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Señores

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO

DIVISIÓN DE NUEVAS CREACIONES

E. _____ S. _____

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO



No. 07-081364-00002-0000

Fecha: 2007-11-27 10:17:14 - DE: 2026 NUECREACION
No. 11 - PALENE: 70 - Ley 379 FASENACIONAL II
No. 444 RESPUESTA AL OFICIO 10

Ref.: Expediente N°. 07-081.364

Solicitud de Patente de Invención titulada: "COMBINACIONES FARMACEUTICAS QUE COMPRENDEN UN UNHIBIDOR DE LA RENINA, UNA ENDOPEPTIDASA NEUTRAL Y OPCIONALMENTE UN DIURETICO Y UN BLOQUEADOR DEL RECEPTOR DE LA ANGIOTENSINA II".

Solicitante: NOVARTIS A.G.

RESPUESTA AL OFICIO N°. 13107 NOTIFICADO
POR FIJACION EN LISTA No. 378, DE FECHA 12 DE OCTUBRE DE 2007,
(EXAMEN DE FORMA)

CARLOS R. OLARTE, mayor de edad y vecino de Bogotá, identificado tal como aparece al pie de mi firma, en mi carácter de apoderado de la sociedad en referencia, me permito dar respuesta al auto emanado de ese Despacho, dentro del término legal previsto en el artículo 39 de la Decisión 486, en los siguientes términos:

1. En respuesta a la primera observación del Examinador, me permito aclarar al despacho que la presente ~~Solicitud entra en Fase Nacional Capítulo I~~ y no Capítulo II como inicialmente se presentó. Para tal efecto, adjunto copia del Reporte Preliminar Internacional de Patentabilidad, el cual, valga la pena aclarar, no contiene anexos.

2. En respuesta a la segunda observación del Examinador, me permito presentar un nuevo título: "COMBINACIONES FARMACEUTICAS QUE COMPRENDEN UN UNHIBIDOR DE LA RENINA, UNA ENDOPEPTIDASA NEUTRAL Y OPCIONALMENTE UN

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INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY (Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44bis)

Applicant's or agent's file reference PC/4-34138A	FOR FURTHER ACTION		See item 4 below
International application No. PCT/US2006/004401	International filing date (day/month/year) 09 February 2006 (09.02.2006)	Priority date (day/month/year) 11 February 2005 (11.02.2005)	
International Patent Classification (8th edition unless older edition indicated) See relevant information in Form PCT/ISA/237			
Applicant NOVARTIS AG			

1.	This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 bis.1(a).		
2.	This REPORT consists of a total of 8 sheets, including this cover sheet. In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead.		
3.	This report contains indications relating to the following items:		
	☒ Box No. I	Basis of the report	
	☐ Box No. II	Priority	
	☒ Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability	
	☐ Box No. IV	Lack of unity of invention	
	☒ Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement	
	☐ Box No. VI	Certain documents cited	
	☐ Box No. VII	Certain defects in the international application	
	☒ Box No. VIII	Certain observations on the international application	
4.	The International Bureau will communicate this report to designated Offices in accordance with Rules 44bis.3(c) and 93bis.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44bis .2).		

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No. +41 22 338 82 70	Date of issuance of this report 16 October 2007 (16.10.2007)
	Authorized officer Beate Gliffo-Schmitt e-mail: pt03.pct@wipo.int

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To:

see form PCT/ISA/220

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WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY
(PCT Rule 43bis.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.
PCT/US2006/004401

International filing date (day/month/year)
09.02.2006

Priority date (day/month/year)
11.02.2005

International Patent Classification (IPC) or both national classification and IPC

INV. A61K31/165 A61K31/192 A61K31/216 A61K31/549 A61K31/41 A61P3/06 A61P3/10 A61P9/00 A61P9/04
A61P9/10 A61P9/12 A61P13/12 A61P27/06

Applicant
NOVARTIS AG

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☒ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:



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Date of completion of
this opinion

see form
PCT/ISA/210

Authorized Officer

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Telephone No. +49 89 2339-8467



**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
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Box No. 1 Basis of the opinion

1. With regard to the language, this opinion has been established on the basis of:
 - ☒ the international application in the language in which it was filed
 - ☐ a translation of the international application into , which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1 (b)).
2. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material:
 - ☐ a sequence listing
 - ☐ table(s) related to the sequence listing
 - b. format of material:
 - ☐ on paper
 - ☐ in electronic form
 - c. time of filing/furnishing:
 - ☐ contained in the international application as filed.
 - ☐ filed together with the international application in electronic form.
 - ☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

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Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of

☐ the entire international application

☒ claims Nos. 1-36 (all in part)

because:

☒ the said international application, or the said claims Nos. 1-36 (I.A. only) relate to the following subject matter which does not require an international search (*specify*):

see separate sheet

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed (*specify*):

☒ no international search report has been established for the whole application or for said claims Nos. 1-36 (all in part)

☐ a meaningful opinion could not be formed without the sequence listing; the applicant did not, within the prescribed time limit:

☐ furnish a sequence listing on paper complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Searching Authority in a form and manner acceptable to it.

☐ furnish a sequence listing in electronic form complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Searching Authority in a form and manner acceptable to it.

☐ pay the required late furnishing fee for the furnishing of a sequence listing in response to an invitation under Rules 13ter.1(a) or (b).

☐ a meaningful opinion could not be formed without the tables related to the sequence listings; the applicant did not, within the prescribed time limit, furnish such tables in electronic form complying with the technical requirements provided for in Annex C-bis of the Administrative Instructions, and such tables were not available to the International Searching Authority in a form and manner acceptable to it.

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in electronic form only, do not comply with the technical requirements provided for in Annex C-bis of the Administrative Instructions.

☐ See Supplemental Box for further details

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

Claims 19-27 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Reference is made to the following documents:

- D1: EP-A-0 498 361 (SCHERING CORP [US]) 12 August 1992 (1992-08-12)
- D2: WO 02/40007 A (NOVARTIS AG [CH]; NOVARTIS ERFIND VERWALT GMBH [AT]; HEWITT WILLIAM [U] 23 May 2002 (2002-05-23)
- D3: WO 03/099279 A (NOVARTIS AG [CH]; NOVARTIS PHARMA GMBH [AT]; HOLMES DAVID GRENVILLE [C] 4 December 2003 (2003-12-04)
- D4: WO 03/059345 A (NOVARTIS AG [CH]; NOVARTIS PHARMA GMBH [AT]; WEBB RANDY LEE [US]; KSAN) 24 July 2003 (2003-07-24)
- D5: WO 03/097098 A (NOVARTIS AG [CH]; NOVARTIS PHARMA GMBH [AT]; FELDMAN DAVID LOUIS [US]) 27 November 2003 (2003-11-27)

Novelty - Article 33(2) PCT

It is noted that components (a) and (b) are optional features in the independent claims.

D1 discloses pharmaceutical compositions for treating hypertension and congestive heart failure comprising a NEP inhibitor and either a renin inhibitor or an angiotensin II antagonist.

D2 discloses compositions comprising a renin inhibitor (Aliskiren), a dual angiotensin converting enzyme/neutral endopeptidase (ACE/NEP) and a diuretic (hydrochlorothiazide).

D3 discloses compositions comprising - apart from a DPP-IV inhibitor - a renin inhibitor, preferably aliskiren, and a NEP inhibitor. A further component is valsartan (claim 10). The

compositions are used for treating a variety of diseases, including diabetes mellitus, hypertension, congestive heart failure and renal failure.

It should be noted that the fact that a medicament works under the guise of an alternative mechanism of action is not considered to be novelty-establishing technical feature when the therapeutic application is the same (cf. comments on Clarity under Item VIII below).

Documents D1-D3 disclose the features of the independent claims 1, 9, 19 and 28 and destroy novelty for these claims.

Inventive Step - Article 33(3) PCT

A full assessment of the inventive step can only be performed when the applicant has provided independent claims that relate to novel subject-matter. The following preliminary remarks can however be made.

D4 describes pharmaceutical compositions comprising a NEP inhibitor N-(3-carboxy-1-oxopropyl)- (4S)-p-phenylphenylmethyl)-4-amino-2R- methylbutanoic acid ethyl ester and angiotensin II antagonist valsartan. These compositions are intended for treating the same diseases as in claims 20 and 29 of the current application. The addition of a diuretic, especially hydrochlorothiazide, is disclosed (page 16, bottom and claim 4).

D5 relates to pharmaceutical compositions comprising a renin inhibitor, preferably aliskiren hemi-fumarate, a calcium channel blocker, and a diuretic, preferably hydrochlorothiazide. The treatment of the same diseases as in claims 20 and 29 of the current application is intended (cf. claims 6-8 of D5).

In view of the lack of substantiated evidence of any synergism or any other unexpected effect between the renin inhibitor and the NEP inhibitor, the subject-matter of claims 1-36 lacks an inventive step over D4 combined with D5

Industrial Applicability - Article 33(4) PCT

For the assessment of the present claims 19-36 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING
AUTHORITY (SEPARATE SHEET)**

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example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

Re Item VIII

Certain observations on the international application

It is noted that the therapeutic application of claims 19 and 28 is defined in terms of a mechanism of action; "condition mediated by angiotensin II and/or neutral endopeptidase activity". As it is not clear what diseases fall under this functional definition, these claims lack clarity under Article 6 PCT. Due to this lack of clarity, the claims are interpreted in view of the diseases listed in claims 20 and 29.

The examples show various formulations for valsartan and aliskiren hemi-fumarate. There is no substantiated evidence that problem is solved, i.e. that the claimed therapeutic effect really exists.

REPUBLICA DE COLOMBIA
SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO

Folio 134

2020
Bogotá D.C.,

Doctor(a)
OLARTE GARCIA CARLOS REINALDO
Apoderado(a) y/o Representante de
NOVARTIS AG

REFERENCIA	Radicación No.	07 81364
	Solicitud internacional	PCT/US2006/004401
	Fecha inicio fase nacional	11/09/2007
	Trámite	11
	Evento	379
	Actuación	416
	Oficio No.	6475
	Folios	1

Teniendo en cuenta que la solicitud de privilegio de patente que se tramita bajo el expediente indicado en la referencia, reúne los requisitos de forma establecidos en la Decisión 486 de la Comisión de la Comunidad Andina, el Tratado de Cooperación en Materia de Patentes (PCT), el Reglamento y la Circular Única de la Superintendencia de Industria y Comercio, se envía el extracto de la solicitud a la Oficina de Comunicaciones para efecto de su publicación en la Gaceta de Propiedad Industrial.

Cúmplase
Dado en Bogotá DC,

24 JUL 2008

ALIX CARMENZA CESPEDES DE VERGEL
Jefe de la división de Nuevas Creaciones

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