for dogs who are greater than 12 months of age. The reason for this is that below 1 year of age, demodicosis and pneumonia were seen at an unacceptable level when Apoquel was given at 3 x and 5 x the regular dose.

In humans, it is not recommended to give some of these JAK inhibitor drugs with CYP3A4 inhibitors like ketoconazole. Dramatic dose reductions are needed when cyclosporine is given with ketoconazole, and giving ketoconazole at the same time as demodicosis doses of Ivermectin can be very dangerous, causing Ivermectin toxicity at what should normally be a safe dose. I have not seen bad side effects giving almost any drug with Apoquel, including ketoconazole. The only possible interaction I have seen so far is with pets getting more sleepy than normal when Apoquel was given with Benadryl, possibly Temaril P, and these were individual cases.

Long term studies of giving Apoquel with other immune suppressants like steroids and cyclosporine have not been done. My clinical experience would suggest that steroids at anti-inflammatory doses of 0.5mg/kg twice daily and taper is seems to be safe for the short term. If steroids are needed with Apoquel, evaluate how well the Apoquel is actually working for the patient. Apoquel is effective very quickly, so there is no need to transition slowly from steroids to Apoquel. Obviously a short transition may be needed to prevent an Addisonian crisis in a pet who has been on high doses or daily steroids for more than a month.
The dose of Apoquel is 0.4-0.6 mg/kg every 12 hours for up to 14 days, then 0.4-0.6 mg/kg once daily thereafter. Apoquel is not FDA approved to use twice daily longer than 14 days. The original intent was to get it FDA approved in dogs for twice daily dosing long term. Apoquel works much, much better for many dogs when it is given twice daily. From what I know, the reason for this is that unacceptable numbers of dogs developed bone marrow suppression when given Apoquel twice daily for longer than the FDA approved time frame of 14 days. The dose range is very strict, I do not recommend going above the recommended dose or bone marrow suppression becomes more likely.

Apoquel works rapidly, most pets see complete relief within 2 days. We typically give it twice daily for 7 days if the pet is very uncomfortable, then go to once daily. If it has not worked after a week, it is very unlikely to work better with continued use in my opinion. Zoetis reports that 60% of moderate to severe atopic dermatitis cases are controlled long term, likely because severe cases would do better on twice daily dosing. It is rare that Apoquel controls pruritus in dogs whose allergies were so severe that they require daily steroids.

I have data for 229 dogs that I started on Apoquel. Currently, 150 of these dogs are still on the medication. Only 10 of these 150 are on twice daily dosing, if these pets could not be on twice daily dosing, the medication would not have worked for them. Of the 79 dogs that stopped the Apoquel, 35 (about 15% of total) were stopped because the Apoquel did not work, 3 were stopped due to side effects: bone marrow suppression in 2 cases, 1 case due to severe pu/pd. Most of the rest stopped because symptoms subsided with the season, some were lost to follow up.

In the cases still on the Apoquel, side effects are as follows: 5 cases of UTIs, 2 cases of pneumonia, 5 cases of otitis (interestingly in several cases who had not had otitis issues prior, or had not had otitis for a long time prior), 4 cases of bone marrow suppression managed by changing the dose of the Apoquel, 1 case of yawning, 1 case of excessive drinking, 1 case of eating grass, 1 case of severe pancreatitis with vomiting/diarrhea when on Apoquel twice daily. I had one case where a German shepherd police dog developed blastomycosis while on Apoquel, but the owner and other dogs who went to the same location up north did as well, so the Apoquel may not have played a role. The dog has since recovered, but no longer does police work.

One 9yo MN lab died at home- had chronic bloody diarrhea (had before with prednisone and cyclosporine) and severe allergic dermatitis and recurrent infections. Owner had declined multiple workups, no autopsy.

One 14yo Cocker was euthanized 2 months after starting due to probable worsening of heart disease, liver disease, true reason for illness not known for sure, no autopsy.

One 7yo MN Basset was stopped 2 months after starting due to multicentric lymphoma. I do not think the Apoquel caused the lymphoma since the dog’s lymph nodes were prominent prior to starting the Apoquel and his brother died of lymphoma at a very young age (6yrs) as well.

UTIs and ear infections seem at an unusually high rate in my opinion. All UTIs reported were in pets who are still currently on the medication and so we have good follow-up, the rate may be higher because we have less data for those pets who are not following up with us.

6 cases (2.6% of total) had bone marrow suppression significant for me to change dose of the Apoquel (4 cases) or stop it (2 cases). Only one of these cases was on twice daily dosing. Steroids and cyclosporine
do not cause bone marrow suppression even at extreme doses, so this is one downside to Apoquel. In these 6 cases, the bone marrow has recovered after a few weeks of stopping Apoquel. Even in cases where the CBC values do not go below normal, it is common for the values to sink towards the low end, the clinical significance of this is not known.

Our protocol for Apoquel is to check a CBC/mini-panel prior to starting Apoquel, then at 3 months, then once yearly. For dogs on twice daily dosing, I recommend a CBC/mini-panel once monthly for 3 months, then at the 5 month point (2 months later), then every 6 months. The CBC is the most important piece of information for monitoring. It is important to make sure the dog does not have liver disease prior to starting the Apoquel. The only exception to this would be liver elevations caused by steroids.

Similarly to the side effect of weight gain seen in humans on JAK inhibitors, I have seen weight gain in dogs on Apoquel, not to the degree seen with prednisone.

Some dermatologists have used Apoquel in cats (desperate cases) with some success, however this use is not FDA approved, high doses are needed, and more than once daily dosing is needed. This may be a future feline drug, but time will tell.

So far, I have not had Apoquel help with conditions other than allergic dermatitis.

We don’t know long term side effects of Apoquel in dogs, time will tell. The product insert warns that Apoquel may exacerbate neoplastic conditions. There is no good evidence of this as of yet, we will keep monitoring. I would recommend Apoquel over cyclosporine in a dog with previous cancer.

In summary, I like Apoquel. The benefits of Apoquel include: rapid onset of action, low likelihood of GI side effects, rare side effects with long term use, and decent price. The downsides include: current supply issues, increased infections, and bone marrow suppression is possible, does not work for everyone, and we do not have long term data. It is a wonderful option for those dogs who do not tolerate steroids or cyclosporine.

Monitor blood work prior to administering this medication (especially in older animals), at 3 months, and then routinely thereafter until we have more information about long term use in dogs.

Feel free to contact me if you have any questions about Apoquel or dermatology cases.