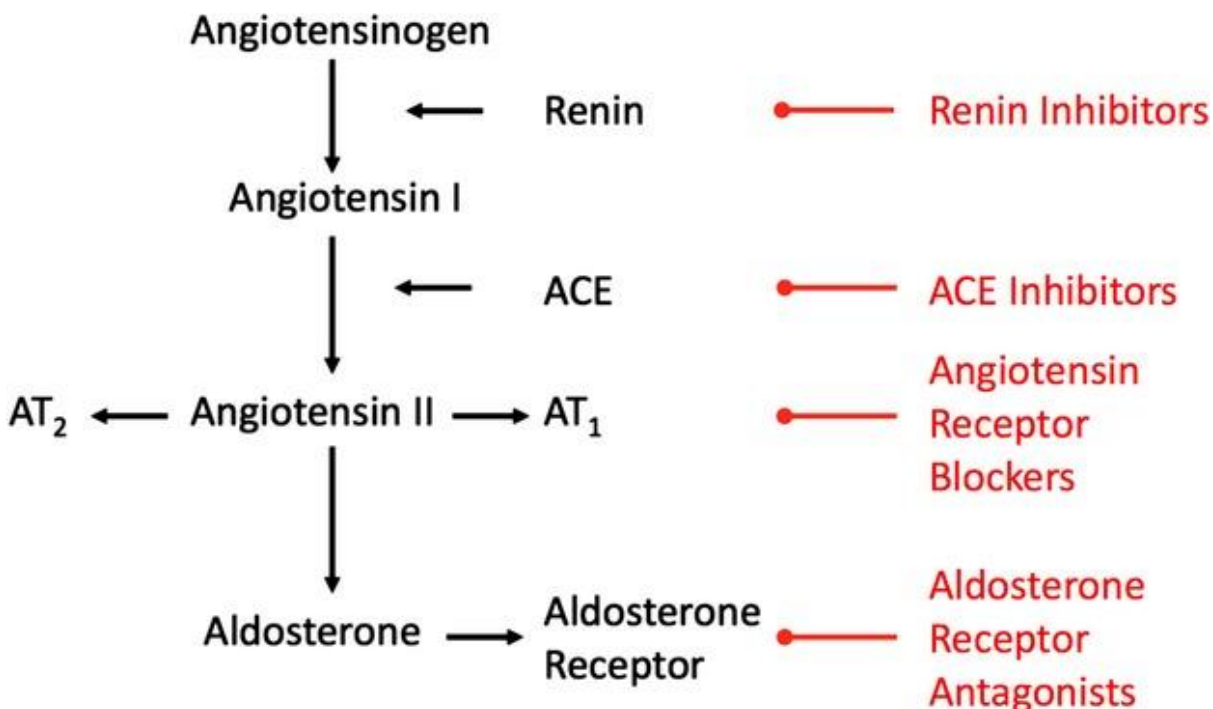


Telmisartan- Fighting that RAAS from a different angle

What's the background to this new drug?

In healthy animals activation of the Renin-Angiotensin-Aldosterone-System (RAAS) helps the body cope with dehydration or hypovolemia by causing vasoconstriction and increased blood volume and thus can be lifesaving. Activation of RAAS can also occur in disease through a variety of mechanisms in heart and renal disease. With chronic ongoing activation in some diseases negative long terms effects are noted on the body and organ systems. These can include hypertension, sodium retention, proteinuria, worsening organ function, fibrosis and vascular injury.

Traditionally ACEi's (Angiotensin converting enzyme inhibitors) have been utilised to prevent conversion of Angiotensin I to Angiotensin II. The end results is to deplete levels of serum aldosterone and Angiotensin II to reduce the negative long terms effects of high serum levels of these enzymes.



Picture taken from: IRIS staging group, JVIM, 2013 "Consensus"

recommendation for standard therapy of glomerular disease in dogs



In some cases, ACE inhibition alone leads to an ineffective RAAS blockade due to alternative enzyme activation pathways and aldosterone production. Furthermore Angiotensin 2 (AT2) receptor activation leads to positive long term effects that oppose the negative actions of AT1 and use of ACEi prevents activation of this receptor.

Thus a need for specific AT1 receptor inhibition was required to provide a more specific down regulation of the complex RAAS system. Telmisartan a specific AT1 receptor blocker fills this role. In recent times this drug has been investigated in the use in heart disease, hypertension (especially in cats) and glomerular disease.

Telmisartan is a relatively new drug to the veterinary world and now widely used amongst the veterinary internal medicine team. There is little published information on its use in dogs however its use in cats for hypertension and proteinuria is growing.

What products are available on the market?

- Licenced product for cats: **Semintra** (liquid) comes in 4mg/ml or a 10mg/ml solution
- Unlicensed product: **Micradis** comes as a tablet in 40mg and 80mg



What adverse effects should I be aware of?

Given this drug is relatively new the long terms

effects are largely unknown

- Reported effects include;
 - o Hypotension,
 - o Anemia
 - o Gastro-intestinal effects (vomiting, diarrhea)
 - o Increase in liver enzymes.
 - o Azotemia



What dose is appropriate for use?

- 1mg/kg q24hours is an acceptable dose in dogs
- 1-3mg/kg q24hours or split into 12hour dosing are reported doses in cats

What is the evidence of use of telmisartan?

Current VSS clinicians are utilising this drug for the following conditions:

- **Systemic hypertensive cats with blood pressures <200mmHg (see below)**
- **Systemic hypertension in dogs that may be refractory to amlodipine and benazepril**
 - o *Caro-Vadillo et al, Vet Record, 2017, "Effect of combination of telmisartan and amlodipine in hypertensive dogs"*
 - o *Acierno et al, JVIM 2018, "ACVIM consensus statement: Guidelines for the identification, evaluation, and management of systemic hypertension in dogs and cats"*
- **Proteinuria in cats as a first line treatment to reduce UPC**
 - o *New studies suggest it is superior to ACEi's; Sent et al, JVIM, 2015; Comparison of Efficacy of long-term oral treatment with telmisartan and Benazepril in cats with chronic kidney disease*
- **Proteinuria in dogs as a first line treatment to reduce UPC**
 - o *Bugbee et al; JVIM 2015 "Telmisartan treatment of refractory proteinuria in a dog"*
 - o *IRIS staging group, JVIM, 2013 "Consensus recommendation for standard therapy of glomerular disease in dogs"*

The use of ARBs to replace ACEi's in dogs and cats with heart disease is unknown and is not recommended at this time.

Some recent interesting studies have investigated the use of telmisartan in a variety of disease conditions in particular of interest is its growing use in cats with hypertension as studied by Glaus and Coleman.

Glaus et al, JVIM 2018, "Efficacy of long-term oral telmisartan treatment in cats with hypertension; Results of a prospective European clinical trial"

- o A robust study of 285 cats with systemic hypertension (<200mmHg, without evidence of target organ damage) received 2mg/kg/SID telmisartan over a 120day period.
- o Reduction of blood pressure was seen at day 14 and progressive to day 28. Long term control was seen at 120days for majority of cats.
- o **Clinical significance:** *Long term use of telmisartan is safe in cats with blood pressures below 200mmHg. Dose/drug changes may not be necessary until the 4 week mark.*

Coleman et al, JVIM 2019 "Safety and efficacy of orally administered telmisartan for the treatment of systemic hypertension in cats; Results of a double blind, placebo-controlled, randomized clinical trial"

- o Robust study of 221 cats given placebo or telmisartan for hypertension
- o **Clinical significance:** *Long term follow up over 6months showed good control of hypertension for majority of cats with systemic hypertension*

Current studies are looking at combination of ARBs and ACEi to cause a more complete RAAS inhibition and provide longer term benefits in patients. The effects of combination treatment are not known at this time and thus not recommended however VSS clinicians are eagerly watching this space.



Want to learn more?

If you find yourself lying awake at night contemplating the amazing world of RAAS and how newly developed drugs might target this system, we not only can relate to your passion but can suggest a therapeutic read of an exciting 20 page FREE ACCESS document of RAAS and its suppression in dogs and cats with the Journal of Veterinary Internal Medicine.

Ames et al, JVIM, 2018, The renin-angiotensin-aldosterone system and its suppression

Alternatively, you can call the VSS internal medicine department to discuss the use of this drug in clinical cases that you see.

Thanks to Dr Luke Johnston for preparing this information.

