

REYES & REYES
A B O G A D O S

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO



No. 11-165084- -00015-0000

Fecha: 2013-10-01 11:04:14 Dep. 2020 DIR.NUEVASCR
Tra. 11 PATENTEIYII Eve: 378 FASENACIONALI
Act. 329 CTOINFORMACION Folios: 15

SEÑOR
SUPERINTENDENTE DE INDUSTRIA Y COMERCIO
E. S. D.

REF: Expediente 11-165-084

TÍTULO SOLICITADO: "SOLUCIÓN BEBIBLE FARMACÉUTICA DE TELMISARTAN"

PUBLICACIÓN: Gaceta 647 de 29 de Junio de 2012, N° de publicación 844.

PRIORIDAD: EP 09160771.3 de 20/05/2009.

SOLICITANTE: BOHERINGER INGELHEIM VETMEDICA, GMBH

APODERADO: CARLOS R. OLARTE

TRÁMITE: REMISIÓN DE INFORMACIÓN

JOSÉ LUIS REYES VILLAMIZAR, mayor de edad, identificado como aparece al pie de mi firma, abogado en ejercicio, titular de la tarjeta profesional número 44655 del Consejo Superior de la Judicatura, obrando en calidad de apoderado de la sociedad **TECNOQUÍMICAS S.A.** dentro del trámite de la referencia, en ejercicio de lo dispuesto por el artículo 42 inciso 2° de la Decisión 486 de 2000, por medio del presente escrito, procedo a presentar argumentos que demuestran que la solicitud de la referencia incumple los requisitos de patentabilidad establecidos por los artículos 14, 16 y 18 de la Decisión 486 de 2000, a pesar del cambio de capítulo reivindicatorio, y que por ello no merece recibir beneficio patentario:

I. RATIFICACIÓN

Comedidamente me permito insistir en los argumentos planteados en la oposición y sustentación respectivas, los cuales, como se dijo en su momento, demuestran que la solicitud de la referencia incumple los requisitos de patentabilidad establecidos por los artículos 14, 16 y 18 de la Decisión 486 de 2000, y que por ello no merece recibir el beneficio patentario aun con los cambios realizados en el capítulo reivindicatorio.

II. COMPLEMENTO DE INFORMACION

- En primer lugar, es importante señalar que la modificación al capítulo reivindicatorio original, que constaba de 18 reivindicaciones y que ahora, presentada en respuesta a oposiciones consta de 17 reivindicaciones, no logra superar en absoluto los argumentos presentados en nuestra oposición, como lo demostraremos más adelante, en tanto la solicitud referida no solamente persiste en carecer de nivel inventivo, como bien lo ha señalado el Señor Examinador en su requerimiento de artículo 45, sino que también mantiene su carencia de Novedad.
- En efecto, la materia original que se pretende proteger, ha quedado intacta al realizarse solamente un cambio consistente en seleccionar el telmisartán como el único antagonista del receptor de angiotensina II para incorporarse a la solución farmacéutica. Por lo demás, prevalecen todas las inconsistencias mencionadas en el memorial de oposición con respecto a claridad y concisión, en tanto no se expresan cantidades, nombres específicos y proporciones de principios activos y azúcares – alcoholes, no se definen valores o rangos precisos de pH, y se caracteriza repetidamente la materia protegible en función de los “resultados por alcanzar”, determinados directamente por los azúcares reductores y no por la invención en sí misma, lo que resulta contrario a la técnica jurídica en esta materia.
- De igual manera, persiste la solicitud en mencionar usos como el carácter “bebible” de la solución, el cual resulta, además, ambiguo. Por si fuera poco, el título no es claro ni técnicamente correcto, existen excepciones (*disclaimers*) que tampoco se encuentran sustentadas por la descripción, lo que hace que,

definitivamente el examen de patentabilidad llevado a cabo por ese Despacho esté bien elaborado y a que por ello sus conclusiones sean las adecuadas.

- De igual manera es del caso resaltar que persisten falencias en cuanto a unidad de invención, en tanto la solicitud pretende proteger un recipiente que hace parte de otro campo técnico.

Siguiendo con nuestro análisis, existen documentos con los cuales tanto esta firma como el Examinador, demostraron en el transcurso del trámite que la presente solicitud colombiana carece, al menos, de nivel inventivo. Veamos:

- **US 2007/026026 “*Oral liquid losartan compositions*”**, publicada en febrero 1 de 2007, revela composiciones líquidas de losartán (un antagonista del receptor de angiotensina II tal como el que pretende protegerse en la presente solicitud colombiana en trámite “Telmisartán”) con excipientes, de tal forma que logra un pH mayor a 9, el cual es estable en soluciones de glicol, glicerina y xilitol y que incluye alcoholes azucarados como el manitol.
- **WO 2004/028505 “*SOLID PHARMACEUTICAL FORMULATIONS COMPRISING TELMISARTAN*”** revela composiciones farmacéuticas sólidas que contienen telmisartán, por lo cual es considerado por el Examinador como el documento más cercano al estado de la técnica ya que, al igual que la solicitud colombiana en trámite, contiene polioles como manitol, sorbitol, xilitol, agentes básicos como arginina, NaOH, KOH, o carbonatos; la única diferencia existente es que la composición de la solicitud en trámite es líquida, sin que esto signifique que tenga efectos ventajosos y el hecho de contener azúcares reductores por debajo de 1000 ppm es meramente un resultado a alcanzar.

Ahora observemos la comparación realizada por el Examinador:

La reivindicación 1 divulga una solución farmacéutica con un valor de pH de 10 o superior que contiene Telmisartan, caracterizada porque contiene uno o más azúcar alcoholes hasta en una concentración total de 40% a 70%, presentando antes de su adición un contenido máximo de azúcares reductores de 1000 ppm (Página 8 del radicado N° 11-165084-00013-0000)

Comparación de las características técnicas **esenciales**, con las del Estado de la Técnica:

Solicitud	D1	D2
Una composición farmacéutica oral líquida	Una composición farmacéutica oral sólida para disolución	Una composición farmacéutica líquida sólida
Contiene Telmisartan	Contiene Telmisartan 3% – 50%	Contiene Losartan potásico
Contiene polioles en proporción entre el 40% – 70%	Contiene entre el 25% – 70% de un diluyente hidrosoluble, que pueden ser eritritol, manitol, sorbitol o xilitol	Contiene un diluyente máximo al 50% que puede ser glicerol (un poliol)

Así las cosas y aunque bajo distintos análisis, se concluye tanto por ese Despacho como por nuestra oficina que la solicitud carece no solamente de novedad sino de todo indicio de nivel inventivo, dado que una persona medianamente conocedora de la materia, teniendo en cuenta la necesidad de incrementar la estabilidad y solubilidad del telmisartán, lograría modificar la tableta para disolución oral líquida con la información de la composición de la anterioridad que proporciona un inhibidor de angiotensina II en solución líquida a pH básico para obtener fácilmente lo que pretende proteger la presente solicitud colombiana en trámite.

Ahora bien, por si no fueren suficientes los argumentos esbozados en la oposición, queremos reiterar ciertos aspectos adicionales que refuerzan la tesis de que dicha solicitud incumple los requisitos de patentabilidad, a la luz de los siguientes documentos:

- **WO 2008/040774, “Angiotensin II receptor antagonist for the prevention or treatment of systemic diseases in cats”**, publicado en abril 10 de 2008, revela un método para enfermedades sistémicas en gatos que consiste en administrar una cantidad terapéuticamente efectiva de un antagonista del receptor de angiotensina II (sartan).

(57) Abstract: The present invention relates to a method of prophylaxis or treatment of systemic diseases in cats, wherein the method comprising administration of a therapeutically effective amount of angiotensin II receptor 1 (AT-1) antagonist (sartan) to a cat in need of such a treatment.

La anterioridad revela que hasta la fecha no se le había encontrado uso en animales a los antagonistas del receptor de angiotensina II y sin embargo, se encuentra que los gatos toleran dosis farmacodinámicamente efectivas de tales antagonistas, por lo cual, la idea de tratar animales terapéuticamente con

telmisartán, tal como se pretende proteger en la solicitud colombiana, ya era algo conocido y usado comúnmente en el estado del arte desde el año 2008, de acuerdo con lo revelado allí:

It was surprisingly found that cats tolerate a pharmacodynamically effective dose of sartans. In a open-label study in nondiabetic, hypertensive human patients with proteinuric nephropathies the effects on renal outcome of low (80 mg once daily) and high dose (80 mg twice daily) telmisartan were compared. The results reinforced the

(...)

El documento al cual nos referimos incluso prefiere el telmisartán tal como pretende protegerse en la actual solicitud ya que encontró ser altamente efectivo en animales con falla renal crónica e hipertensión arterial cuya vía de administración incluía incluso la oral, tal como consta a continuación:

(pág 8):

valsartan. Those which are particularly preferred according to the present invention are irbesartan, losartan und telmisartan. All of these sartans, or pharmaceutical salts

(...)

(pág 9):

Thus, according to a further embodiment, the present invention relates to a method for the prophylaxis or treatment of a systemic disease in cats, preferably of chronic kidney disease, e.g. chronic renal failure, wherein the method comprising administration of a therapeutically effective amount of telmisartan or pharmaceutically acceptable salt thereof, preferably of a telmisartan as mentioned above. More preferably said telmisartan is Micardis®.

(...)

(pág 10):

Thus, according to another aspect, the present invention relates to a method for the prophylaxis or treatment of a systemic disease in cats, preferably of chronic kidney disease, e.g. chronic renal failure, wherein the method comprising administration of a therapeutically effective amount of angiotensin II receptor 1 (AT-1) antagonist (sartan), preferably telmisartan or pharmaceutically acceptable salt thereof, to that cat in need of such a treatment, wherein the therapeutically effective amount of such angiotensin II receptor 1 (AT-1) antagonist is about 0.01 to about 10 mg/kg of body weight. Preferably, said therapeutically effective amount of such angiotensin II (...)

(pág 11):

In cases when angiotensin II receptor 1 (AT-1) antagonist, preferably telmisartan is administered by oral, rectal, nasal or inhalative route a dosage of about 0.03 to about 10 mg/kg of body weight is preferred. Preferably, said therapeutically effective (...)

Observamos también cómo el documento sugiere el uso del telmisartán en forma de elixir, es decir, en forma de solución farmacéutica para administración oral que contiene al menos un ingrediente activo y como es bien sabido por cualquier experto medianamente versado en la materia, un elixir¹ está conformado por azúcares alcoholes que enmascaran el sabor y que puede estar conformado por gliceroles, sorbitol, estabilizantes, antioxidantes, conservantes, etc, veamos:

(pág 13):

¹ <http://es.m.wikipedia.org/wiki/Elixir>

Telmisartan and the other active compounds can be orally administered in a wide variety of different dosage forms, i.e., they may be formulated with various pharmaceutically acceptable inert carriers in the form of tablets, capsules, lozenges, troches, hard candies, powders, sprays, aqueous suspensions, elixirs, syrups, and the like. Such carriers include solid diluents or fillers, sterile aqueous media and various non-toxic organic solvents. Moreover, such oral pharmaceutical formulations can be suitably sweetened and/or flavoured by means of various agents of the type commonly employed for such purposes. In general, the compounds of this invention are present in such oral dosage forms at concentration levels ranging from about 0.5% to about 90% by weight of the total composition, in amounts which are sufficient to provide the desired unit dosages. Other suitable dosage forms for the compounds of this invention include controlled release formulations and devices well known to those who practice in the art.

(...)

(pág 13, 14):

When aqueous suspensions and/or elixirs are desired for oral administration, the essential active ingredient therein may be combined with various sweetening or flavouring agents, colouring matter or dyes and, if so desired, emulsifying agents and/or water, ethanol, propylene glycol, glycerine and various like combinations thereof.

These preformulated combinations of active substances are generally incorporated with one or more formulation adjuvants such as mannitol, sorbitol, xylitol, saccharose, calcium carbonate, calcium phosphate, lactose, croscarmellose sodium salt (cellulose carboxymethylether sodium salt, cross-linked), crospovidone, sodium starch glycolate, hydroxypropylcellulose (low-substituted), maize starch,

Así las cosas, recalcamos como se hizo desde el inicio de este trámite, que la presente solicitud no es nueva:

Para terminar con el análisis de la reivindicación 1, es necesario resaltar que “el pH de 10 o superior” no es una característica técnica esencial toda vez que, como bien lo indica el Examinador en el artículo 45, es un dato no limitado y no sustentado mediante UN componente específico dentro de la formulación que proporcione la especificación en mención y su ventaja diferencial contra el estado de la técnica, por tanto, el objeto de esta solicitud, tal como aparece en las reivindicaciones 1 y sus dependientes, no es nuevo con respecto a la publicación internacional **WO 2008/040774**.

NOVEDAD CO 11-165-084	
CARACTERÍSTICAS DE LA REIVINDICACION INDEPENDIENTE 1	WO 2008/040774
Solución farmacéutica	SI
TELMISARTÁN	SI
caracterizada porque están contenidos uno o más azúcar-alcoholes	SI

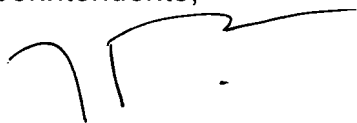
De esta forma se evidencia que la solicitud colombiana en trámite no solamente carece de cualquier indicio de actividad inventiva como lo analiza el Examinador en su artículo 45, sino que de acuerdo al cambio actual de capítulo reivindicatorio **NO ES NUEVA** ya que, comparando elemento por elemento se observa fácilmente que los 3 (tres) elementos característicos de la reivindicación independiente, es decir: una solución farmacéutica, que contiene telmisartán, con uno o más azúcares alcoholes habían sido divulgados previamente en el estado de la técnica, es decir, ya se habían utilizado formulaciones iguales, para el tratamiento de insuficiencia renal e hipertensión en animales.

En conclusión, queda irrefutablemente demostrado que aún con la modificación al capítulo reivindicatorio, la presente solicitud colombiana en trámite carece de todos los requisitos de patentabilidad. Por todo lo anterior, ruego se analicen los argumentos expuestos con el rigor y detenimiento habituales y que en consecuencia se decrete, además de la negación de la solicitud en comento, el archivo del expediente que la contiene.

III. PRUEBAS

- La publicación internacional WO 2008/040774, "*angiotensin II receptor antagonist for the prevention or treatment of systemic diseases in cats*", págs 4 a 14.

Señor Superintendente,



JOSE LUIS REYES VILLAMIZAR

C.C. 79.152.473 de Usaquén

T.P. 44655 del C. S de la J.

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
10 April 2008 (10.04.2008)

PCT

(10) International Publication Number
WO 2008/040774 A2

(51) International Patent Classification:

A61K 31/41 (2006.01) A61P 9/00 (2006.01)
A61K 31/4184 (2006.01) A61P 13/12 (2006.01)

(74) Agent: HAMMANN, Heinz; Boehringer Ingelheim GmbH, Binger Str. 173, 55216 Ingelheim Am Rhein (DE).

(21) International Application Number:

PCT/EP2007/060531

(22) International Filing Date: 4 October 2007 (04.10.2007)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:

06121905.1 6 October 2006 (06.10.2006) EP

(71) Applicant (for all designated States except US):

BOEHRINGER INGELHEIM VETMEDICA GMBH [DE/DE]; Binger Str. 173, 55216 Ingelheim Am Rhein (DE).

(72) Inventors; and

(75) Inventors/Applicants (for US only): STARK, Marcus [DE/DE]; Armenruhstr. 18, 65203 Wiesbaden (DE). SENT, Ulrike [DE/DE]; Ernst Barlach Str. 5, 65195 Wiesbaden (DE). LANG, Ingo [DE/DE]; An der Selzer Muehle 40a, 55218 Ingelheim Am Rhein (DE).

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

— without international search report and to be republished upon receipt of that report

(54) Title: ANGIOTENSIN II RECEPTOR ANTAGONIST FOR THE PREVENTION OR TREATMENT OF SYSTEMIC DISEASES IN CATS

(57) Abstract: The present invention relates to a method of prophylaxis or treatment of systemic diseases in cats, wherein the method comprising administration of a therapeutically effective amount of angiotensin II receptor 1 (AT-1) antagonist (sartan) to a cat in need of such a treatment.

WO 2008/040774 A2

ANGIOTENSIN II RECEPTOR ANTAGONIST FOR
THE PREVENTION OR TREATMENT OF SYSTEMIC DISEASES IN CATS

5 FIELD OF INVENTION:

The present invention relates to the field of veterinary medicine, especially to the prophylaxis or treatment of systemic diseases in cats. In particular, the present invention relates to a method of prophylaxis or treatment of systemic diseases in cats, wherein the method comprising administration of a therapeutically effective
10 amount of angiotensin II receptor 1 (AT-1) antagonist (sartan) to a cat in need of such a treatment.

BACKGROUND OF THE INVENTION:

The prevalence of renal disease is high in aged cats, whereas chronic renal failure is
15 considered the most important one. The prevalence of chronic kidney disease (CKD) in cats is reported to reach up to 20% with 53% of cats were older than 7 years (Lefebvre, Toutain 2004, *J. Vet. Pharm. Therap.* 27, 265 – 281; Wolf AM North. Am. Vet. Congress 2006). Survival in cats with mild to moderate azotemia and extrarenal clinical signs (IRIS stage 2 & 3) ranged from 1 to 3 years. Early management and
20 therapy is considered to successfully influence prognosis for CKD (Wolf AM North Am. Vet Congress 2006)

Chronic renal failure (CRF), at least in its final stage is, regardless of the underlying causes, characterized by irreversible structural lesions of the kidney. Thereby,
25 progressive irreversible lesions initially localized to one portion of the nephron (e.g. glomeruli, peritubular capillaries, tubules or interstitial tissue), are eventually responsible for the development of lesions in the remaining, but initially unaffected portions of nephrons due to their functional interdependencies. New nephrons cannot be formed to replace others irreversibly destroyed by disease . In a study of biopsy
30 findings in cats with primary renal azotemia, tubulointerstitial nephritis was observed in 70%, glomerulonephropathy occurred in 15%, lymphoma in 11% and amyloidosis was observed in 2% of the samples. CRF is recognized by reduced kidney function or the presence of kidney damage (Polzin, Osborne, Ross 2005 in : Ettinger SJ,

Feldman CE (eds.) Textbook of Veterinary Internal Medicine, 6th, Vol 2. Chapter 260, 1756 -1785).

Angiotensin II plays an important part in pathophysiology, particularly as the most
5 potent agent for increasing blood pressure in humans. It is known that in addition to
its effect of raising blood pressure Angiotensin II also has growth-promoting effects
which contribute to left ventricular hypertrophy, vascular thickening, atherosclerosis,
renal failure and stroke. In small animals, inhibition of the effects of Angiotensin II, via
either ACE inhibitors have been shown to exhibit renoprotective effects through their
10 simultaneous capacity to decrease blood pressure and control proteinuria.

Current therapy aims to delay the progression of the disease in cats by improving
renal function, especially glomerular function by maintaining glomerular perfusion.
This includes dietary protein restriction, modification of dietary lipid intake, phosphate
15 restriction and treatment with angiotensin-converting enzyme (ACE) inhibitors (*P.J.
Barber (2004) The Kidney, in: Chandler EA, Gaskell CJ, Gaskell RM (eds.) Feline
Medicine and Therapeutics, 3rd edition, Blackwell Publishing, Oxford, UK).*

ACE inhibitors, especially enalapril, benazepril, imidapril and ramipril, have been
20 initially developed in small animal medicine to control chronic heart failure (CHF).
Based on the pathophysiological role of the renin-angiotensin-aldosterone system
(RAAS) in progression of chronic heart failure and in progression of renal damage,
these agents have been shown to be useful in the treatment of chronic kidney
disease (CKD) in order to delay progression of disease and reduce morbidity and
25 suffering in small animals, including cats. Sound evidence for this is probably the
recent approval of benazepril in Europe for the treatment of feline CRF (*Lefebvre
Toutain, 2004 J Vet Pharm Therap 27, 265-281*). However, the renoprotection of
ACE inhibitor was likely mediated by the effect on proteinuria rather than by blood
pressure reduction. This has been shown for ramipril, since the effect on blood
30 pressure was comparable to that of placebo while the proteinuria was reduced
(*Remuzzi et al., 2006 J Clin Invest 116, (2) 288-296*).

- 3 -

From a clinical point of view, ACE inhibitors are not the preferred target to block the RAAS because of the lack of specificity for Angiotensin I and the "angiotensin escape" phenomenon; where alternate enzymatic pathways such as cathepsin, trypsin or the heart chymase can also convert Angiotensin I. Moreover, during long term treatment with ACE inhibitors, ACE activity is upregulated and Angiotensin I levels are high due to the stimulated renin secretion (*Burnier & Brunner 2000 The Lancet, 355 637-645*).

Thus, one objective of the present invention consists in providing a new therapeutic approach for the treatment or prophylaxis of cats against chronic kidney disease.

A further more general aspect of the present invention consists in providing a new therapeutic approach for the treatment or prophylaxis of cats against systemic diseases; preferably against systemic diseases which are related to Angiotensin II or associated with the renin-angiotensin-aldosterone system (RAAS).

DESCRIPTION OF THE INVENTION:

Description of Figures:

Figure 1: Inhibition of blood pressure increase by angiotensin II receptor 1 antagonist

Detailed Description of the Invention:

Before the embodiments of the present invention it shall be noted that as used herein and in the appended claims, the singular forms "a", "an", and "the" include plural reference unless the context clearly dictates otherwise. Thus, for example, reference to "a preparation" includes a plurality of such preparations, reference to the "carrier" is a reference to one or more carriers and equivalents thereof known to those skilled in the art, and so forth. Unless defined otherwise, all technical and scientific terms used herein have the same meanings as commonly understood by one of ordinary skill in the art to which this invention belongs. All given ranges and values may vary by 1 to 5 % unless indicated otherwise or known otherwise by the person skilled in the art, therefore, the term "about" was omitted from the description. Although any methods and materials similar or equivalent to those described herein can be used in the practice or testing of the present invention, the preferred methods, devices, and

- 4 -

materials are now described. All publications mentioned herein are incorporated herein by reference for the purpose of describing and disclosing the substances, excipients, carriers, and methodologies as reported in the publications which might be used in connection with the invention. Nothing herein is to be construed as an admission that the invention is not entitled to antedate such disclosure by virtue of prior invention.

The solution to the above technical problem is achieved by the description and the embodiments characterized in the claims.

10

To date, the use of angiotensin II receptor 1 antagonists (sartans) in cats is not described for any indication. Blockage of angiotensin II receptor 1 is a treatment concept which differs from blockage of angiotensin converting enzyme as known from the ACE-inhibitors. Receptor blockage is more specific and complete and further downstream in the physiologic cascade of the RAAS system. The present invention is based on various unexpected findings:

15

It was surprisingly found that cats tolerate a pharmacodynamically effective dose of sartans. In a open-label study in nondiabetic, hypertensive human patients with proteinuric nephropathies the effects on renal outcome of low (80 mg once daily) and high dose (80 mg twice daily) telmisartan were compared. The results reinforced the concept that more effective RAAS inhibition achieved by a high dose of 160 mg daily. This dose corresponds to a plasma level of about 2800 ± 2400 ng/ml ($C_{max} \pm SD$), which exceeds the no-effect doses in toxicities studies in animals such as dogs and rats (Investigator brochure 1994, data on file) The resulting dose of about 2 to 3 mg/Kg body weight and day was thus expected to be toxic in cats. Pilot-toxicity studies have surprisingly shown, that such a dose (up to 3 mg/kg) is well tolerable in cats.

20

25

Moreover, it was found that sartans effectively blocks the angiotensin II receptor 1 also in cats. This finding was all the more unexpected, as the absolute bioavailability in cats is very low and the mean residence time and plasma half life are rather short in cats as compared to human beings. The oral bioavailability was calculated to

30

33,6% as compared to human beings. The mean t_{max} oral was 0,44 hours and the C_{max} oral was 138,1 ng/ml. The mean $t_{1/2}$ oral was 2,17 hours. The mean AUC → ~ oral was calculated to 150 (ng x h /ml), and the mean V/f oral was 20,4 l/kg. The mean AUC → ~ intravenous was calculated to 385 (ng x h /ml). The mean $t_{1/2}$ intravenous was 2,25 hours and the mean V/f oral was 8,8 l/kg. From this information, which was newly generated, it can be concluded that sartans, preferably telmisartan, can be used to treat cats with systemic diseases, preferably with chronic kidney disease, such as for example chronic renal failure, including chronic renal insufficiency.

10

Table 1: Abbreviations

Abbreviation	Pharmacokinetic parameters
AUC	area under the plasma concentration time curve
C max	maximum measured plasma concentration
V/f	Volume of distribution (V) whereas f is the absolute bioavailability
MRT	mean residence time
t 1/2	terminal half-live
t max	time to reach Cmax

Thus, according to one embodiment, the present invention relates to a method for the prophylaxis or treatment of a systemic disease in cats, wherein the method comprising administration of a therapeutically effective amount of angiotensin II receptor 1 (AT-1) antagonist (sartan) to that cat in need of such a treatment.

The term "systematic disease" as used herein means but is not limited to cardiovascular such as dilated cardiomyopathy (DCM), mitral valve insufficiency (MI), hypertrophic cardiomyopathy (HCM); and other acquired or hereditary heart diseases, e.g. cardiopulmonary diseases, systemic hypertension for example hypertension associated with renal diseases, chronic renal failure and other vascular

20