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Superintendencia de Industria y Comercio
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SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO



No. 07-076601-00002-0000

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Referencia : Expediente No. 07.076.601
Asunto : Solicitud de patente para: **2-FENILINDOLES
COMO ANTAGONISTAS DEL RECEPTOR DE LA
PROSTAGLANDINA D2**
Solicitante : **AVENTIS PHARMACEUTICALS, INC.**
Fecha solicitud: 26 de julio de 2007

1. Yo, Emilio FERRERO, obrando como apoderado del solicitante en el asunto de la referencia, doy respuesta al Oficio N° 13101, notificado por fijación en lista de fecha 12 de octubre de 2007.

2. Mediante el Oficio N° 13101 se puso en conocimiento del solicitante el resultado del examen de forma realizado por ese Despacho, requiriéndole para completar el siguiente requisito:

2.1. Traducción de los anexos del Reporte de Examen Preliminar Internacional: Adjunto al presente escrito el correspondiente Reporte Preliminar Internacional sobre Patentabilidad, expedido por la Administración encargada, el cual consta de 11 hojas, 7 del informe y 4 de anexos. Igualmente presento la traducción al español de las 4 páginas correspondientes a anexos.

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference US20030165WO		FOR FURTHER ACTION		See Form PCT/PEA/410
International application No. PCT/US2006/002738		International filing date (day/month/year) 25.01.2006	Priority date (day/month/year) 26.01.2005	
International Patent Classification (IPC) or national classification and IPC INV. C07D209/12				
Applicant Aventis Pharmaceuticals Inc				
1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36. 2. This REPORT consists of a total of <u>7</u> sheets, including this cover sheet. 3. This report is also accompanied by ANNEXES, comprising: a. ☒ sent to the applicant and to the International Bureau a total of <u>4</u> sheets, as follows: ☒ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions). ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box. b. ☐ (sent to the International Bureau only) a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in electronic form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 602 of the Administrative Instructions).				
4. 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				
Date of submission of the demand 2006-10-31		Date of completion of this report 30.03.2007		
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80288 Munich Tel. +49 89 2339 - 0 Tlx: 623886 epmu d Fax: +49 89 2339 - 4466		Authorized officer Von Daacke, Axel Telephone No. +49 89 2339-8266 		

**INTERNATIONAL PRELIMINARY REPORT
ON PATENTABILITY**

International application No.
PCT/US2006/002736

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Box No. I Basis of the report

1. With regard to the language, this report is based on

- ☒ 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 (under Rules 12.3(a) and 23.1(b))
 - ☐ publication of the international application (under Rule 12.4(a))
 - ☐ international preliminary examination (under Rules 55.2(a) and/or 55.3(a))

2. With regard to the elements* of the international application, this report is based on (replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report):

Description, Pages

1-20, 22-69	as originally filed
21	filed with telefax on 31.10.2006

Claims, Numbers

6-54	as originally filed
1-5	filed with telefax on 31.10.2006

- ☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing

3. ☐ The amendments have resulted in the cancellation of:

- ☐ the description, pages
- ☐ the claims, Nos.
- ☐ the drawings, sheets/figs
- ☐ the sequence listing (specify):
- ☐ any table(s) related to sequence listing (specify):

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

- ☐ the description, pages
- ☐ the claims, Nos.
- ☐ the drawings, sheets/figs
- ☐ the sequence listing (specify):
- ☐ any table(s) related to sequence listing (specify):

* If item 4 applies, some or all of these sheets may be marked "superseded."

**INTERNATIONAL PRELIMINARY REPORT
ON PATENTABILITY**

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

1. 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. 1-54 (part)

because:

☒ the said international application, or the said claims Nos. 46-54 (IA) relate to the following subject matter which does not require an international preliminary examination (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 said claims Nos. 1-54 (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 Preliminary Examining 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 Preliminary Examining 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) and 13ter.2.

☐ 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 Preliminary Examining 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 separate sheet for further details

**INTERNATIONAL PRELIMINARY REPORT
ON PATENTABILITY**

International application No.
PCT/US2006/002736

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	<u>1-54</u>
	No: Claims	
Inventive step (IS)	Yes: Claims	<u>1-54</u>
	No: Claims	
Industrial applicability (IA)	Yes: Claims	<u>1-45</u>
	No: Claims	

2. Citations and explanations (Rule 70.7):

see separate sheet

Box No. VI Certain documents cited

1. Certain published documents (Rule 70.10)

and / or

2. Non-written disclosures (Rule 70.9)

see separate sheet

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

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III NON-ESTABLISHMENT

1. Claims 46-54 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).
2. Due to the lack of structural information within the claims, the claimed object concerning the functional definitions "prodrugs" and "acid bioisosteres" have not been searched.

The following assessment of novelty and inventive step has been performed on the searched matter.

V REASONED STATEMENT

1. PRIOR ART

The documents cited in the International Search Report

- D1: CACCHI, SANDRO ET AL: "Palladium-catalyzed cyclization of o-alkynyltrifluoroacetanilides with allyl esters. A regioselective synthesis of 3-allylindoles" JOURNAL OF ORGANIC CHEMISTRY, 63(4), 1001-1011
CODEN: JOCEAH; ISSN: 0022-3263, 1998, XP002381255
- D2: EP-A1-0 639 567 (OTSUKA PHARMACEUTICAL FACTORY, INC., JAPAN) 22 February 1995 (1995-02-22)
- D3: FUKUYAMA, TOHRU ET AL: "A Novel Tin-Mediated Indole Synthesis" JOURNAL OF THE AMERICAN CHEMICAL SOCIETY, 116(7), 3127-8
CODEN: JACSAT; ISSN: 0002-7863, 1994, XP002381256
- D4: EP-A-1 600 440 (ONO PHARMACEUTICAL CO., LTD) 30 November 2005 (2005-11-30)
- D5: WO 2004/106302 A (ASTRAZENECA AB; BONNERT, ROGER; RASUL, RUKHSANA) 9 December 2004 (2004-12-09)

have been considered for the examination procedure. **See also Section VI, last paragraph.**

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2. NOVELTY

The subject-matter of Claims 1-3 is novel in view of D1-D3 (Article 33(2) PCT). D1-D3 disclose related compounds which are, however, not covered by the claims in questions, either due to the lack of definitions (i.e. R cannot denote R1S, R3 cannot denote alkenyl) or due to the disclaimer at the end of Claim 1.

3. INVENTIVE STEP

The claimed subject-matter appears also to fulfil the requirements of Article 33(3) PCT for the following reasons.

The closest state of the art for the present application is represented by D4 and D5 (D4 relates to a family member of the prepublished Japanese patent application WO2004/078719). Both documents disclose structurally related compounds as prostaglandin D2 antagonists. However, the 2-position of the indole nucleus is substituted by aliphatic groups and not by phenyl as in the present compounds. None of the cited documents D4 and D5, either alone or in its combination, makes obvious the presently claimed compounds. The present examples include IC_{50} values concerning the alleged activity. It can thus be assumed that the problem underlying the present application, i.e. the provision of further PG D2 antagonists may be expected as having been solved by the compounds as claimed in Claim 1.

4. INDUSTRIAL APPLICABILITY

No objection for Claims 1-45. For the assessment of the present Claims 46-54 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 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.

VI CERTAIN DOCUMENTS CITED

D1: DATABASE CHEMCATS [Online] CHEMICAL ABSTRACT SERVICE,
COLUMBUS, OHIO, US; XP002381259 retrieved from STN

This document discloses 2-phenyl indoles which are not covered by Claims 1-3 due
to the lack of the definition $R = R1S$.

VIII CERTAIN OBSERVATIONS (CLAIMS)

1. Due to the use of the functional terms "prodrug" and "bioisosteric acid", the claims
are not clear in the sense of Art. 6 PCT. Functional definitions may be allowed in
compound claims only in exceptional cases where a certain product cannot be
defined otherwise, i.e. in form of structural terms.

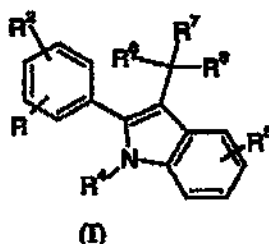
those skilled in the art that certain compounds of the invention may also exhibit geometrical isomerism. It is to be understood that the present invention includes individual geometrical isomers and stereoisomers and mixtures thereof, including racemic mixtures, of compounds of Formula (XVI) hereinabove. Such isomers can be separated from their mixtures, by the application or adaptation of known methods, for example chromatographic techniques and recrystallization techniques, or they are separately prepared from the appropriate isomers of their intermediates. Additionally, in situations where tautomers of the compounds of Formula (XVI) are possible, the present invention is intended to include all tautomeric forms of the compounds.

Particular Embodiments of the Invention

One particular embodiment of the invention is a compound of Formula (XVI) wherein n is 1 to 3, or 0 when R³ is carboxy, acid bisoester, or -C(O)-NY²Y², or a pharmaceutically acceptable salt, hydrate, or solvate thereof, a pharmaceutically acceptable prodrug thereof, or a pharmaceutically acceptable salt, hydrate or solvate of the prodrug.

Another particular embodiment of the invention is a compound of Formula (XVI) wherein n is 1, or a pharmaceutically acceptable salt, hydrate, or solvate thereof, a pharmaceutically acceptable prodrug thereof, or a pharmaceutically acceptable salt, hydrate or solvate of the prodrug.

Another particular embodiment of the invention is a compound of Formula (XVI) wherein the compound is of Formula (I):



or a pharmaceutically acceptable salt, hydrate, or solvate thereof, a pharmaceutically acceptable prodrug thereof, or a pharmaceutically acceptable salt, hydrate or solvate of the prodrug.

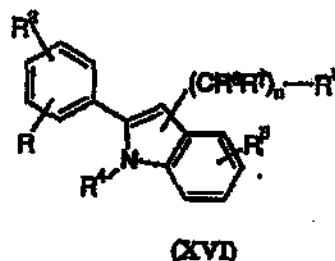
Another particular embodiment of the invention is a compound of Formula (I) wherein:

R is R¹SO₂, R¹SO-, R¹S-, R¹-C(=O)-NH- or R¹-SO₂-NH-;

R¹ is alkyl, alkenyl or alkynyl, each of which is optionally substituted by one or more aliphatic group substituents,

We claim:

1. A compound of Formula (XVI):



wherein:

R is R^1SO_2 , R^1SO , R^1CO , $R^1C(=O)NH$, or R^1SO_2NH ;

R¹ is alkyl, alkenyl, or alkynyl, each of which is optionally substituted by one or more aliphatic group substituents,

cycloalkyl, cycloalkenyl, aryl, heteroaryl, heterocyclyl, heterocyclenyl, or multicyclic alkyl, each of which is optionally substituted by one or more ring group substituents, or $-NRR''$ when R is R^1SO_2 or R^1CO ;

R² is hydrogen,

aryl, heteroaryl, cycloalkyl, cycloalkenyl, heterocyclyl, heterocyclenyl, or multicyclic alkyl, each of which is optionally substituted by one or more ring group substituents, or

alkyl, alkenyl or alkynyl, each of which is optionally substituted by one or more aliphatic group substituents;

R³ is hydrogen, alkyl, alkenyl or alkynyl;

R⁴ is hydrogen, halo, alkyl, alkenyl, alkynyl, haloalkyl, haloalkenyl, haloalkynyl, alkoxy, alkenyloxy or alkynyloxy;

R⁵ is acyl, cyano, carboxy, acid bioisostere, $-C(O)NY^1Y^2$,

aryl or heteroaryl, each of which is optionally substituted by one or more ring group substituents,

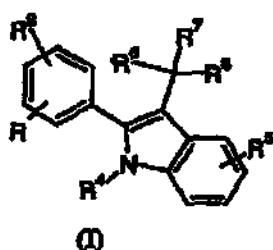
alkyl or alkynyl, each of which is optionally substituted by one or more aliphatic group substituents, or

alkoxy, alkenyloxy or alkynyloxy, each of which is optionally substituted by one or more aliphatic group substituents;

Y¹ and Y² are each independently hydrogen, alkylsulfonyl, arylsulfonyl, arylamino, heteroarylsulfonyl, heteroarylamino, or

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- alkyl, alkenyl or alkynyl, each of which is optionally substituted by one or more aliphatic substituent groups;
- R^4 is hydrogen, acyl, aroyl, heteroaryl, alkylsulfonyl, arylsulfonyl, arylalkylsulfonyl, heteroarylsulfonyl, heteroarylalkylsulfonyl, $-C(O)-NY^4Y^5$, $-C(O)-O-Y^6$,
- 5 alkyl, alkenyl or alkynyl, each of which is optionally substituted by aryl, heteroaryl, carboxy, alkoxy, carbonyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, aroyl, heteroaroaryl or acyl, or (C_2-C_6) -alkyl, alkenyl or alkynyl, each of which is substituted by halo, hydroxy, alkoxy, amino, alkylamino or dialkylamino;
- 10 Y^4 and Y^5 are each *independently* hydrogen, alkyl, alkenyl or alkynyl; Y^6 is alkyl, alkenyl or alkynyl;
- R^5 is hydrogen, halo, carboxy, cyano, nitro, hydroxy, alkyl, alkenyl, alkynyl, haloalkyl, haloalkenyl, haloalkynyl, alkoxy, alkenyloxy, alkynyloxy, haloalkoxy, haloalkenyloxy or haloalkynyloxy;
- R^6 and R^7 are each *independently*, hydrogen, alkyl, alkenyl or alkynyl;
- 15 R^8 is alkyl, alkenyl, or alkynyl, each of which is optionally substituted by one or more aliphatic group substituents, or aryl, heteroaryl, cycloalkyl, cycloalkenyl, heterocyclyl, heterocyclylenyl, or multicyclic alkaryl, each of which is optionally substituted by one or more ring group substituents; and
- n is 1 to 6, or 0 when R^3 is carboxy, acid bioisostere, or $-C(O)-NY^1Y^2$;
- 20 provided that when R^1 is amino, then R^4 is hydrogen and n is 1 to 6;
- or a pharmaceutically acceptable salt, hydrate, or solvate thereof, a pharmaceutically acceptable prodrug thereof, or a pharmaceutically acceptable salt, hydrate or solvate of the prodrug, provided that the prodrug is not 2-(4-acetyl-phenyl)-1H-indole-3-carboxylic acid methyl ester.
- 25 2. The compound according to claim 1, wherein n is 1 to 3, or 0 when R^3 is carboxy, acid bioisostere, or $-C(O)-NY^1Y^2$, or a pharmaceutically acceptable salt, hydrate, or solvate thereof, a pharmaceutically acceptable prodrug thereof, or a pharmaceutically acceptable salt, hydrate or solvate of the prodrug.
- 30 3. The compound according to claim 1, wherein n is 1, or a pharmaceutically acceptable salt, hydrate, or solvate thereof, a pharmaceutically acceptable prodrug thereof, or a pharmaceutically acceptable salt, hydrate or solvate of the prodrug.
4. The compound according to claim 1, wherein the compound is of Formula (I):



or a pharmaceutically acceptable salt, hydrate, or solvate thereof, a pharmaceutically acceptable prodrug thereof, or a pharmaceutically acceptable salt, hydrate or solvate of the prodrug.

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5. The compound according to claim 4, wherein:

R is R^1SO_2 , R^1SO , R^1CO , $R^2-C(=O)-NH$ or R^3-SO_2-NH ;

R^1 is alkyl, alkenyl or alkynyl, each of which is optionally substituted by one or more aliphatic group substituents,

10 aryl, heteroaryl, or heterocyclyl, each of which is optionally substituted by one or more ring group substituents, or

$-NRR''$ when R is R^1SO_2 ;

R' is hydrogen,

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aryl, heteroaryl, cycloalkyl, heterocyclyl, arylcycloalkyl, or cycloalkylaryl, each of which is optionally substituted by one or more ring group substituents, or alkyl, alkenyl or alkynyl, each of which is optionally substituted by one or more aliphatic group substituents;

R'' is hydrogen, alkyl;

R^2 is hydrogen, halo, alkyl, alkenyl, alkynyl, haloalkyl, or alkoxy;

20 R^3 is acyl, cyano, carboxy, acid bisoester, $-C(O)-NY^1Y^2$, alkyl, which is optionally substituted by one or more aliphatic group substituents, or alkoxy, which is optionally substituted by one or more aliphatic group substituents, Y^1 and Y^2 are each independently hydrogen, alkylsulfonyl, arylsulfonyl, arylamino, heteroarylsulfonyl, heteroarylamino, or

25 alkyl, which is optionally substituted by one or more aliphatic substituent groups;

R^4 is hydrogen, acyl, alkylsulfonyl, arylsulfonyl, arylalkylsulfonyl, heteroarylsulfonyl, heteroarylalkylsulfonyl, $-C(O)-NY^3Y^4$, $-C(O)-O-Y^4$,

alkyl, alkenyl or alkynyl, each of which is optionally substituted by carboxy, alkoxycarbonyl or acyl, or

30 (C_2-C_6) -alkyl, alkenyl or alkynyl, each of which is substituted by hydroxy, alkoxy, amino, alkylamino or dialkylamino;

aquellos expertos en la técnica que ciertos compuestos de la invención pueden exhibir isomerismo geométrico. Se debe entender que la presente invención incluye isómeros geométricos individuales y estereoisómeros y mezclas de estos, que incluyen mezclas racémicas, de compuestos de Fórmula (XVI) aquí. Tales isómeros se pueden separar de sus mezclas, por la aplicación o adaptación de métodos conocidos, por ejemplo técnicas de cromatografía y técnicas de recristalización, o ellos se preparan separadamente de los isómeros apropiados o sus intermediarios. Adicionalmente, en situaciones en donde los tautómeros de los compuestos de Fórmula (XVI) son posibles, la presente invención se entiende que incluye todas las formas tautoméricas de los compuestos.

Modalidades Particulares de la Invención

Una modalidad particular de la invención es un compuesto de Fórmula (XVI) en donde n es 1 a 3, o 0 cuando R^3 es carboxi, bioisoster ácido, o $-C(O)-NY^1Y^2$, o una sal farmacéuticamente aceptable, hidrato, o solvato de este, una prodroga farmacéuticamente aceptable de este, o una sal farmacéuticamente aceptable, hidrato o solvato de la prodroga.

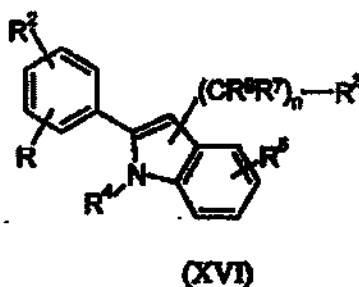
Otra modalidad particular de la invención es un compuesto de Fórmula (XVI) en donde n es 1, o una sal farmacéuticamente aceptable, hidrato, o solvato de este, una prodroga farmacéuticamente aceptable de este, o una sal farmacéuticamente aceptable, hidrato o solvato de la prodroga.

Otra modalidad particular de la invención es un compuesto de Fórmula (XVI) en donde el compuesto es de Fórmula (I):

REIVINDICACIONES

Reivindicamos:

1. Un compuesto de Fórmula (XVI):



en donde:

R es R^1SO_2 , R^1SO -, R^1S -, R^1CO -, $R^8-C(=O)-NH$ -, o R^8-SO_2-NH -;

R^1 es alquilo, alquenilo, o alquinilo, cada uno de los cuales es opcionalmente sustituido por uno o más sustituyentes de grupo alifático,

cicloalquilo, cicloalquenilo, arilo, heteroarilo, heterociclilo, heterociclenilo, o alcarilo multicíclico, cada uno de los cuales es opcionalmente sustituido por uno o más sustituyentes de grupo de anillo, o

$-NR'R''$ cuando R es R^1SO_2 o R^1CO -;

R' es hidrógeno,

arilo, heteroarilo, cicloalquilo, cicloalquenilo, heterociclilo, heterociclenilo, o alcarilo multicíclico, cada uno de los cuales es opcionalmente sustituido por uno o más sustituyentes de grupo de

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anillo, o alquilo, alquenilo o alquinilo, cada uno de los cuales es opcionalmente sustituido por uno o más sustituyentes de grupo alifático;

Rⁿ es hidrógeno, alquilo, alquenilo o alquinilo;

R² es hidrógeno, halo, alquilo, alquenilo, alquinilo, haloalquilo, haloalquenilo, haloalquinilo, alcoxi, alqueniloxi o alquiniloxi;

R³ es acilo, ciano, carboxi, bioisoster ácido, -C(O)-NY¹Y²,

aroilo o heteroaroilo, cada uno de los cuales es opcionalmente sustituido por uno o más sustituyentes de grupo de anillo,

alquilo, alquenilo o alquinilo, cada uno de los cuales es opcionalmente sustituido por uno o más sustituyentes de grupo alifático, o

alcoxi, alqueniloxi o alquiniloxi, cada uno de los cuales es opcionalmente sustituido por uno o más sustituyentes de grupo alifático;

Y¹ y Y² son cada uno independientemente hidrógeno, alquilsulfonilo, arilsulfonilo, arilamino, heteroarilsulfonilo, heteroarilamino, o

alquilo, alquenilo o alquinilo, cada uno de los cuales es opcionalmente sustituido por uno o más grupos sustituyentes alifáticos;

R⁴ es hidrógeno, acilo, aroilo, heteroarilo, alquilsulfonilo, arilsulfonilo, arilalquilsulfonilo, heteroarilsulfonilo, heteroarilalquilsulfonilo, -C(O)-NY⁴Y⁵, -C(O)-O-Y⁶,

alquilo, alquenilo o alquinilo, cada uno de los cuales es opcionalmente sustituido por aroilo, heteroarilo, carboxi, alcoxicarbonilo, aminocarbonilo, alquilaminocarbonilo, dialquilaminocarbonilo, aroilo, heteroarilo o acilo, o

alquilo-(C₂-C₆), alquenilo o alquinilo, cada uno de los cuales se sustituye por halo, hidroxilo, alcoxi, amino, alquilamino o dialquilamino;

Y⁴ y Y⁵ son cada uno independientemente hidrógeno, alquilo, alquenilo o alquinilo;

Y⁶ es alquilo, alquenilo o alquinilo;

R⁵ es hidrógeno, halo, carboxi, ciano, nitro, hidroxilo, alquilo, alquenilo, alquinilo, haloalquilo, haloalquenilo, haloalquinilo, alcoxi, alqueniloxi, alquiniloxi, haloalcoxi, haloalqueniloxi o haloalquiniloxi;

R⁶ y **R⁷** son cada uno independientemente, hidrógeno, alquilo, alquenilo o alquinilo;

R⁸ es alquilo, alquenilo, o alquinilo, cada uno de los cuales es opcionalmente sustituido por uno o más sustituyentes de grupo alifático, o

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arilo, heteroarilo, cicloalquilo, cicloalquenilo, heterociclilo, heterociclenilo, o alcarilo multicíclico, cada uno de los cuales es opcionalmente sustituido por uno o más sustituyentes de grupo de anillo; y

n es 1 a 6, o 0 cuando R^3 es carboxi, bioisoster ácido, o $-C(O)-NY^1Y^2$;

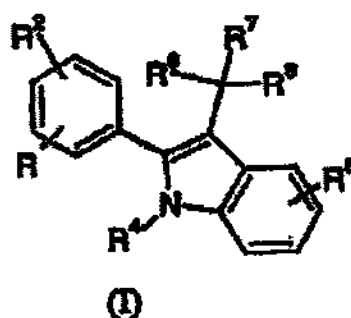
dado que cuando R^1 es amino, entonces R^4 es hidrógeno y n es 1 a 6;

o una sal farmacéuticamente aceptable, hidrato, o solvato de este, una prodroga farmacéuticamente aceptable de este, o una sal farmacéuticamente aceptable, hidrato o solvato de la prodroga, dado que la prodroga no es éster de metilo de ácido 2-(4-acetil-fenil)1H-indol-3-carboxílico.

2. El compuesto de acuerdo con la reivindicación 1, en donde n es 1 a 3, o 0 cuando R^3 es carboxi, bioisoster ácido, o $-C(O)-NY^1Y^2$, o una sal farmacéuticamente aceptable, hidrato, o solvato de este, una prodroga farmacéuticamente aceptable de este, o una sal farmacéuticamente aceptable, hidrato o solvato de la prodroga.
3. El compuesto de acuerdo con la reivindicación 1, en donde n es 1 o una sal farmacéuticamente aceptable, hidrato, o solvato de este, una prodroga farmacéuticamente aceptable de este, o una sal farmacéuticamente aceptable, hidrato o solvato de la prodroga.

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4. El compuesto de acuerdo con la reivindicación 1, en donde el compuesto es de Fórmula (I):



o una sal farmacéuticamente aceptable, hidrato, o solvato de este, una prodroga farmacéuticamente aceptable de este, o una sal farmacéuticamente aceptable, hidrato o solvato de la prodroga.

5. El compuesto de acuerdo con la reivindicación 4, en donde:

R es R^1SO_2 , R^1SO , R^1S , $R^8-C(=O)-NH$ - o R^8-SO_2-NH -;

R^1 es alquilo, alquenilo o alquinilo, cada uno de los cuales es opcionalmente sustituido por uno o más sustituyentes de grupo alifático,

arilo, heteroarilo, o heterociclilo, cada uno de los cuales es opcionalmente sustituido por uno o más sustituyentes de grupo de anillo, o

$-NR^1R^{11}$ cuando R es R^1SO_2 ;

R' es hidrógeno,

arilo, heteroarilo, cicloalquilo, heterociclilo, arilcicloalquilo, o cicloalquilarilo, cada uno de los cuales es opcionalmente sustituido por uno o más sustituyentes de grupo de anillo, o

alquilo, alquenilo o alquinilo, cada uno de los cuales es opcionalmente sustituido por uno o más sustituyentes de grupo alifático;

R" es hidrógeno, alquilo;

R² es hidrógeno, halo, alquilo, alquenilo, alquinilo, haloalquilo, o alcoxi;

R³ es acilo, ciano, carboxi, bloisoster ácido, $-C(O)-NY^1Y^2$, alquilo, que se sustituye opcionalmente por uno o más sustituyentes de grupo alifático, o

alcoxi, que se sustituye opcionalmente por uno o más sustituyentes de grupo alifático,

Y¹ y Y² son cada uno independientemente hidrógeno, alquilsulfonilo, arilsulfonilo, arilamino, heteroarilsulfonilo, heteroarilamino, o

alquilo, que se sustituye opcionalmente por uno o más grupos sustituyentes alifáticos;

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REPUBLICA DE COLOMBIA
SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO

Folio 3/1

2020
Bogotá D.C.,

Doctor(a)
FERRERO EMILIO
Apoderado(a) y/o Representante de
AVIANTIS PHARMACEUTICALS INC.

REFERENCIA	Radicación No.	07 76601
	Solicitud internacional	PCT/US2006/002736
	Fecha inicio fase nacional	26/08/2005
	Trámite	11
	Evento	379
	Actuación	416
	Oficio No.	6459
	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.

Cumplase
Dado en Bogotá DC,

22 JUL. 2008

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

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