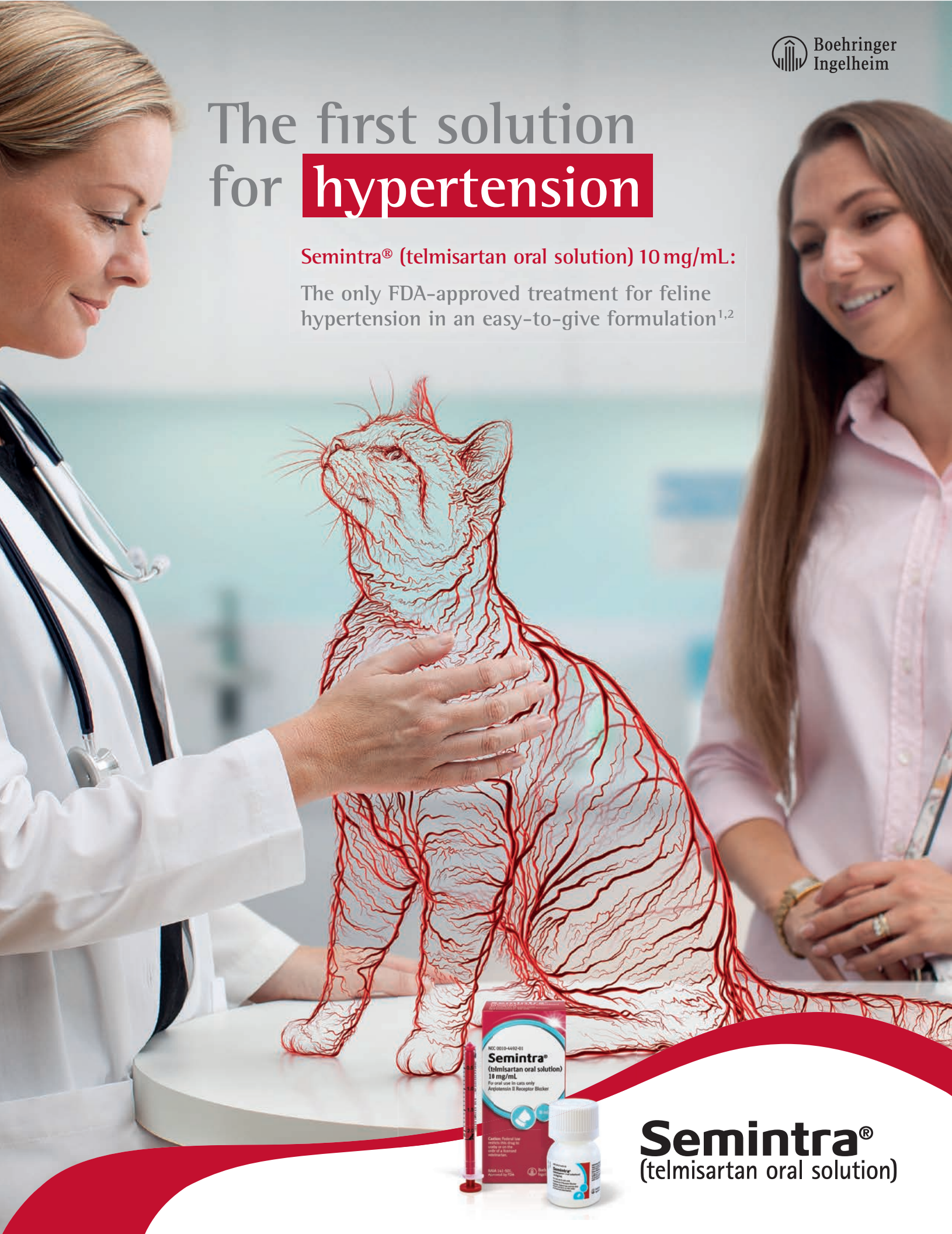
Boehringer Ingelheim

The first solution for hypertension

Semintra® (telmisartan oral solution) 10 mg/mL:

The only FDA-approved treatment for feline hypertension in an easy-to-give formulation[1,2]



Semintra®
(telmisartan oral solution)

Hypertension in cats

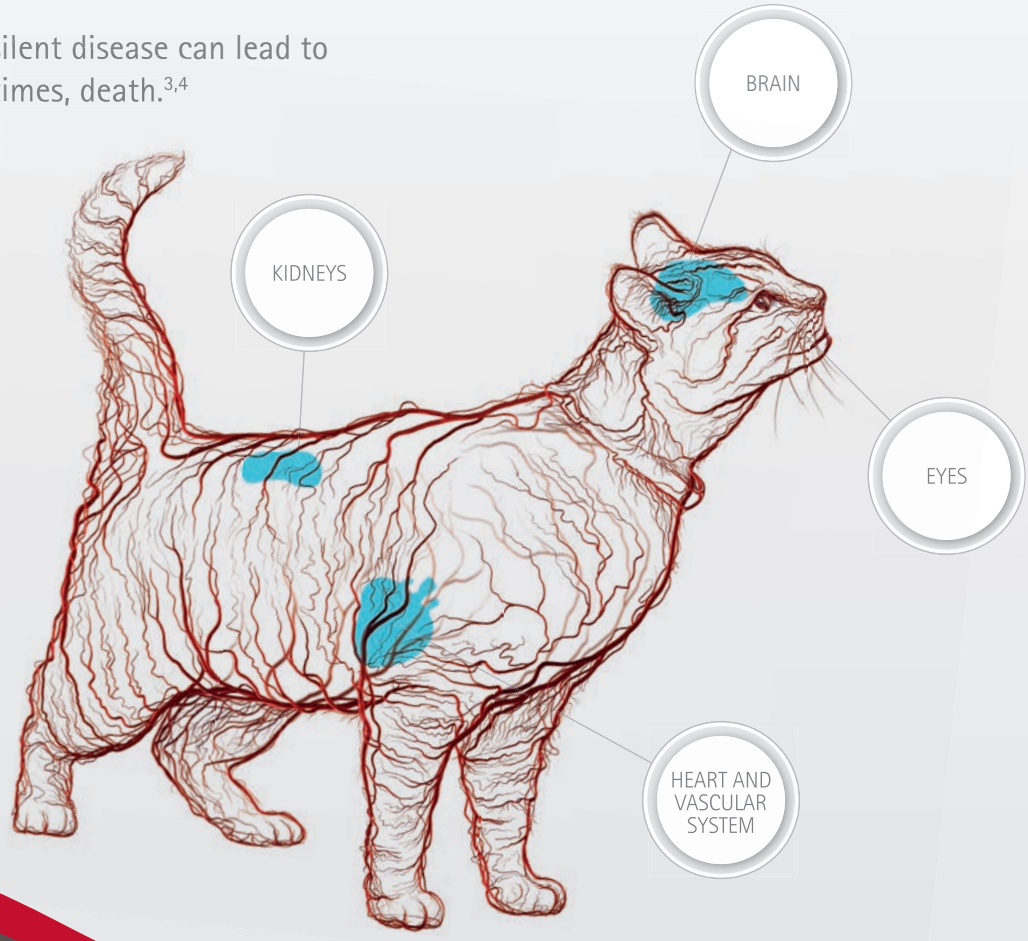
A silent disease

While hypertension can be a common problem in older cats, the condition can be difficult to diagnose.[3,4]

Hypertension can affect many parts of the body before detection and is strongly associated with target organ damage[3,4]:

- Eyes
- Heart and vascular system
- Brain
- Kidneys

Without treatment, this silent disease can lead to serious illness and, sometimes, death.[3,4]



Most often develops as secondary hypertension to diseases such as CKD and hyperthyroidism[3]

Primary hypertension

About 20% of diagnosed cases are classified as idiopathic hypertension, with no specific cause identified.[3]

Secondary hypertension

Up to 74% of hypertensive cats have CKD[5,6]

Up to 65% of cats with CKD are hypertensive[7–9]

The RAAS-hypertension connection

The pathophysiology of the renin-angiotensin-aldosterone system (RAAS) and hypertension is very complex in cats. What we do know is that activation of RAAS can increase blood pressure and promote the retention of salt and water to increase effective circulating blood volume. Chronic, excessive RAAS activation can result in systemic hypertension.[10,11]

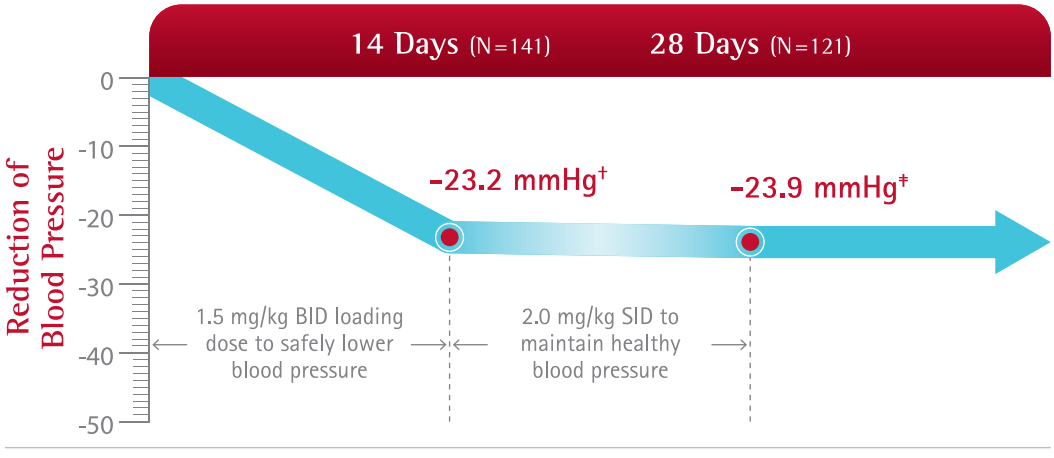
Semintra® (telmisartan oral solution) 10 mg/mL

The only angiotensin receptor blocker (ARB) for first-line treatment of hypertension in cats

- Because ARBs feature a unique, targeted mode of action that specifically blocks the harmful vasoconstrictive effects of the RAAS, SEMINTRA is shown to quickly lower blood pressure within 14 days*
- Shown to be effective in cats with primary and secondary hypertension
- Proven to be safe and effective[12-15]

*For cats with blood pressure ≤ 200 mmHg

SEMINTRA: Proven to lower systolic blood pressure[12,14]



A pilot dose determination laboratory study was conducted to evaluate the effectiveness of multiple oral doses and dose strategies of telmisartan on the reduction of systolic blood pressure (SBP) in clinically normal, healthy laboratory cats within a 14-day time period.[15]

† Endpoint at day 14 was significant reduction from baseline compared to placebo ($P < 0.0005$).

‡ A clinically relevant reduction in group mean SBP was predefined to be ≥ 20 mmHg in the telmisartan group from baseline to Day 28. The number of cats available at Day 28 for comparison is less than at enrollment because of removal of cats for hypertension rescue or adverse reactions.

IMPORTANT SAFETY INFORMATION

SEMINTRA is for oral use in cats only. SEMINTRA has not been evaluated in cats with systolic blood pressure > 200 mmHg. The safe use of SEMINTRA has not been evaluated in cats with hepatic disease, cats less than 9 months of age, or cats that are pregnant, lactating, or intended for breeding. The safe use of SEMINTRA with other anti-hypertensive medications has not been evaluated. Mild anemia or

SEMINTRA: Flexible dosing to safely lower and maintain blood pressure in cats

- SEMINTRA offers a dose-dependent response—an initial 1.5-mg/kg (0.68 mg/lb) dose twice daily for 14 days lowers blood pressure to a healthy level quickly, followed by a 2-mg/kg (0.91 mg/lb) once-daily dose to maintain control[15]
- Dose may be reduced by 0.5-mg/kg (0.23 mg/lb) increments to a minimum of 0.5 mg/kg to optimize dosing and prevent hypotensive state

SEMINTRA: Easily given as an oral liquid

EASY-TO-USE SYRINGE

— Flexible delivery of dose straight into the mouth or on top of food[2]
— Selection of accurate dose

ISFM easy to give
www.icatcare.org/vets

SAFE FOR LONG-TERM ADMINISTRATION

— Safety shown to extend through 6 months in multiple studies[12–15]

CONVENIENT LIQUID FORMULATION

As demonstrated in a study:
— 91.2% of cat owners prefer a liquid formulation[2]

Semintra®
(telmisartan oral solution)

non-regenerative anemia has been reported. The most common side effects reported in field studies include vomiting, diarrhea, lethargy, dehydration, poor appetite, and weight loss. If side effects should occur, pet owners should contact their veterinarian. For additional information, see the full prescribing information enclosed.

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Boehringer Ingelheim

Semintra®

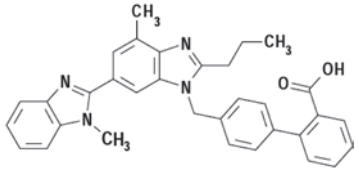
(telmisartan oral solution) 10 mg/mL

For oral use in cats only
Angiotensin II Receptor Blocker

35 mL

Caution: Federal law restricts this drug to use by or on the order of a licensed veterinarian.

Description: SEMINTRA (telmisartan oral solution) is a clear, colorless to yellowish viscous solution containing 10 mg/mL telmisartan. Telmisartan is an orally active, non-peptide, selective angiotensin II subtype 1 (AT1) receptor blocker. The chemical name of telmisartan is 4'-[(1,4'-dimethyl-2'propyl[2,6'-bi-1H-benzimidazol]-1'-yl)methyl]-[1,1'-biphenyl]-2-carboxylic acid. Its empirical formula is C33H30N4O2, its molecular weight is 514.63, and its structural formula is:



Indication: SEMINTRA is indicated for the control of systemic hypertension in cats.

Dosage and Administration: Always provide the Client Information Sheet with each prescription.

The initial dose of SEMINTRA is 1.5 mg/kg (0.68 mg/lb) orally twice daily for 14 days, followed by 2 mg/kg (0.91 mg/lb) orally once daily. The dose may be reduced by 0.5 mg/kg (0.23 mg/lb) increments to a minimum of 0.5 mg/kg (0.23 mg/lb) orally once daily to manage SEMINTRA-induced hypotension.

SEMINTRA can be administered directly into the mouth, or next to or on top of a small amount of food. Do not mix into food. SEMINTRA should be administered using the dosing syringe provided in the package. The dosing syringe fits onto the bottle and has 0.1 mL incremental marks. The dose should be rounded to the nearest 0.1 mL. After administration close the bottle tightly with the cap. Rinse the dosing syringe with water and let air dry.

If the cat vomits within 30 minutes of dosing, the cat may be re-dosed.

Information for Cat Owners

Always provide the Client Information Sheet with each prescription and review it with the cat owner. Advise cat owners that adverse reactions can occur with use of SEMINTRA. The most common adverse reactions reported during the field studies included vomiting, diarrhea, lethargy, weight loss, anemia and dehydration.

Contraindications: Do not use in cats with a hypersensitivity to telmisartan.

Human Warnings: Not for human use. Keep out of reach of children.

SEMINTRA is an angiotensin II antagonist/angiotensin receptor blocker (ARB). Pregnant women should avoid contact with SEMINTRA because substances that act on the renin-angiotensin-aldosterone system (RAAS) such as angiotensin receptor blockers (ARBs) can cause fetal and neonatal morbidity and death during pregnancy in humans.

Precautions: SEMINTRA has not been evaluated in cats with systolic blood pressure >200 mm Hg.

SEMINTRA can cause mild anemia or nonregenerative anemia. Cats should be monitored for anemia when initiating treatment with SEMINTRA.

SEMINTRA may cause inappetence and weight loss in some cats. Cats should be monitored for weight loss when initiating treatment with SEMINTRA. Use with caution in cats with a history of vomiting, inappetence or weight loss.

The safe use of SEMINTRA in cats with hepatic disease has not been evaluated. SEMINTRA is metabolized by the liver.

The safe use of SEMINTRA has not been evaluated in cats less than 9 months of age.

The safe use of SEMINTRA has not been evaluated in cats that are pregnant, lactating, or intended for breeding. See **Human Warnings**.

The safe use with other anti-hypertensive medications has not been evaluated.

Adverse Reactions:

28-day Field Effectiveness Study Safety was evaluated in a 28-day field study in 288 cats (192 SEMINTRA group cats, 96 control group cats) that received at least one dose of study drug. The control product was a vehicle control without telmisartan. Cats enrolled in the study had a median age of 14 years (7-20 years), and weighed 1.93-11.4 kg. SEMINTRA was administered orally at 1.5 mg/kg twice daily for 14 days, then 2 mg/kg once daily until study end; the control was administered at a volume equivalent to SEMINTRA. One hundred fourteen (59.4%) SEMINTRA group cats and 42 (43.8%) control group cats had at least one adverse reaction. Adverse reactions that occurred in at least 5% of either treatment group are presented in Table 1 below.

Table 1 Adverse Reactions in the 28-Day Field Study[a]

Clinical Sign	SEMINTRA N=192	Control N=96
Vomiting	46 (24.0%)	14 (14.6%)
Diarrhea	18 (9.4%)	4 (4.2%)
Lethargy	13 (6.8%)	3 (3.1%)
Weight loss	13 (6.8%)	5 (5.2%)
Decreased appetite/ Inappetence	13 (6.8%)	7 (7.3%)
Non-regenerative anemia	11 (5.7%)	2 (2.1%)
Dehydration	10 (5.2%)	4 (4.2%)
Retinal lesions (target organ damage)	4 (2.1%)	6 (6.3%)

Additional adverse reactions that occurred in <5% of the SEMINTRA group included (in order of decreasing frequency): anorexia, gagging, arrhythmia, cough, heart murmur, and regenerative anemia. Additional adverse reactions representing 2-5% of the control group included azotemia, not drinking and renal failure.

Seven cats (five SEMINTRA and two control) either died or were euthanized during the study. None of the SEMINTRA group deaths were considered related to treatment.

5-month Field Effectiveness and Safety Study The long-term safety of SEMINTRA was evaluated in an open label, 5 month field effectiveness and safety study in 107 cats that received at least one dose of SEMINTRA. Cats enrolled in the study had a mean age of 14.1 years (7-20 years) and weighed 1.92- 11.4 kg. SEMINTRA was administered orally at 2 mg/kg once daily. Ninety-four cats (87.9%) had at least one adverse reaction during the study. Adverse reactions that occurred in at least 5% of cats are presented in Table 2 below.

Table 2 Adverse Reactions in the 5-Month Study[a]

Clinical Sign	SEMINTRA N = 107
Weight loss	37 (34.6%)
Vomiting	32 (29.9%)
Dehydration	18 (16.8%)
Non-regenerative anemia	17 (15.8%)
Anorexia	14 (13.1%)
Diarrhea	12 (11.2%)
Lethargy	12 (11.2%)
Decreased appetite/ Inappetence	11 (10.3%)
Heart murmur	10 (9.3%)
Death, Euthanasia, Found dead	9 (8.4%)
Cough	8 (7.5%)
Retinal lesions (target organ damage)	6 (5.6%)

Adverse reactions representing <5% of the study population were (in order of decreasing frequency): elevated liver enzymes, renal failure, tachycadia, arrhythmia, azotemia, depression, loose stool, constipation, gagging, hypotension, regenerative anemia, renal insufficiency, and vocalization.

Nine cats died or were euthanized during the study. Three cats had progressive chronic kidney disease that may have been affected by telmisartan treatment, concurrent disease, or inadequate control of hypertension. The other six cats died of causes unrelated to treatment (e.g. neoplasia).

To report suspected adverse drug events, for technical assistance, or to obtain a copy of the Safety Data Sheet (SDS), contact Boehringer Ingelheim Vetmedica, Inc. at 1-888-637-4251. For additional information about adverse drug experience reporting for animal drugs, contact FDA at 1-888-FDA-VETS or online at www.fda.gov/reportanimalae.

Clinical Pharmacology: Telmisartan is a selective angiotensin II subtype AT1 receptor blocker, with no relevant affinity for other receptors in general receptor-binding assays. Telmisartan is metabolized to the 1-O-acylglucuronide of telmisartan, which, in cats treated for 6 days at 1 mg/kg, was shown to be present in the plasma at levels approximately 21% of that of unchanged parent compound.

Following an oral dose of 1 mg/kg telmisartan once daily for five days, the time to reach mean peak plasma concentration (Tmax) was 21 minutes and 32 minutes for fasted and fed cats, respectively. There was a higher systemic exposure to telmisartan in the fasted cats based on the maximum concentration (Cmax) and area under the concentration vs time curve (AUC). The mean terminal elimination half-life was approximately 8 hours. The mean systemic exposure of telmisartan (Cmax and AUC) was approximately 60% lower for female cats compared to male cats. However, dose adjustment for female cats is not necessary. An increase in dose from 1 to 5 mg/kg once daily resulted in a greater than proportional increase in telmisartan exposure. There could be low to moderate accumulation of drug upon repeated once daily or twice daily administrations of 1.5-2 mg/kg.

Effectiveness: Effectiveness was demonstrated in a 28-day multi-center, controlled, randomized and masked field study in client-owned cats with hypertension, and in an open label 5-month field study.

28-Day Field Study
In the 28-day study, 288 cats with hypertension (systolic blood pressure [SBP] 160-200 mmHg) were enrolled in the study and randomized to treatment with SEMINTRA (telmisartan oral solution) (n=192) or vehicle control (n=96). The study population included cats with hypertension associated with chronic kidney disease or controlled hyperthyroidism, or idiopathic hypertension. The per protocol population for effectiveness was 141 SEMINTRA treated cats and 79 control cats. SEMINTRA was administered orally at 1.5 mg/kg twice daily for 14 days, then 2 mg/kg once daily until study end; the vehicle control was administered at a mL/kg volume equivalent to SEMINTRA. The two primary variables for effectiveness were comparison of the SEMINTRA and control group mean SBP (mSBP) from baseline to Day 14, and a decrease in mSBP >20 mmHg in the SEMINTRA group from baseline to Day 28. Cats with SBP >180 mmHg at Days 14 or 28 were rescued and removed from the study. There was a statistically significant difference between the mSBP for the SEMINTRA group compared to the control group at Day 14 (p=0.0005). At Day 14 the SEMINTRA group mSBP decreased by 23.2 mmHg, and the control group mSBP decreased by 7.3 mmHg. At Day 28, the SEMINTRA group mSBP decreased 23.9 mmHg compared to baseline.

5-Month Field Study
One hundred-seven cats from the SEMINTRA group that had successfully completed the 28-day study were enrolled in a 5-month open label study. At the beginning of the 5-month study most cats were administered SEMINTRA at 2 mg/kg once daily. Cats that experienced hypotension (defined as SBP <120 mmHg) at 2 mg/kg once daily could have the SEMINTRA dose reduced to 1 mg/kg once daily. Cats that experienced hypotension at 1 mg/kg once daily could have the SEMINTRA dose reduced again to 0.5 mg/kg once daily. Cats were evaluated for SBP, target organ damage (TOD; primarily assessed by retinal photographs), clinical pathology and adverse reactions. SBP was measured on Days 28, 56, 98, 140 and 182 and retinal photographs and clinical pathology were collected on Days 28, 98 and 182. Seventy-three (68.2%) cats completed the study (Day 182), 8 cats were removed for hypertension (SBP >180 mmHg), 2 cats were removed for hypotension, 10 cats were removed by the owner or for owner noncompliance, 8 cats were removed for new or worsening TOD, and 6 cats were removed for adverse reactions unrelated to TOD. Twenty-six cats had dose reductions to 1 mg/kg once daily to manage hypotension. Of these 26 cats, 10 had an additional dose reduction to 0.5 mg/kg once daily.

Table 3 Distribution of Cats by SBP Range and Study Day in the 5-Month Study[a]

SBP Range (mm Hg)	Baseline N=107 n (%)	Day 28 N=107 n (%)	Day 56 N=102 n (%)	Day 98 N=91 n (%)	Day 140 N=80 n (%)	Day 182 N=69 n (%)
≤ 150	0 (0%)	58 (54.2%)	55 (53.9%)	61 (67%)	44 (55%)	41 (59.4%)
>150-160	4 (3.7%)	19 (17.8%)	19 (18.6%)	17 (18.7%)	21 (26.2%)	16 (23.2%)
>160-170	38 (35.5%)	18 (16.8%)	14 (13.7%)	10 (11%)	12 (15%)	7 (10.1%)
>170-180	28 (26.2%)	12 (11.2%)	10 (9.8%)	2 (2.2%)	3 (3.8%)	4 (5.8%)
> 180	37 (34.6%)	0 (0%)	4 (3.9%)	1 (1.1%)	0 (0%)	1 (1.5%)

[a] SBP obtained at unscheduled visits are not represented. Cats that were removed for missing >3 doses prior to SBP measurement are not included.

The most commonly used concomitant treatments during the 5-month study included (in order of frequency) antibiotics, anesthesia/sedatives/analgesia, nutritional supplements, vaccines, prescription diets, antiparasitics, thyroid treatment, antiemetics and fluid therapy.

Animal Safety: In a six-month target animal safety study, healthy cats 9 to 13 months old were administered telmisartan orally, once daily at 0, 1, 3, or 5 mg/kg body weight.

Control cats (0 mg/kg) received saline at a volume equal to the 5 mg/kg dose. There were eight cats per group (4 males, 4 females).

All cats survived the study, and there were no telmisartan-related effects on clinical observations, physical examination, body weight, ophthalmic examination, coagulation parameters, urinalysis, and gross necropsy.

Blood pressure was lower in the groups administered telmisartan compared to the control group. Blood pressure was lower starting at week 4 in the 1 mg/kg group, at week 2 in the 3 mg/kg group, and during the first week in the 5 mg/kg group. This is an expected pharmacologic effect of telmisartan. Food consumption in the 3 and 5 mg/kg group cats was lower than that of the control group.

Telmisartan-related effects on hematology parameters included lower red blood cell count, hemoglobin, hematocrit, and reticulocytes in the 3 and 5 mg/kg group cats. One 5 mg/kg group cat also had mild generalized depletion of the hematopoietic cells on bone marrow histology. In some 5 mg/kg group cats, decreases in red blood cell precursors on bone marrow cytology were considered telmisartan-related.

Blood urea nitrogen (BUN) was statistically significantly higher for the 3 mg/kg group at weeks 12 and 16, and for the 5 mg/kg group at weeks 2, 4, 7, 12, 16, 20, and 25, when compared to the control group. There were no clinical signs associated with the changes in BUN.

There was a telmisartan-related effect on lower heart weight in the 3 and 5 mg/kg groups compared to the control group, but the histopathology was normal in all treated cats. On kidney histology, there was minimal to mild hypertrophy of the juxtaglomerular apparatus in the 1, 3, and 5 mg/kg group cats. Kidney histology was normal in control group cats.

Storage Conditions: Store at or below 25°C (77°F) with excursions permitted up to 40°C (104°F). Once the bottle is opened, use the contents within six months.

How Supplied: SEMINTRA (telmisartan oral solution), 10 mg/mL, 35 mL fill volume, is supplied in a 45 mL plastic bottle with a dosing syringe. NDC 0010-4492-01

Approved by FDA under NADA # 141-501

Marketed by:

Boehringer Ingelheim Animal Health USA Inc.
Duluth, GA 30096

Made in Spain

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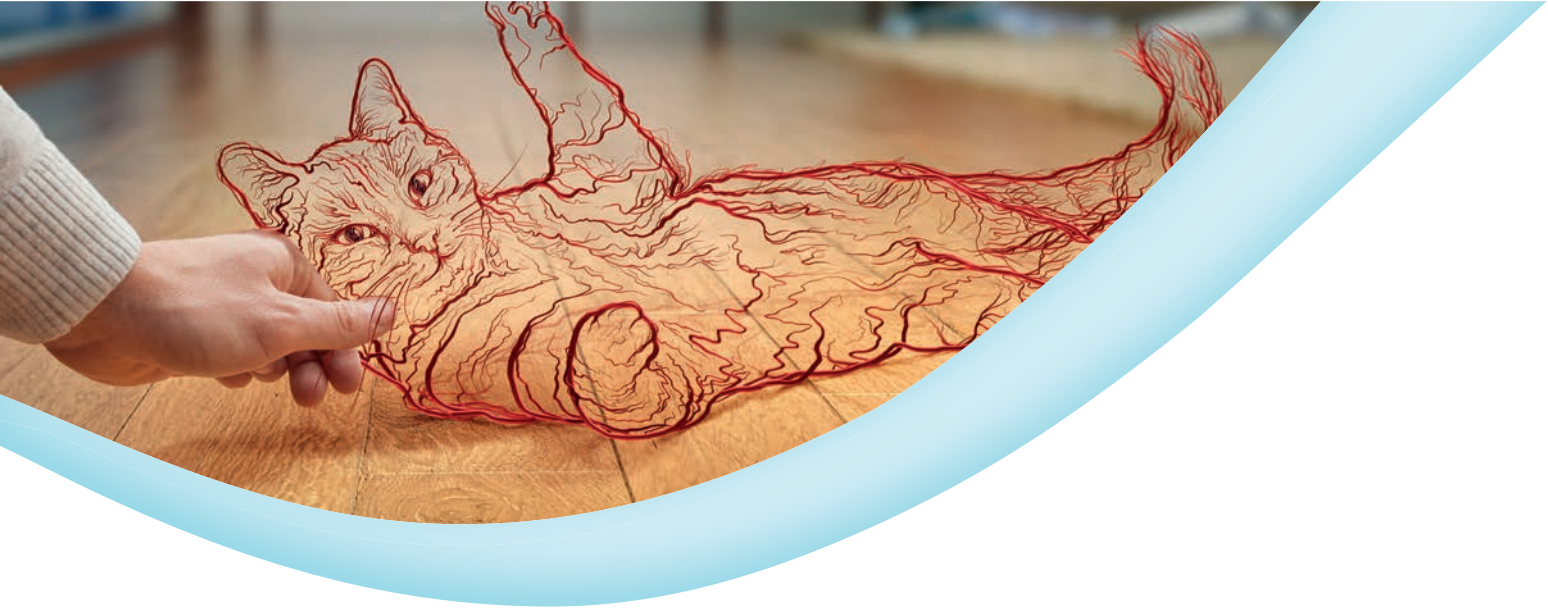

The first solution for feline hypertension

- The only ARB for first-line treatment of hypertension in cats
- Easy-to-use syringe allows for accurate dosing and flexible dosing
- Safe for long-term administration, with once-daily dosing after 14 days

Discover the entire portfolio of feline products available from Boehringer Ingelheim.

For more information about SEMINTRA for feline hypertension, please talk to your Boehringer Ingelheim representative.

References: 1. Semintra® (telmisartan oral solution) Prescribing Information. Boehringer Ingelheim Vetmedica, Inc. 2018. **2.** Zimmering T. Ease of use of Semintra® and its effects on quality of life—update on cat owner feedback ("EASY Programme") [abstract]. In: Proceedings from the 21st Federation of European Companion Animal Veterinary Associations (FECAVA); October 15–17, 2015; Barcelona, Spain. Poster. **3.** Elliott J, Fletcher M, Syme HM. Idiopathic feline hypertension: epidemiologic study [abstract]. *J Vet Intern Med.* 2003;17:754. **4.** Taylor SS, Sparkes AH, Briscoe K, et al. ISFM Consensus Guidelines on the diagnosis and management of hypertension in cats. *J Feline Med Surg.* 2017;19(3):288–303. **5.** Maggio F, DeFrancesco TC, Atkins CE, et al. Ocular lesions associated with systemic hypertension in cats: 69 cases (1985–1998). *J Am Vet Med Assoc.* 2000;217:695–702. **6.** Littman MP. Spontaneous systemic hypertension in 24 cats. *J Vet Intern Med.* 1994;8:79–86. **7.** Stiles J, Polzin D, Bistner SI. The prevalence of retinopathy in cats with systemic hypertension and chronic renal failure or hyperthyroidism. *J Am Anim Hosp Assoc.* 1994;30:564–572. **8.** Syme HM, Barber PJ, Markwell PJ, et al. Prevalence of systolic hypertension in cats with chronic renal failure at initial evaluation. *J Am Vet Med Assoc.* 2002;220:1799–1804. **9.** Kobayashi DL, Peterson ME, Graves TK, et al. Hypertension in cats with chronic renal failure or hyperthyroidism. *J Vet Intern Med.* 1990;4:58–62. **10.** Williams TL, Elliott J, Syme HM. Renin-angiotensin-aldosterone system activity in hyperthyroid cats with and without concurrent hypertension. *J Vet Intern Med.* 2013;27(3):522–529. **11.** Syme H. Hypertension in small animal kidney disease. *Vet Clin North Am Small Anim Pract.* 2011;41(1):63–89.
12. Coleman, A et al, 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 *J Vet Intern Med.* 2019; 1-11. **13.** Glaus TM, et al Efficacy of long-term oral telmisartan treatment in cats with hypertension: Results of a prospective European clinical trial. *J Vet Intern Med.* 2018;1–10. **14.** Semintra® (telmisartan oral solution) [Freedom of Information Summary]. St. Joseph, MO: Boehringer Ingelheim Vetmedica, Inc.; 2018.
15. Coleman A, et al. Evaluation of orally administered telmisartan for the reduction of indirect systolic arterial blood pressure in awake, clinically normal cats *J Feline Med Surg.* 2018; 1-6.

Please see inside for full Prescribing Information.

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(telmisartan oral solution)