164244-004

Semintra

4 mg/ml
oral solution for cats

Boehringer Ingelheim

Marketing authorisation holder
Rhone Ma Malaysia Sdn Bhd (200001023279)
Lot 18A & 18B, Jalan 241,
Seksyen 51A, 46100 Petaling Jaya,
Selangor

Manufacturer responsible for batch release
Boehringer Ingelheim
Promeco S.A. de C.V.
Calle Maiz No. 49, Barrio Xaltocan,
C.P. 16090, Mexico City, Mexico.

Active substance and other ingredient
One ml contains:
Telmisartan 4 mg
Benzalkonium chloride 0.1 mg

Clear, colourless to yellowish viscous solution.

Indication
Reduction of proteinuria associated with chronic kidney disease (CKD) in cats.
Treatment of systemic hypertension in cats.

Contraindications
Do not use during pregnancy or lactation.
See section "Pregnancy or lactation".
Do not use in cases of hypersensitivity to the active substance or to any of the excipients.

Adverse events
Cats:

Rare (1 to 10 animals / 10,000 animals treated):	Gastrointestinal signs (regurgitation[1], vomiting[2], diarrhoea[2]). Elevated renal parameters (creatinine and/or blood urea nitrogen), chronic renal failure.
Very rare (<1 animal / 10,000 animals treated, including isolated reports):	Elevated liver enzymes[3] Decreased red blood cell counts (see section "Special precautions for use")

[1] Mild and intermittent
[2] Vomiting and diarrhoea are commonly reported when given at the initial treatment dose of 2 mg/kg for systemic hypertension. Mild and transient
[3] Values normalised within a few days following cessation of therapy.

Reporting adverse events is important. It allows continuous safety monitoring of a veterinary medicinal product. Reports should be sent, preferably via a veterinarian, to either the marketing authorisation holder or its local representative or the national competent authority via the national reporting system.

Target species
Cats

Dosage, routes and method of administration
Oral use.

The product is to be administered once daily directly into the mouth or with a small amount of food.
Semintra® is an oral solution and is well accepted by most cats.
The solution should be given using the measuring syringe provided in the package. The syringe fits onto the bottle and has a ml scale.

CKD – amounts to be administered once daily:
The recommended dose is 1 mg telmisartan/kg body weight.

Dosing: 1 mg telmisartan/kg body weight	
Strength [mg/ml]	Dosage/kg bodyweight [ml]
4	0.25

Systemic hypertension – amounts to be administered once daily:
The initial recommended dose is 2 mg telmisartan/kg body weight.

Dosing: 2 mg telmisartan/kg body weight	
Strength [mg/ml]	Dosage/kg bodyweight [ml]
4	0.5

After 4 weeks, the dosage of telmisartan may be reduced in cats with systolic blood pressure (SBP) of less than 140 mmHg (in 0.5 mg/kg increments) at the discretion of the veterinarian.
If the SBP increases over the course of the disease the daily dose may be increased again up to 2 mg/kg.
The target SBP range is between 120 and 140 mmHg. If SBP is below the target or if there are concurrent signs of hypotension, please refer to section "Special precautions for use".
Systemic hypertension associated with CKD – amounts to be administered once daily:
The dosing regimen for hypertensive cats with concomitant chronic kidney disease is as described above for systemic hypertension except that for these cats the recommended minimum effective dose is 1 mg/kg.

Advice on correct administration



Push down and turn cap to open the bottle. Attach the dosing syringe to the plug-in adapter of the bottle by gently pushing.

Turn the bottle/syringe upside down. Pull the plunger out until the end of the plunger corresponds to the amount needed in ml.
Separate the dosing syringe from the bottle.



Push the plunger to empty the contents of the syringe directly into the mouth of the cat...



... or onto a small amount of food.

After administration of the veterinary medicinal product close the bottle tightly with the cap...



... wash the measuring syringe with water and let it dry.

To avoid contamination, use the provided syringe only to administer the veterinary medicinal product.

Withdrawal period
Not applicable.

Special precautions for storage
Keep out of the sight and reach of children.
This veterinary medicinal product does not require any special storage conditions.
Do not use after the expiry date stated on the carton and the bottle after EXP.
Shelf life after first opening of the bottle: 6 months.

Special precautions for use
Special precautions for use in target species
The safety and efficacy of telmisartan has not been tested in cats under the age of 6 months.
It is good clinical practice to monitor the blood pressure of cats receiving the veterinary medicinal product which are under anaesthesia. Due to the mode of action of the veterinary medicinal product, transient hypotension may occur.
Symptomatic treatment, e.g. fluid therapy, should be provided in case of any clinical signs of hypotension.
The dosage of telmisartan should be reduced if systolic blood pressure (SBP) is consistently lower than 120 mmHg or if there are concurrent signs of hypotension.
As known from substances acting on the Renin-Angiotensin-Aldosterone System (RAAS), a slight decrease in red blood cell count may occur. Red blood cell count should be monitored during therapy.

Substances acting on the RAAS may lead to a reduction in glomerular filtration rate and worsening renal function in cats with severe kidney disease. The safety and efficacy of telmisartan in such patients has not been investigated. When using this product in cats with severe kidney disease, it is advisable to monitor renal function (plasma creatinine concentration).
In cats with hypertension it is good clinical practice to regularly monitor blood pressure.

Special precautions to be taken by the person administering the veterinary medicinal product to animals
In case of accidental ingestion, seek medical advice immediately and show the package leaflet or the label to the physician.
Avoid eye contact. In case of accidental eye contact, rinse eyes with water.
Wash hands after use.
Pregnant women should take special care to avoid contact with the product because substances acting on the RAAS, such as Angiotensin Receptor Blockers (ARBs) and ACE inhibitors (ACEis), have been found to affect the unborn child during pregnancy in humans. People with hypersensitivity to telmisartan or other sartans/ARBs should avoid contact with the veterinary medicinal product.

Special precautions for the protection of the environment
Not applicable.

Pregnancy or lactation
The safety of Semintra® has not been established in breeding, pregnant or lactating cats.
Do not use during pregnancy or lactation.
See section "Contraindications".

Interaction with other medicinal products and other forms of interaction
During concomitant therapy with amlodipine at the recommended dose for the reduction of proteinuria associated with chronic kidney disease (CKD) in cats, no clinical evidence of hypotension was observed.
No drug-drug interactions are known from available data in cats with CKD and/or hypertension for the use of telmisartan and other medicinal products that lower blood pressure (such as amlodipine) or interfere with RAAS (such as ARBs or ACEis). The combination of such agents may lead to additive hypotensive effects or may alter renal function.

Overdose (symptoms, emergency procedures, antidotes), if necessary
After administration of up to 5 mg/kg body weight for 6 months to young adult healthy cats, adverse reactions observed were consistent with those mentioned in section "Adverse reactions". Administration of the product at overdose (up to 5 mg/kg body weight for 6 months) resulted in marked reductions in blood pressure, decreases in red blood cell count (effects attributable to the pharmacological activity of the product) and increases in Blood Urea Nitrogen (BUN).
In the event that hypotension does occur, symptomatic treatment, e.g. fluid therapy, should be provided.

Incompatibilities
In the absence of compatibility studies, this veterinary medicinal product must not be mixed with other veterinary products.

Pharmacodynamic properties
Telmisartan is an orally active and specific angiotensin II receptor (subtype AT_1) antagonist which causes a dose-dependent decrease in mean arterial blood pressure in mammalian species, including the cat.
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 treatment with 1mg/kg.
In a further clinical trial in cats with hypertension a reduction in mean systolic blood pressure was achieved with a dose of 2 mg/kg. Due to the combination of these pharmacodynamic properties, telmisartan is an appropriate treatment for cats with concomitant hypertension and CKD.
Telmisartan displaces angiotensin II from its binding site at the AT_1 receptor subtype.
Telmisartan selectively binds to the AT_1 receptor and does not show affinity for other receptors, including AT_2 or other less characterised AT receptors.
Stimulation of the AT_1 receptor is responsible for pathologic effects of angiotensin II in the kidney and other organs associated with angiotensin II such as vasoconstriction, retention of sodium and water, increased aldosterone synthesis and organ remodelling. Effects associated with stimulation of the AT_2 receptor such as vasodilatation, natriuresis and inhibition of inappropriate cell growth are not suppressed.
The receptor binding is long lasting due to the slow dissociation of telmisartan from the AT_1 receptor binding site. Telmisartan does not exhibit any partial agonist activity at the AT_1 receptor.
Hypokalaemia is associated with CKD, however telmisartan does not affect potassium excretion, as shown in the clinical field trial in cats.

Pharmacokinetic properties
Absorption
Following oral administration of telmisartan to cats, plasma-concentration-time curves of the parent compound are characterised by rapid absorption, with maximum plasma concentrations (C_{max}) achieved after 0.5 hours (t_{max}). For both, C_{max}-values, and AUC-values, a dose proportional increase over the dose range from 0.5 mg/kg to 3 mg/kg was observed. As determined by AUC, food consumption does not affect the overall extent of absorption of telmisartan.
Telmisartan is highly lipophilic and has rapid membrane permeability kinetics, which facilitates easy distribution into tissue.
No significant gender effect was seen.

No clinically relevant accumulation was observed following multiple dose administration once daily for 21 days.
The absolute bioavailability after oral administration was found to be 33%.

Distribution
In vitro studies in human, dog, mouse and rat plasma showed a high plasma protein binding (> 99.5%), mainly to albumin and α-1-acid glycoprotein.

Metabolism
Telmisartan is metabolised by conjugation to the glucuronide of the parent compound. No pharmacological activity has been shown for the conjugate. From *in vitro* and *ex vivo* studies with feline liver microsomes it can be concluded that telmisartan is effectively glucuronidated in the cat.
The glucuronidation resulted in the formation of the 1-*O*-acylglucuronide metabolite of telmisartan.

Elimination
The terminal elimination half life ($t_{1/2}$) ranged from 7.3 hours to 8.6 hours, with mean value 7.7 hours. After oral administration, telmisartan is almost exclusively excreted in faeces mainly as the unchanged active substance.

Disposal of unused product or waste materials
Medicines should not be disposed of via wastewater or household waste. Ask your veterinary surgeon how to dispose of medicines no longer required. These measures should help to protect the environment.

Date on which the package leaflet was last approved
DD.MM.YY

Other information
Pack sizes of one plastic bottle filled with 30 ml or one plastic bottle filled with 100 ml.
One measuring syringe.
Not all pack sizes may be marketed.

Semintra® is a registered trademark of Boehringer Ingelheim Vetmedica GmbH, used under licence.

For any information about this veterinary medicinal product, please contact the local representative of the marketing authorisation holder.

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