Semintra

# Frequently Asked Questions

Boehringer Ingelheim

# Contents

# Frequently Asked Questions

## PHARMACOKINETICS AND PHARMACODYNAMICS

### 1. What is Semintra®?

Semintra® (telmisartan) is an oral solution that is well accepted by most cats. It is an angiotensin receptor blocker (ARB) licensed for the reduction of proteinuria associated with chronic kidney disease (CKD) in cats.

### 2. How quickly does Semintra® work?

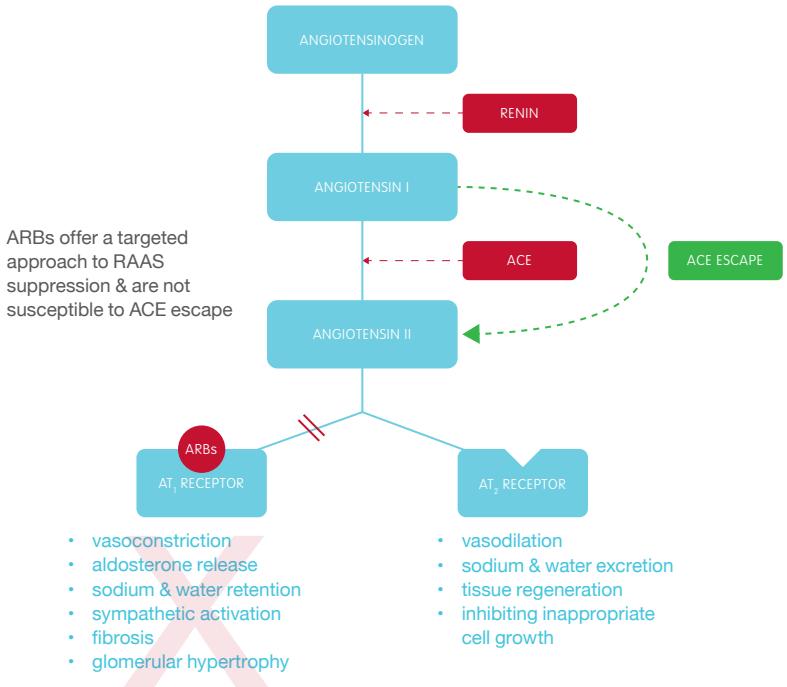
Semintra® works quickly, providing a reduction of proteinuria within the first 7 days after the start of treatment.[1]

### 3. What is Semintra®'s mode of action?

Semintra® is a specific angiotensin II receptor (type $AT_1$) blocker (ARB). It selectively binds to the $AT_1$ receptor and does not show affinity for other AT receptors. The receptor binding is long-lasting due to the slow dissociation of Semintra® from the $AT_1$ receptor binding site. By selectively blocking the $AT_1$ receptor, Semintra® blocks the pathological effects of angiotensin II, such as vasoconstriction, retention of sodium and water and increased aldosterone synthesis, while still allowing beneficial effects associated with stimulation of the $AT_2$ receptor, such as vasodilation and natriuresis. The active ingredient in Semintra® causes a dose-dependent decrease in mean arterial pressure in mammalian species including the cat, and in a clinical trial in cats with chronic kidney disease, a reduction in proteinuria was seen within the first 7 days after the start of the treatment.[1]

### 4. What is ACE escape?

ACE escape results from production of angiotensin II by pathways other than angiotensin converting enzyme, which can blunt the efficacy of ACEIs over time. ACE escape has been documented in cats and other species treated with ACE inhibitors.[2] ACE escape does not occur with Semintra®, because it specifically targets the $AT_1$ receptor and blocks the detrimental effects of angiotensin II.



## 5. How quickly is Semintra® absorbed?

Semintra® is rapidly absorbed, with maximum blood concentrations achieved after half an hour following oral administration. Food consumption does not affect the overall extent of absorption of telmisartan.

## 6. What is the half life of Semintra®?

The half life of Semintra® is 7.7 hours, with telmisartan's high affinity for and slow dissolution from the $AT_1$ receptor providing a 24 hour duration of effect.

# CONCURRENT TREATMENTS & CONDITIONS

## 7. Can I combine Semintra® treatment and a renal diet?

Yes.

## 8. Can I combine Semintra® treatment with amlodipine treatment?

Yes. During concomitant therapy with amlodipine at the recommended dose no clinical evidence of hypotension was observed.[1]

## 9. Can I use Semintra® instead of renal diets?

The reduced phosphorus contained in renal diets has been shown to improve survival in cats with CKD. We would therefore not recommend using Semintra® instead of renal diets. Renal diets are for treating different CKD-related conditions.

## 10. Can I use Semintra® with phosphate binders?

Yes. During the pivotal clinical field study some cats were also given phosphate binders, and concomitant use was well tolerated during the course of the study.[3]

# DOSING AND ADMINISTRATION

## 11. Can Semintra® and an ACE-inhibitor be used together?

While sequential blockade of the RAAS was thought to provide more aggressive mitigation of RAAS-mediated negative outcomes, a therapeutic advantage was not realized in human medicine; however increased intolerance was. As such, this is no longer recommended in people and we suggest extrapolating the same recommendation to cats. In fact, as ACE-inhibitors reduce the production of ANGII, they will indiscriminately effect both the $AT_1$ and $AT_2$ receptors, potentially mitigating the beneficial effects of Semintra® through its selective $AT_1$ receptor blockade.

## 12. How is Semintra® given?

Semintra® is an easy-to-use oral solution. It can be given directly into the mouth or by adding it to a small amount of food, whichever the owner and/or cat prefers.

## 13. Should Semintra® be given with or without food?

Food consumption does not affect the absorption of Semintra®; therefore it can be given directly into the mouth or onto a small amount of food. We would recommend that administration and the timing of food are kept consistent from day to day to ensure consistent absorption.

## 14. What is the dose?

Semintra® is given once a day with a recommended dose of 1 mg/kg bodyweight, when used for the management of CKD. The solution should be given using the bodyweight-calibrated syringe, which is provided in the package.

## 15. Can the Semintra® syringe be accidentally used by an owner on a Metacam® bottle or vice-versa?

The Semintra® syringe has been designed so that it cannot fit onto a Metacam® bottle and likewise the Semintra® bottle will not fit a Metacam® syringe.

## 16. How long can I give Semintra® for?

There is no maximum duration for Semintra® treatment: cats should be given Semintra® once daily for the rest of their life.

## 17. What do you mean when you say that Semintra® is “well accepted by most cats”?

A clinical trial assessed how well cats took Semintra®. It concluded that Semintra® was “well accepted by most cats” and the assessed acceptance of Semintra® was good or very good in 91.7% of all treatments.[4] This was recognized by the International Society for Feline Medicine in 2013, when they presented Semintra with their EASY to Give Award.[5]

## 18. I normally treat my CKD cats with benazepril but I don’t analyse their urine for protein. If I want to use Semintra®, do I now need to check for proteinuria first?

Both benazapril and Semintra® are licensed for the reduction of proteinuria associated with CKD in cats. Therefore, you can use Semintra® where you would have previously used benazapril.

## 19. Can I reduce the Semintra® dose?

Based on Semintra® dose-determination studies, Boehringer Ingelheim (Canada) Ltd. recommends the dose of 1 mg/kg a day be maintained when treating CKD in cats.[6]

## 20. With Metacam® I can dose accurately for small cats using a "drop dosing" dose rate – can I do this with Semintra®?

The bottle for Semintra® was not calibrated for a special drop size and thus using drops as a measure for an accurate dosing is not supported. Please use the syringe provided with the package – the lowest body weight that can be dosed using this syringe is 0.5 kg.

## 21. Do I need to monitor cats that are on Semintra®?

There are no specific monitoring requirements for cats that are receiving Semintra® listed on the Canadian package insert, apart from a recommendation to monitor the blood pressure of cats receiving Semintra® which are under anaesthesia as part of good clinical practice. We would recommend you continue to monitor cats which receive Semintra® as you would cats with CKD that receive benazepril.

## 22. Is a washout period required when switching from an ACE-inhibitor to Semintra®?

No, one can begin to administer Semintra® within 24 hours of stopping an ACE-inhibitor.

## 23. Can Semintra® be used as an anti-hypertensive treatment?

While recently published data supports efficacy as an anti-hypertensive in cats when used at a dose multiple of the current CKD dose, it is not licensed as such in Canada and so would be considered off-label use. If you have further questions, please call to discuss with one of our technical services veterinarians.

# ADVERSE REACTIONS AND OVERDOSE

## 24. What is Semintra®'s safety profile?

Semintra® is well tolerated by most cats. After administration of up to 5-fold of the recommended dose for 6 months, vomiting, reductions in blood pressure and RBC numbers, and higher BUN values in the higher dose groups vs controls were seen in some animals.[1] Elevated liver enzymes have been rarely observed. No clinically relevant accumulation was observed following multiple dose administration once daily for 21 days.[1] After oral administration, the active ingredient in Semintra® is almost exclusively excreted in the feces.[1] As such, Semintra® does not require dose adjustment with CKD progression.

## 25. On the package insert it says that Semintra® can cause low blood pressure (hypotension). Is this something I should be concerned about?

During clinical trials, Semintra® was administered at up to 5-fold of the recommended dose for 6 months which resulted in marked reductions in blood pressure and was expected due to Semintra®'s mode of action on the RAAS. This effect is unlikely to be observed under clinical conditions – in fact during the 6 month period of the field trial using Semintra® at the normal dose, no cats showed any signs of hypotension (low blood pressure).[1]

## 26. What are the most common adverse effects which I might expect to see with Semintra®?

The Canadian package insert states that the following adverse reactions were observed in a clinical study: The following mild and transient gastrointestinal signs have rarely been observed: mild and intermittent regurgitation, vomiting, diarrhea or soft feces. Elevated liver enzymes have been very rarely observed and values normalised within a few days following cessation of therapy.

Effects attributable to the pharmacological activity of the product observed at the recommended treatment dose included reductions in blood pressure and decreases in RBC counts. The reduction in blood pressure seen did not result in clinical problems, and the decrease in RBC count was considered to be of limited clinical relevance.

## 27. What if a dose of Semintra® is missed?

There is no need to worry if you happen to miss or forget a dose of Semintra®. Do not increase the dose or dose frequency. Simply wait until the next scheduled dose is due and give as normal.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**REFERENCES:**

1. Semintra® Canadian label/package insert.
2. Akasu M, Urata H, Kinoshita A. (1998) Differences in Tissue Angiotensin II-Forming Pathways by Species and Organs In Vitro. *Hypertension* 32:514-520.
3. Sent U. et al. Comparison of Efficacy of Long-term Oral Treatment with Telmisartan and Benazepril in Cats with Chronic Kidney Disease. *J Vet Intern Med* 2015;29:1479.
4. Sent U, Lang I, Moore G (2013) Characterisation of Telmisartan in Cats. Abstract in: *Proceedings of the ISFM World Feline Veterinary Congress*, Barcelona, June 26-30, 2013.
5. ISFM Semintra Easy-to-Give Award http://www.icatcare.org/cat-campaigns/easy-give.
6. EMA CVMP Assessment Report for Semintra® (2013).




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