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SUPERINTENDENTE DE INDUSTRIA Y COMERCIO

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REF: EXPEDIENTE 03-113-785

TÍTULO SOLICITADO: "Composiciones farmacéuticas de amlodipina y atorvastatina"

PUBLICACIÓN: Gaceta 554 de 29-07-2005, número de publicación 287

PRIORIDAD: US 60/309.133 de 31/06/2001

SOLICITANTE: WARNER-LAMBERT COMPANY LLC

APODERADO: CARLOS R. OLARTE

TRÁMITE: SUSTENTACIÓN DE OPOSICIÓN

JOSÉ LUIS REYES VILLAMIZAR, identificado como aparece al pie de mi firma, reconocido apoderado del opositor en el trámite de la referencia, estando dentro de los términos de la prórroga solicitada, por medio del presente escrito me permito ratificar y sustentar los argumentos del escrito principal de oposición, también radicado dentro del plazo de ley ante esa entidad.

#### I. RATIFICACIÓN

Reitero a su Despacho la solicitud de negar el beneficio patentario para la totalidad de las reivindicaciones contenidas en el expediente en referencia, por los argumentos que fueron definidos en el escrito de oposición del 25 de octubre de 2005. En efecto, es evidente que la composición farmacéutica que contiene Amlodipina y Atorvastatina en donde los dos componentes se combinan para formar una composición final para una forma de dosificación sólida carece de Novedad y de Nivel inventivo, debido a la materia revelada en la

PCT/WO/99/11259 publicada en marzo 11 de 1999, es decir, antes de la fecha de prioridad de la solicitud en trámite.

En esta publicación internacional se revela una combinación farmacéutica que comprende Atorvastatina y Amlodipino o las sales de adición farmacéuticamente aceptables de cada compuesto, preferiblemente se refiere a la sal Hemicálcica de Atorvastatina y a la sal de Besilato de Amlodipina, los kits que contienen dichas combinaciones y el método par emplearlas en el tratamiento de angina pectoris, aterosclerosis entre otros, así como los vehículos y diluentes entre los que se encuentran Carbonato de Calcio y Fosfato de Calcio, junto con varios desintegrantes y lubricantes y rangos de dosificación coincidentes.

La solicitud colombiana en trámite pretende además, proteger un estuche que comprende a) Amlodipino, b) Atorvastatina, c) el vehículo en forma de dosificación unitaria y d) un recipiente. Esta pretensión es improcedente a la luz de la Decisión 486, pues resulta evidente su intención de amparar un método terapéutico. En cuanto al recipiente del literal d) hago notar que éste carece por completo de novedad y nivel inventivo, en especial considerando que el mismo solo se caracteriza en función de la cantidad que pueda albergar de producto y de la forma farmacéutica, pero no por sus propias características o propiedades; además permite la entrega de una manera adecuada ya sea al paciente o al cuerpo médico, del medicamento que es necesario en el tratamiento de determinada patología.

## II. COMPLEMENTO DE INFORMACIÓN

Como adición a lo expuesto en el punto precedente y en el escrito inicial de oposición, ruego al Despacho se sirva tener en cuenta de igual manera lo consignado a continuación:

A. La aplicación internacional WO 00/64443 "SYNERGISTIC EFFECTS OF AMLODIPINE AND ATORVASTATIN" publicada el 2 de noviembre de 2000 y con prioridades US 60/130,665 de 23-04-1999, US 60/145,305 de 23-07-1999, US 60/151,121 de 27-08-1999 y US 60/166,592 de 19-11-1999, que según el Informe del estado de la Técnica practicado a la WO 03/011283 A1 publicada en febrero 13 de 2003 y con prioridad US 60/309,133 de 31-07-2001 (Solicitud equivalente a la Colombiana 03-113-785) es un documento señalado dentro de

la categoría "X"-*documento de particular relevancia; la invención reclaraza no puede ser considerada nueva o que involucre nivel inventivo* - en la cual se revelan composiciones farmacéuticas que comprenden:

- a) una cantidad terapéuticamente efectiva de Amlodipina o derivados de la misma como Besilato de Amlodipina;
- b) una cantidad terapéuticamente efectiva de un compuesto de Atorvastatina seleccionado del grupo que consiste de la sal Hemicálcica de Atorvastatina y metabolitos hidroxilados de Atorvastatina; y
- c) agentes de formulación farmacéuticamente aceptables

Estas combinaciones de Amlodipina con Atorvastatina o metabolitos de ésta muestran un efecto antioxidante sinérgico en la prevención de la peroxidación lipídica, el cual es atribuido a las estructuras químicas de estos compuestos y a su interacción molecular con moléculas de fosfolípidos; esto hace que la combinación en cuestión pueda ser usada para tratar desórdenes cardiovasculares.

Como se puede observar y teniendo en cuenta lo revelado en las reivindicaciones de la solicitud colombiana en trámite, podemos concluir en este caso que, en esta anterioridad ya se proponía la combinación de Atorvastatina y Amlodipino con un evidente efecto sinérgico en el tratamiento de enfermedades cardiovasculares, en consecuencia, la materia revelada en la publicación Internacional PCT WO 00/64443 pertenece al estado del arte, y, que en consecuencia, las reivindicaciones de la solicitud 03-113-785 por lo menos carecen de nivel inventivo.

- B. La aplicación internacional WO 00/73271 A1 "MUTUAL SALT OF AMLODIPINE AND ATORVASTATIN" publicada el 7 de diciembre de 2000 y con prioridad US 60/136,269 de 27-05-1999, que según el Informe del estado de la Técnica practicado a la WO 03/011283 A1 publicada en febrero 13 de 2003 y con prioridad US 60/309,133 de 31-07-2001 (Solicitud equivalente a la Colombiana 03-113-785) es un documento señalado dentro de la categoría "X"- tal como el explicado en el numeral A-, la cual se refiere a la sal mutua de Amlodipina y Atorvastatina, composiciones farmacéuticas de los mismos y a métodos de tratamiento de angina pectoris, aterosclerosis y combinación de hipertensión e hiperlipidemia.

Más específicamente en las reivindicaciones 16 a 19 de la anterioridad WO 00/73271 se menciona que la composición farmacéutica de la invención comprende una cantidad farmacéuticamente aceptable de Amlodipino o una sal del mismo, preferiblemente su sal de Besilato y una cantidad farmacéuticamente aceptable de Atorvastatina o una sal de la misma, preferiblemente la sal Hemicálcica de Atorvastatina.

C. Una vez más se puede observar que esta anterioridad también sugiere la combinación de dos principios activos como son Atorvastatina o una sal aceptable de la misma y de Amlodipino o una sal aceptable del mismo, utilizada en el tratamiento de de diversas enfermedades de tipo cardiovascular entre las que se puede mencionar a la Angina pectoris, aterosclerosis, hipertensión y hiperlipidemia, entre otros. Así, las reivindicaciones de la solicitud 03-113-785 en trámite, carecen al menos de nivel inventivo por obra de lo descrito anteriormente.

Por lo todo lo expuesto, reitero mi solicitud para que sea negada la solicitud en cuestión y como consecuencia de ello, se ordene el archivo del expediente debido al evidente incumplimiento de lo dispuesto en los artículos 14, 16, 18 y 20d de la Decisión 486 de 2000.

### **III. PRUEBAS**

Ruego que se tengan como tales, sin perjuicio de que el Despacho considere oficiosamente, en particular de las allegadas por el suscrito a los expedientes mencionados en este escrito, la siguiente:

1. Aplicación Internacional WO 00/64443 publicada 2 de noviembre de 2000, páginas 5, 6, 31-33, 35, 38-39.
2. Aplicación Internacional WO 00/73271 A1 publicada 7 de diciembre de 2000, páginas 6, 22-24.

Señor Superintendente,



**JOSÉ LUIS REYES VILLAMIZAR**

C.C. 79.152.473 de Usaquén

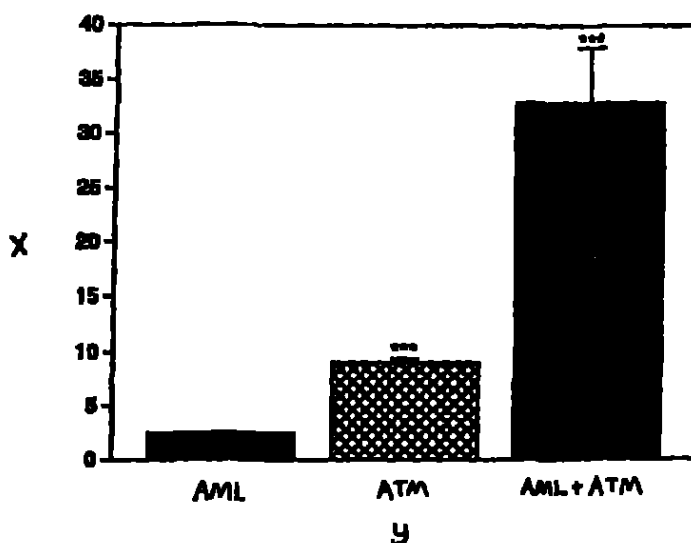
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## INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

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| (30) Priority Data:<br>60/130,665      23 April 1999 (23.04.99)      US<br>60/145,305      23 July 1999 (23.07.99)      US<br>60/151,121      27 August 1999 (27.08.99)      US<br>60/166,592      19 November 1999 (19.11.99)      US |  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                                                        |
| (71)(72) Applicant and Inventor: <b>MASON, R., Preston [US/US];<br/>Post Office Box 585, Sewickley, PA 15143 (US).</b>                                                                                                                 |  | Published<br><i>With international search report.</i>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                                                        |
| (74) Agents: <b>COHEN, Jerry et al.; Perkins, Smith &amp; Cohen, LLP,<br/>One Beacon Street, Boston, MA 02108 (US).</b>                                                                                                                |  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                                                                        |

(54) Title: SYNERGISTIC EFFECTS OF AMLODIPINE AND ATORVASTATIN



## (57) Abstract

The combination of amlodipine with either atorvastatin or atorvastatin metabolite shows a synergistic antioxidant effect on lipid peroxidation in human low-density lipoproteins and membrane vesicles enriched with polyunsaturated fatty acids. Inhibition of oxy-radical damage by this drug combination was observed at therapeutic levels in a manner that could not be reproduced by the combination of amlodipine with other statins or the natural antioxidant, vitamin E. The basis for this potent activity is attributed to the chemical structures of these compounds and their molecular interactions with phospholipid molecules, as determined by x-ray diffraction analyses. This combination therapy can be used to treat cardiovascular disorders, especially coronary artery disease, by increasing the resistance of low-density lipoproteins and vascular cell membranes against oxidative modification.

significantly enhance patient compliance with therapeutic regimens.

Therefore, it is an object of this invention to provide a combination therapy that will treat the multiple pathological processes involved in arterial and related heart disease. These include, but are not limited to, hypertension and hyperlipidemia. It is also an object of this invention to develop useful and convenient dosage levels and forms of such a combination therapeutic. Preferably, this pharmaceutical composition would have synergistic effects on these hallmarks of arterial and related heart disease, such that the individual effects of the components of this composition would be enhanced by their combination.

Thus, this invention encompasses a therapeutic goal for the treatment of CAD that entails the development of drugs that can simultaneously target multiple underlying disease processes that contribute to atherosclerosis, thereby altering the course of the disease. Therefore, using this invention, CAD therapy may have increased positive outcomes if the use of an antihypertensive agent and HMG-CoA reductase inhibitor was combined in a single delivery system.

#### Summary of the Invention

Unexpectedly, when AML and AT were combined, they had a synergistic effect in preventing lipid peroxidation in human low-density lipoproteins (LDL) and lipid membranes; this effect occurred in addition to their well-established

therapeutic effects on both dyslipidemia and hypertension. The activity of the combination is considered synergistic as the measured effect significantly exceeded any additive effects of the two drugs. Therefore, these agents have heretofore unrecognized synergistic antioxidant effects, a property that would enable these agents to increase the resistance of LDL and vascular cell membranes to oxidative modification during atherogenesis. Indeed, oxidative modification of lipids is a well-established cause of injury to the endothelium and underlying smooth muscle (Ross R. Atherosclerosis -- An inflammatory disease. *N. Engl. J. Med.* 1999; 340:115-126; Diaz MN, Frei B, Vita JA, Keaney JF. Antioxidants and atherosclerotic heart disease. *N. Engl. J. Med.* 1997; 337:408-416). Lipophilic agents that protect against lipid peroxidation have been shown to reduce lesion development in various models of atherosclerosis as well as clinical studies (Diaz MN, Frei B, Vita JA, Keaney JF. Antioxidants and atherosclerotic heart disease. *N. Engl. J. Med.* 1997; 337:408-416). Moreover, the benefit associated with hypolipidemic therapy is attributed to both its effect on plasma very low-density lipoproteins (VLDL), LDL, and high-density lipoproteins (HDL) levels and, as a consequence, to a reduction in the potential formation of atherogenic oxidized lipoproteins.

Scientific analyses that support the combined use of AML (Norvasc<sup>®</sup>) and AT (Lipitor<sup>®</sup>) in a single delivery system for the treatment of cardiovascular disease are described in this invention. Specifically, the synergistic antioxidant activities of

1. A pharmaceutical composition comprising:
  - (a) a therapeutically effective amount of amlodipine;
  - (b) a therapeutically effective amount of an atorvastatin compound selected from the group consisting of atorvastatin and hydroxylated atorvastatin metabolite; and
  - 5 (c) pharmaceutically acceptable formulation agents.
2. The pharmaceutical composition of claim 1 wherein amlodipine comprises a therapeutically effective derivative of amlodipine.
- 10 3. The pharmaceutical composition of claim 2 wherein the therapeutically effective derivative of amlodipine comprises amlodipine besylate.
4. The pharmaceutical composition of claim 1 wherein the atorvastatin compound comprises a therapeutically effective derivative of the atorvastatin compound.
- 15 5. The pharmaceutical composition of claim 4 wherein the therapeutically effective derivative of the atorvastatin compound is a hemicalcium salt.
6. The pharmaceutical composition of claim 1 wherein said pharmaceutical
- 20 composition reduces the risk of arterial and related heart disease.

7. The pharmaceutical composition of claim 6 wherein said arterial and related heart disease is selected from the group consisting of hypertension, hyperlipdemia, atherosclerosis, arteriosclerosis, coronary artery disease, myocardial infarction, congestive heart failure, stroke, and angina pectoris.

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8. The pharmaceutical composition of claim 1 wherein said pharmaceutical composition lowers blood pressure.

9. The pharmaceutical composition of claim 8 wherein said pharmaceutical composition lowers blood pressure to a level consistent with a reduced risk of arterial and related heart disease.

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10. The pharmaceutical composition of claim 8 wherein said pharmaceutical composition lowers blood pressure to a level statistically equivalent to normal.

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11. The pharmaceutical composition of claim 1 wherein said pharmaceutical composition lowers systemic lipid concentrations.

12. The pharmaceutical composition of claim 11 wherein said pharmaceutical composition lowers systemic lipid concentrations to a level consistent with a reduced risk of arterial and related heart disease.

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13. The pharmaceutical composition of claim 11 wherein said pharmaceutical composition lowers systemic lipid concentrations to a level statistically equivalent to normal.

5 14. The pharmaceutical composition of claim 1 wherein said pharmaceutical composition lowers blood pressure and systemic lipid concentrations.

15. The pharmaceutical composition of claim 14 wherein said pharmaceutical composition lowers blood pressure and systemic lipid concentrations to a level  
10 consistent with a reduced risk of arterial and related heart disease.

16. The pharmaceutical composition of claim 14 wherein said pharmaceutical composition lowers blood pressure and systemic lipid concentrations to a level statistically equivalent to normal.

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17. The pharmaceutical composition of claim 1 wherein said pharmaceutical composition concomitantly lowers blood pressure and systemic lipid concentrations.

18. The pharmaceutical composition of claim 17 wherein said pharmaceutical  
20 composition concomitantly lowers blood pressure and systemic lipid concentrations to a level consistent with a reduced risk of arterial and related heart disease.

least partially from reduced lipid oxidation.

25. A pharmaceutical composition comprising:

- (a) a therapeutically effective amount of amlodipine;
- 5 (b) a therapeutically effective amount of an atorvastatin compound selected from the group consisting of atorvastatin and hydroxylated atorvastatin metabolite; and
- (c) pharmaceutically acceptable formulation agents wherein said pharmaceutical composition lowers blood pressure and systemic lipid concentrations.

- 10 26. The pharmaceutical composition of claim 25 wherein amlodipine comprises a therapeutically effective derivative of amlodipine.

27. The pharmaceutical composition of claim 26 wherein the therapeutically effective derivative of amlodipine comprises amlodipine besylate.

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28. The pharmaceutical composition of claim 25 wherein the atorvastatin compound comprises a therapeutically effective derivative of the atorvastatin compound.

29. The pharmaceutical composition of claim 28 wherein the therapeutically
- 20 effective derivative of the atorvastatin compound is a hemicalcium salt.

41. The pharmaceutical composition of claim 40 wherein said arterial and related heart disease is selected from the group consisting of hypertension, hyperlipdemia, atherosclerosis, arteriosclerosis, coronary artery disease, myocardial infarction, congestive heart failure, stroke, and angina pectoris.

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42. The pharmaceutical composition of claim 35 wherein said pharmaceutical composition lowers blood pressure and systemic lipid concentrations to a level consistent with a reduced risk of arterial and related heart disease.

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43. The pharmaceutical composition of claim 35 wherein said pharmaceutical composition lowers blood pressure and systemic lipid concentrations to a level statistically equivalent to normal.

44. A pharmaceutical composition comprising:

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- (a) a therapeutically effective amount of amlodipine;
  - (b) a therapeutically effective amount of an atorvastatin compound selected from the group consisting of atorvastatin and hydroxylated atorvastatin metabolite; and
  - (c) pharmaceutically acceptable formulation agents wherein said pharmaceutical composition synergistically lowers blood pressure and systemic lipid
- 20 concentrations.

45. The pharmaceutical composition of claim 44 wherein amlodipine comprises a

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therapeutically effective derivative of amlodipine.

46. The pharmaceutical composition of claim 45 wherein the therapeutically effective derivative of amlodipine comprises amlodipine besylate.

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47. The pharmaceutical composition of claim 44 wherein the atorvastatin compound comprises a therapeutically effective derivative of the atorvastatin compound.

48. The pharmaceutical composition of claim 47 wherein the therapeutically effective derivative of the atorvastatin compound is a hemicalcium salt.

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49. The pharmaceutical composition of claim 44 wherein said pharmaceutical composition reduces the risk of arterial and related heart disease.

50. The pharmaceutical composition of claim 49 wherein said arterial and related heart disease is selected from the group consisting of hypertension, hyperlipdemia, atherosclerosis, arteriosclerosis, coronary artery disease, myocardial infarction, congestive heart failure, stroke, and angina pectoris.

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51. The pharmaceutical composition of claim 44 wherein said pharmaceutical composition synergistically lowers blood pressure and systemic lipid concentrations to a level consistent with a reduced risk of arterial and related heart disease.

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(74) Agents: SPIEGEL, Allen, J. et al.; c/o Simpson, Allison,  
Urquhart-Dykes & Lord, 30 Welbeck Street, London W1M  
7PG (GB).

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(71) Applicant (for all designated States except US): PFIZER  
PRODUCTS INC. [US/US]; Eastern Point Road, Groton,  
CT 06340 (US).

(72) Inventor; and

Published:

(75) Inventor/Applicants (for US only): CHANG, George  
[US/US]; Pfizer Inc., Central Research Division, Eastern  
Point Road, Groton, CT 06340 (US). HAMANAKA,  
Ernest, Seichi [CA/US]; Pfizer Inc., Central Research  
Division, Eastern Point Road, Groton, CT 06340 (US).

— With international search report.

For two-letter codes and other abbreviations, refer to the "Guid-  
ance Notes on Codes and Abbreviations" appearing at the begin-  
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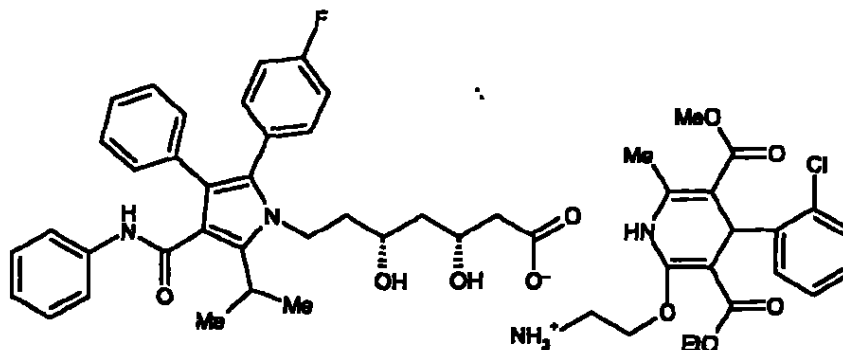
(54) Title: MUTUAL SALT OF AMLODIPINE AND ATORVASTATIN

(57) Abstract: This invention relates to a neutral salt of amlodipine and atorvastatin, pharmaceutical compositions thereof and methods of treating angina pectoris, atherosclerosis and combined hypertension and hyperlipidemia in mammals with such a neutral salt and compositions. This invention also relates to methods of managing cardiac risk in a mammal presenting with symptoms of cardiac risk, including humans by administering such a neutral salt and compositions.

## SUMMARY OF THE INVENTION

This invention is directed to a compound which is an atorvastatin salt of amlodipine. It is to be understood that the phrase "amlodipine salt of atorvastatin" is synonymous with the phrase "atorvastatin salt of amlodipine." Those phrases are used interchangeably throughout this specification and appendant claims.

This invention is particularly directed to an atorvastatin salt of amlodipine which is a compound of formula I,



This invention is still more particularly directed to a compound of formula I wherein the carbon atom at the 4-position of the dihydropyridine ring has the (R)-configuration, e.g., 7-[2-(4-fluoro-phenyl)-5-isopropyl-3-phenyl-4-phenylcarbamoyl-pyrrol-1-yl]-3,5-dihydroxy-heptanoate salt with 2-(2-amino-ethoxymethyl)-4(R)-(2-chloro-phenyl)-6-methyl-1,4-dihydro-pyridine-3,5-dicarboxylic acid 3-ethyl ester 5-methyl ester.

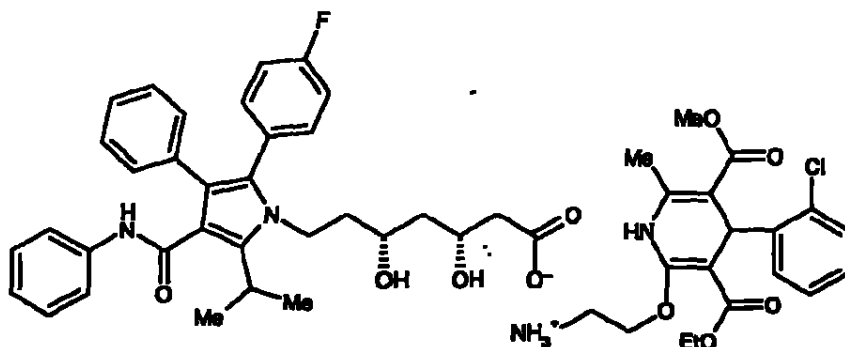
This invention is also more particularly directed to a compound of formula I wherein the carbon atom at the 4-position of the dihydropyridine ring has the (S)-configuration, 7-[2-(4-fluoro-phenyl)-5-isopropyl-3-phenyl-4-phenylcarbamoyl-pyrrol-1-yl]-3,5-dihydroxy-heptanoate salt with 2-(2-amino-ethoxymethyl)-4(S)-(2-chloro-phenyl)-6-methyl-1,4-dihydro-pyridine-3,5-dicarboxylic acid 3-ethyl ester 5-methyl ester.

This invention is also directed to pharmaceutical compositions comprising a compound of formula I and a pharmaceutically acceptable carrier, vehicle or diluent.

This invention is also directed to methods of treating angina pectoris in a mammal suffering from angina pectoris comprising administering to said mammal an angina pectoris treating effective amount of a compound of formula I.

## CLAIMS

1. A compound which is an atorvastatin salt of amlodipine.
2. A compound of claim 1 which is



3. A compound of claim 2 wherein the carbon atom at the 4-position of the dihydropyridine ring has the (R)-configuration.
4. A compound of claim 2 wherein the carbon atom at the 4-position of the dihydropyridine ring has the (S)-configuration.
5. A pharmaceutical composition comprising a compound of claim 1 and a pharmaceutically acceptable carrier, vehicle or diluent.
6. A method of treating angina pectoris in a mammal suffering from angina pectoris comprising administering to said mammal an angina pectoris treating effective amount of a compound of claim 1.
7. A method of treating angina pectoris in a mammal suffering from angina pectoris comprising administering to said mammal an angina pectoris treating effective amount of a pharmaceutical composition of claim 5.
8. A method of treating hypertension and hyperlipidemia in a mammal suffering from hypertension and hyperlipidemia comprising administering to said mammal a hypertension and hyperlipidemia treating effective amount of a compound of claim 1.
9. A method of treating hypertension and hyperlipidemia in a mammal suffering from hypertension and hyperlipidemia comprising administering to said mammal a hypertension and hyperlipidemia treating effective amount of a pharmaceutical composition of claim 5.
10. A method of treating atherosclerosis in a mammal suffering from atherosclerosis comprising administering to said mammal an antiatherosclerosis effective amount of a compound of claim 1.

11. A method of claim 10 wherein said atherosclerosis is manifested by a slowing of the progression of atherosclerotic plaques.
12. A method of claim 10 wherein said atherosclerosis is manifested by a regression of atherosclerotic plaques.
- 5 13. A method of treating atherosclerosis in a mammal suffering from atherosclerosis comprising administering to said mammal an antiatherosclerosis effective amount of a pharmaceutical composition of claim 5.
14. A method of managing cardiac risk in a mammal at risk of suffering an adverse cardiac event, comprising administering to said mammal a cardiac risk  
10 treating effective amount of a compound of claim 1.
15. A method of managing cardiac risk in a mammal at risk of suffering an adverse cardiac event, comprising administering to said mammal a cardiac risk treating effective amount of a pharmaceutical composition of claim 5.
16. A pharmaceutical composition comprising an amount of a compound  
15 of claim 1 and amlodipine or a pharmaceutically acceptable salt thereof.
17. A pharmaceutical composition of claim 16 comprising amlodipine besylate.
18. A pharmaceutical composition comprising an amount of a compound of claim 1 and atorvastatin or a pharmaceutically acceptable salt thereof.
- 20 19. A pharmaceutical composition of claim 18 comprising the hemicalcium salt of atorvastatin.
20. A method of treating angina pectoris in a mammal suffering from angina pectoris comprising administering to said mammal an effective amount of a pharmaceutical composition of claim 16.
- 25 21. A method of treating angina pectoris in a mammal suffering from angina pectoris comprising administering to said mammal an effective amount of a pharmaceutical composition of claim 18.
22. A method of treating atherosclerosis in a mammal comprising administering to said mammal an atherosclerosis treating effective amount of a  
30 pharmaceutical composition of claim 16.
23. A method of treating atherosclerosis in a mammal comprising administering to said mammal an atherosclerosis treating effective amount of a pharmaceutical composition of claim 18.

24. A method of managing cardiac risk in a mammal comprising administering to said mammal a cardiac risk treating effective amount of a pharmaceutical composition of claim 16.
- 5 25. A method of managing cardiac risk in a mammal comprising administering to said mammal a cardiac risk treating effective amount of a pharmaceutical composition of claim 18.
26. A method of treating a mammal suffering from hypertension and hyperlipidemia comprising administering to said mammal a hypertension and hyperlipidemia treating effective amount of a pharmaceutical composition of claim 16.
- 10 27. A method of treating a mammal suffering from hypertension and hyperlipidemia comprising administering to said mammal a hypertension and hyperlipidemia treating effective amount of a pharmaceutical composition of claim 18.
28. A method of delivering amlodipine *in vivo* by administering a compound of claim 1 or a pharmaceutically acceptable salt thereof to a mammal.
- 15 29. A method of claim 28 wherein said mammal is a human.
30. A method of delivering atorvastatin *in vivo* by administering a compound of claim 1 or a pharmaceutically acceptable salt thereof to a mammal.
31. A method of claim 30 wherein said mammal is a human.
32. A method of treating a mammal comprising administering to said mammal an amount of a compound of claim 1 and an amount of amlodipine or a pharmaceutically acceptable salt thereof.
- 20 33. A method of treating a mammal comprising administering to said mammal an amount of a compound of claim 1 and an amount of atorvastatin or a pharmaceutically acceptable salt thereof.
- 25 34. A method of treating a mammal with amlodipine comprising administering to said mammal a compound of claim 1.
35. A method of treating a mammal with atorvastatin comprising administering to said mammal a compound of claim 1.

2020  
Bogotá, D.C.,

**Doctor:**  
**Carlos Olarte**  
**Apoderado**

**Oficio N°:** 1497

**ASUNTO:**

|                   |           |
|-------------------|-----------|
| Radicación PCT N° | 03-113785 |
| Trámite           | 011       |
| Evento            | 379       |
| Actuación         | 440       |
| Folios            | 024       |

Con fundamento en lo previsto por el artículo 43 de la Decisión 486 de la Comisión de la Comunidad Andina, se le comunica que la oposición presentada por el doctor José Luis Reyes Villamizar, en su calidad de apoderado de Tecnoquímicas S.A., reúne los requisitos formales exigidos por la ley al momento de su presentación.

En cumplimiento de lo dispuesto en la citada norma, se le concede el término de sesenta (60) días hábiles siguientes a la fecha de notificación del presente oficio, para que haga valer sus argumentaciones y presente pruebas.

Notifíquese el presente oficio conforme a lo dispuesto en el numeral 5.2, literal e), del capítulo quinto del título primero de la Circular Única N° 10 de 2001.

  
**ALIX CARMENZA CESPEDES DE VERGEL**  
Jefe de la División de Nuevas Creaciones.

El anterior requerimiento fue notificado por fijación en lista de fecha, 10 FEB. 2006.

202021

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10- Feb-2006 -

Frederick 101111.

2020  
Bogotá, D.C.,

**D ctor:**  
**Carlos Olarte**  
**Apoderado**

**Oficio N°:** 1433

**ASUNTO:**

|                   |           |
|-------------------|-----------|
| Radicación PCT N° | 03-113785 |
| Trámite           | 011       |
| Evento            | 379       |
| Actuación         | 440       |
| Folios            | 012       |

Con fundamento en lo previsto por el artículo 43 de la Decisión 486 de la Comisión de la Comunidad Andina, se le comunica que la oposición presentada por el doctor Luis Fernando Rincón, en su calidad de apoderado de Procaps S.A., reúne los requisitos formales exigidos por la ley al momento de su presentación.

En cumplimiento de lo dispuesto en la citada norma, se le concede el término de sesenta (60) días hábiles siguientes a la fecha de notificación del presente oficio, para que haga valer sus argumentaciones y presente pruebas.

Notifíquese el presente oficio conforme a lo dispuesto en el numeral 5.2, literal e), del capítulo quinto del título primero de la Circular Única N° 10 de 2001.

  
**ALIX CARMENZA CESPEDES DE VERGEL**  
Jefe de la División de Nuevas Creaciones.

**10 FEB. 2021**

El anterior requerimiento fue notificado por fijación en lista de fecha, \_\_\_\_\_.

202021

107/P.1 PCT

449

23-113785

Título: Composiciones farmacéuticas de  
amlodipina y atorvastatina.

Solicitante: WARNER LAMBERT COMPANY LLC

Dirección: 201 Tabor Road, Morris Plains,  
New Jersey 07950, Estados  
Unidos de América.

Aipoderado CARLOS R. OLARTE.

Fecha: Diciembre 31, 2003.

Rehro copia hastado.  
10- feb-2006.  
Frederick Toms