



The Pet Oncologist

## FAQs – Palladia® in Pets



**What is Palladia®? What are the pros and cons? What cancers can I try it on? How frequent are the visits? What are the side effects? Vets, here are some answers to some ‘Frequently Asked Questions’ about Palladia® in dogs & cats.**

### ***What is Palladia® (toceranib)?***

Tyrosine kinases are cell signalling proteins that are overstimulated in cancer cells. Inhibiting these proteins with tyrosine kinase inhibitors have the potential to decrease cancer cell growth, proliferation and survival by targeting tyrosine kinase cell signalling proteins (such as *c-kit*, vascular endothelial growth factor receptor and platelet-derived growth factor receptor). Palladia® is an example of a tyrosine kinase inhibitor that can work by the above mechanism. It can also suppress angiogenesis (i.e. anti-angiogenesis) and stimulate the immune response against cancer (i.e. immunomodulation). If cancer loses their blood vessel supply, it will eventually starve itself of oxygen and nutrients, and thus die. Although Palladia® is an anti-cancer medication, it is not chemotherapy, which directly results in cancer cell killing.

### ***What are the pros and cons of Palladia®?***

Palladia® is an attractive treatment option for many owners because they can administer the medication orally to their pets at home, three times a week.

However, the cons are that it has the potential to cause a variety of side effects (such as gastrointestinal side effects, hypertension, proteinuria, neutropenia, hepatopathy, shifting lameness, pancreatitis and cardiotoxicity). It is crucial that pet owners alert veterinarian of any side effects (even if mild). It also needs to be administered by pet owners safely at home and can be an expensive option long-term, particularly in heavy dogs. Moreover, once started, it is considered life-long therapy for as long as it keeps pets in remission, and because it does not necessarily always target cancer cell killing, it can sometimes take an average of 6-12 weeks before a response occurs. Therefore, in pets with rapidly diving tumours, sometimes there may not be enough time to see a response to therapy.

It is important to be aware that stable disease is considered a success if the pet has a good quality of life.

Although Palladia® is not chemotherapy, please refer to handout entitled 'Handling Chemotherapy Medications at Home' for important handling and administration instructions, as well as handling of pet's bodily wastes. It is essential to review and be familiar with Palladia® side effects before administration. The Pet Oncologist can provide veterinarians with a Palladia® drug information handout.

### **When can I consider Palladia® in pets?**

Many cancers have the potential to respond to Palladia®. It can be considered in a situation where pets have unfavourable prognostic factors (such as metastasis [i.e. cancer spread]), when surgery or other forms of therapy are not possible, when pets have failed standard of care, or if owners wish to try an oral anti-cancer medication to administer to their pets at home. Sometimes Palladia® is not considered the standard of care, but it can be helpful and as a 'trial and see' approach.

In **dogs**, the main indications are as follows:

- Mast cell tumours (*London et al. Clin Cancer Res 2009, London et al. Clin Cancer Res 2003*)
  - Macroscopic (i.e. metastasis, unresectable, recurrent) (*Carlsten et al JVIM 2012*)
  - *c-kit* mutation positive
  - No longer responsive to traditional chemotherapy
  - High grade (*Olsen et al. Vet Med Sci 2018*)
  - High-risk (*Horta et al. Oncol Lett 2018*)
- Gastrointestinal stromal tumours (GISTs) (*Berger et al. JVIM 2018, Elliott et al. JSAP 2017*)
- Carcinomas (*London et al. VCO 2012*)
  - Apocrine gland anal sac adenocarcinomas (*Heaton et al. JVIM 2020, Elliott JAVMA 2019*)
  - Squamous cell carcinomas (*de Vos et al. VCO 2012*)
  - Head and neck carcinomas
    - Thyroid carcinomas (*Sheppard-Olivares et al. VCO 2020*)
    - Nasal carcinomas
- Bladder transitional cell carcinoma (*Gustafson et al. JAAHA 2019*)
- Metastatic osteosarcomas (*Kim et al. Can Vet J 2017, Laver et al VCO 2017, Chan et al. AVP 2016, London et al. VCO 2012*)

Other consideration in dogs:

- Stage III insulinoma (*Flesner et al. JAAHA 2019*)
- Heart base tumours (*Lew et al. VCO 2019*)
- Inoperable, metastatic, or recurrent pheochromocytomas (*Musser et al. BMC Vet Res 2018*)
- Inoperative massive hepatocellular carcinoma (*Heishima et al. JAAHA 2018*)
- Inflammatory mammary gland carcinoma (*Rossi et al. VCO 2018*)
- Multiple drug-resistant T-cell lymphoma (*Yamazaki et al. JVMS 2017*)
- Lymphangiosarcoma (*Kim et al. Can Vet J 2018, Marcinowska et al. JSAP 2013*)
- Chronic monocytic leukaemia (*Perez et al. Anticancer Drugs 2013*)

In **cats**, the main indications are as follows: (*Harper et al. JFMS 2017, Merrick et al. VCO 2017*)

- Mast cell tumours (*Berger et al. JFMS 2018*)
- Carcinomas, particularly oral squamous cell carcinoma (*Olmsted et al. JFMS 2017, Wiles et al. JFMS 2017, Azevedo et al. JFMS Open Rep 2017*)

Other considerations in cats:

- Gastrointestinal stromal tumours (GISTs) (*McGregor et al. Aust Vet J 2020*)
- Pancreatic carcinoma (*Dedeaux et al. Can Vet J 2018*)

Palladia® can be safely combined with other anti-cancer therapies, such as metronomic chemotherapy, radiation therapy and some conventional chemotherapy drugs. It can also be safely combined with non-steroidal anti-inflammatory drugs (NSAIDs, such as piroxicam) and prednisolone. However, it is important **not** to administer NSAIDs or prednisolone on the same days as Palladia® because this combination can cause life-threatening gastrointestinal ulceration. NSAIDs or prednisolone can be safely administered on the off-Palladia® days.

### ***How frequent are the visits?***

When I start Palladia®, I typically recommend a recheck one to two weeks later, two weeks later, four weeks later, six weeks later, eight weeks later, then every 2-3 months after that. Each visit will usually consist of a physical examination, body weight, blood pressure, cancer measurement, complete blood count, serum biochemistry panel, and urinalysis (and if indicated urine protein: creatinine ratio).

### ***What are the side effects?***

In **dogs**, approximately 20% to 25% experience a side effect from Palladia®, that is usually gastrointestinal signs, weight loss or lethargy. However, uncommon side effects (such as hypertension, proteinuria, neutropenia, hepatopathy, shifting lameness, pancreatitis, cardiotoxicity) may occur. Most side effects (if picked up early) resolve with temporary discontinuation of Palladia®, dose reduction or addition of supportive medications. It is uncommon for a side effect to result in hospitalisation (<5%). Some dogs require dose adjustments and more frequent visits in the first month to try to get the Palladia® dosage right for the individual dog.

In **cats**, approximately 20% to 70% experience a side effect from Palladia®, that is usually mild and temporary gastrointestinal signs (predominately anorexia) or bone marrow suppression (neutropenia and thrombocytopaenia). However, uncommon side effects (such as hepatopathy, azotaemia and lethargy) may occur. Most side effects (if picked up early) resolve with temporary discontinuation of Palladia®, dose reduction or addition of supportive medications. It is uncommon for a side effect to result in hospitalisation (<5%). Some cats require dose adjustments and more frequent visits in the first month to try to get the Palladia® dosage right for the individual cat.

**Vets, I hope this information helps you understand a bit more about the use of Palladia® in pets. If you have a question about Palladia® or have a pet that you think may benefit from Palladia®, please do not hesitate to get in touch. Email: [info@thepetoncologist.com](mailto:info@thepetoncologist.com).**