



No. 13-296682- -00001-0000

Fecha: 2014-04-04 08:48:05 Dep. 2020 DIR.NUEVASCR
Tra. 11 PATENTEIYII Eve: 378 FASENACIONALI
Act. 400 OPOSIOBSRVTER Follos: 36

DIRECCIÓN DE NUEVAS CREACIONES
PRESENTACIÓN DE OPOSICIÓN

1. Oposición a solicitud de:

- ☒ Patente de invención
☐ Registro de Diseño Industrial
☐ Patente de Modelo de Utilidad
☐ Esquema de Trazado de Circuitos Integrados

Número de expediente: 13 296682

Solicitante: AVENTIS PHARMACEUTICALS, INC

Apoderado: LUZ CLEMENCIA DE PAEZ

Título de la Nueva Creación: COMPOSICIÓN FARMACÉUTICA QUE COMPRENDE FEXOFENADINA

Gaceta: 683

2. Datos del Opositor

☐ Persona Natural ☒ Persona Jurídica
PROCAPS S.A.

Nombre o denominación /Razón social completa

WALTER TANAKA TATEKAWA

Nombre del representante legal

Documento de identificación: C.C. ☐ C.E. ☐ NIT ☒ Otro ☐ Cuál _____

Número 890106527-5 _____

Dirección. CALLE 80 78B 201 _____ Ciudad BARRANQUILLA

Teléfono 055 3719900 Fax: _____ Correo electrónico _____

☐ Autorizo expresamente a la Superintendencia de Industria y Comercio para que todas las comunicaciones sean enviadas a través de la dirección de correo electrónico

3. Datos del representante o apoderado:

MORENO BOHORQUEZ ELIANA ISaura

51.975.664

83823

Apellidos y Nombre

Documento de identificación

Tarjeta profesional

Dirección del representante

CRA 13 119-95 OFICINA 104

Dirección electrónica
negocios@optimum-co.com

No. Fax
(571)6121979

Número telefónico
(571)2131213

En caso de haber presentado poder general para asuntos que se adelanten ante la Delegatura de Propiedad Industrial, sírvase indicar el número de su radicación o protocolo de poder general:

4. Fundamentos de la oposición

Causal: Art14, 16, 18,20 y 30 de la decisión 486 de la CAN no cumple con los requisitos De patentabilidad.

Justificación: La presente solicitud no cumple con los requisitos de patentabilidad dado que lo revelado, ya se encontraba en el estado de la técnica o es posible derivarlo de la misma tal y como se demostrará en el capítulo “fundamento de hecho”.

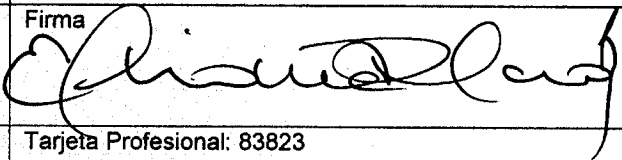
Prórroga: SI ☐ NO ☐

5. Anexos

- ☒ Comprobante de pago de la tasa.
- ☒ Poder, si fuera el caso.
- ☒ Fundamentos de la oposición. Se anexan 9 folios (obligatorios indicar cuántos).
- ☒ Anexo de fundamentos de la oposición. Se anexan 17 folios (obligatorios indicar cuántos)
- ☒ Copias para traslado.
- ☐ Copia de la solicitud y sus anexos en formato magnético.

6. Firma

Nombre del Firmante
ELIANA ISAURA MORENO BOHORQUEZ
CC. 51.975.664

Firma

Tarjeta Profesional: 83823

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO

NIT : 800.176.089-2

- / -

3



Industria y Comercio
SUPERINTENDENCIA

RECIBO DE CAJA

No. 14 - 0036468

Bogotá D.C., Abril 04 de 2014 - 08:42:36

RECIBIDO DE : PROCAPS S.A.

NI 890.106.527

*** Soporte del Pago ***

TIPO PAGO	BANCO	CUENTA	No. PAGO	FECHA PAGO	VR. PAGO
CONSIGNACION	BANCO DE BOGOTA	062754387	543529136	03/04/2014	335.000.00

*** Conceptos Pagados ***

CANT.	RENTISTICO	CONCEPTO	Vr. UNDITARIO	Vr. CONCEPTO
1	50005-01-04	PRESENTACION DE OBSERVACIONES A SOLICITUDES	335.000.00	335.000.00
12		OPOSICION POR CADA CLASE-MARCAS Y LEMAS COMERCIALES		\$335.000.00
				=====

SON: **TRESCIENTOS TREINTA Y CINCO MIL PESOS MONEDA CORRIENTE**

Responsable: _____

Recibo de Caja Aplicado al Expediente No. _____

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO



No. 13-296682-00001-0000

Fecha: 2014-04-04 08:48:05 Dep. 2020 DIR.NUEVASCR
Tra. 11 PATENTEIYII Eve: 378 FASENACIONALI
Act. 400 OPOSIOBSERVTER Folios: 36

Sede Centro: Carrera 13 No. 27 - 00 Pisos 3,4,5 y 10 Bogotá, D.C.- Colombia

Web: www.sic.gov.co e-mail: Info@sic.gov.co Conmutador: (571) 5870000 Fax: (571) 5870284 Línea: 018000-910165 Call Center: (571) 6513240

Abril 4 de 2014 - 08:42:37

Señor Director,
DIRECCIÓN DE NUEVAS CREACIONES
Superintendencia de Industria y Comercio
E. S. D.

Referencia : Expediente N° 13 296682
Asunto : Oposición a la solicitud de patente de Invención titulada
"COMPOSICIÓN FARMACÉUTICA QUE COMPRENDE
FEXOFENADINA"
Solicitante : AVENTIS PHARMACEUTICALS, INC.
Opositora : PROCAPS S.A.

Publicada en la Gaceta de la Propiedad Industrial
N° 683 del 10 de enero de 2014

Yo, *ELIANA ISAURA MORENO BOHÓRQUEZ*, abogada en ejercicio, identificada como aparece al pie de su firma, con tarjeta profesional No. 83823 del Consejo Superior de la Judicatura, en mi condición de apoderada de la sociedad PROCAPS S.A. conformada bajo las leyes de la República de Colombia y domiciliada en la ciudad de Barranquilla, Colombia, atentamente manifiesto que estando dentro del término de ley y por orden expresa de mi representada, presento oposición a la concesión del registro de la Patente de Invención titulada "COMPOSICIÓN FARMACÉUTICA QUE COMPRENDE FEXOFENADINA", cuyo titular AVENTIS PHARMACEUTICALS, INC., y pido a Usted declarar fundada esta oposición y en consecuencia negar el registro de la patente solicitada.

1. INTERÉS PARA ACTUAR

Conforme a lo dispuesto en el artículo 42 de la Decisión 486 de 2000 de la CAN, estando dentro del término estipulado por la ley, manifiesto el legítimo interés de nuestra representada para oponerse al registro de la patente de la referencia, atendiendo a que la solicitud pretendida no cumple con los requisitos dispuestos en la ley como se analizará más adelante y de ser concedida afectaría directamente la comercialización de algunos productos de mi representada, que contienen, en particular *FEXOFENADINA*. Por lo tanto, solicito respetuosamente a ese Despacho se sirva tener en cuenta la presente oposición dentro del trámite administrativo que se surte en esta Superintendencia.

2. FUNDAMENTOS DE HECHOS

- 2.1. La solicitud objeto de la presente fue presentada el 19 de diciembre de 2013, reivindicando prioridad bajo las solicitudes IN2011CH01727 del 2011-05-20; US201161499856P del 2011-06-22; y, EP20110305923 del 2011-07-13; y fue publicada en Colombia, en la Gaceta de la Propiedad Industrial N° 683 del 10 de enero de 2014, cuya publicación internacional corresponde a la WO2012159960 del 2012-11-29.
- 2.2. La solicitud colombiana 13 296682 objeto de la presente oposición se refiere a una formulación farmacéutica de hidrocloreuro de fexofenadina en un sistema de disolvente adecuada como una composición líquida de relleno. En otro aspecto, la invención también se refiere a un proceso para la preparación de dicha formulación farmacéutica y al uso de dicha composición para la preparación de un fármaco para el tratamiento de reacciones alérgicas en un paciente.
- 2.3. En primera instancia, se debe advertir que las reivindicaciones se refieren a usos y métodos de tratamiento y no sólo a la composición farmacológica o a un método de fabricación mediante la cual se obtenga un producto tangible y según la legislación, decisión 486 de la Comunidad Andina de Naciones, Artículo 14.-

“Los Países Miembros otorgarán patentes para las invenciones, sean de producto o de procedimiento (...)”, los usos no están contemplados como patentables; y, Artículo 20.- “No serán patentables (...) d) los métodos terapéuticos o quirúrgicos para el tratamiento humano o animal, así como los métodos de diagnóstico aplicados a los seres humanos o a animales”. Solo serán patentables los productos o procedimientos. Por lo tanto a luz de la norma, dicha materia referente métodos de tratamiento no sería patentable.

2.4. Ahora bien, con base en el artículo 14 de la Decisión 486 de la CAN consagra lo siguiente: *“Los países miembros otorgarán patentes para las invenciones, sean de producto o procedimiento, en todos los campos de la tecnología, siempre que sean nuevas, tengan nivel inventivo y sean susceptibles de aplicación industrial”.* Así las cosas, las invenciones objeto de patente deben ser nuevas y tener nivel inventivo. Bien, pues antes de la fecha de prioridad de esta solicitud se encuentran los siguientes documentos que afecta la patentabilidad de la presente solicitud:

- D1: WO2005062722 publicada el 14 de julio de 2005.

2.5. Ahora bien, el documento D1, proporciona una composición farmacéutica de liberación inmediata oral que comprende una cantidad terapéuticamente eficaz de fexofenadina o sus sales farmacéuticamente aceptables para mejorar la disolución de un agente de unión termofundible y excipientes farmacéuticamente aceptables. Esta anterioridad D1, particularmente en la página 1 líneas 9 a 18, página 4 líneas 10 a 29, página 5 líneas 1 a 7 y líneas 14 a 32, así como los ejemplos 1 a 4, describe una composición oral que comprende clorhidrato de fexofenadina y una mezcla de tensioactivos hidrófilos e hidrófobos en cantidades superiores a 60 p%. El surfactante hidrófilo no iónico puede ser polisorbato 80 - "sorbitán". Los ejemplos 1 a 4 de esta anterioridad D1, ilustran todas las concentraciones del ingrediente activo hasta 30p%. Como tal, esta anterioridad D1, también revela una composición que incluye hidrocloreto de fexofenadina en combinación con surfactantes con buenas propiedades de velocidad de liberación. En las reivindicaciones 1 y 2, dicha anterioridad D1, define una

composición farmacéutica de liberación inmediata oral que comprende una cantidad terapéuticamente eficaz de fexofenadina o sus sales farmacéuticamente aceptables, una cantidad para mejorar la disolución de un agente de unión termofundible y excipientes farmacéuticamente aceptables, en el que el agente se selecciona de un agente hidrofílico, un agente hidrófobo y/o mezclas de los mismos. Como se evidencia, la materia pretendida ya se había divulgado con anterioridad en el documento D1. Por lo tanto, este documento objeto de oposición a la luz del documento D1 carece evidentemente de NOVEDAD.

2.6. En consecuencia y de acuerdo a lo descrito anteriormente, se deriva que la solicitud colombiana 13 296682 no puede pretender un monopolio por patente toda vez que lo que pretende no cumple con dos de los tres requisitos necesarios para su protección.

2.7. Que por consiguiente, respecto a la solicitud pretendida se tiene que:

2.8.1 CARENCIA DE NOVEDAD. Según la decisión 486 de la Comunidad Andina de Naciones, Artículo 16.- *“Una invención se considerará nueva cuando no está comprendida en el estado de la técnica. El estado de la técnica comprenderá todo lo que haya sido accesible al público por una descripción escrita u oral, utilización, comercialización o cualquier otro medio antes de la fecha de presentación de la solicitud de patente o, en su caso, de la prioridad reconocida.”*. A la fecha de prioridad, el 20 de mayo de 2011, ya era conocido, pues como se demostró, era parte del arte anterior con base en los documento D1, una formulación farmacéutica de hidrocloreuro de fexofenadina en un sistema de disolvente adecuada como una composición líquida de relleno, sobre el cual busca protección en el capítulo reivindicatorio.

2.8.2 CARENCIA DE APLICACIÓN INDUSTRIAL. La Decisión 486 de la CAN consagra en su artículo 14 lo siguiente: *“Los países miembros otorgarán patentes para las invenciones, sean de producto o procedimiento, en todos los campos de la tecnología, siempre que sean nuevas, tengan nivel inventivo y sean*

susceptibles de aplicación industrial". La presente solicitud carece de aplicación Industrial ya que como se demostró anteriormente, algunas cláusulas reclaman un método de tratamiento y estos no son aplicables industrialmente porque primero no se obtiene un producto o proceso; y segundo no es reproducible o repetible a escala industrial. Por lo tanto, el objeto de la presente invención referido a métodos de tratamiento, no cumple con el requisito de la aplicación industrial.

2.9 Dado lo anterior, es posible deducir que la solicitud y lo reivindicado no es objeto de patentabilidad pues es contrario a lo que dicta la Decisión 486 de la Comunidad Andina de Naciones, Artículo 14.- *"Los Países Miembros otorgarán patentes para las invenciones, sean de producto o de procedimiento, en todos los campos de la tecnología, siempre que sean nuevas, tengan nivel inventivo y sean susceptibles de aplicación industrial."* La solicitud pretendida no cumple con dos de los tres requisitos de patentabilidad.

2.10 Por todo lo anterior, atentamente solicito a usted que se sirva declarar fundada *"COMPOSICIÓN FARMACÉUTICA QUE COMPRENDE FEXOFENADINA"*, cuyo titular AVENTIS PHARMACEUTICALS, INC., solicitud Colombiana que apareció publicada en la Gaceta de la Propiedad Industrial N° 683 del 10 de enero de 2014.

3. PRUEBAS

De conformidad con lo dispuesto por las normas vigentes, solicito a usted tener como prueba en este asunto los siguientes:

- D1: WO2005062722 publicada el 14 de julio de 2005.

4. FUNDAMENTO DE DERECHO

Fundamento esta observación en las normas legales siguientes:

- 4.1. Artículo 45 de la Decisión 486 de la Comisión del Acuerdo de Cartagena.
- 4.2. En las demás normas concordantes.

5. ANEXOS

Para los efectos correspondientes anexo al presente escrito los siguientes documentos:

1. Poder para actuar en el presente.
2. Documento que acredita al representante legal de PROCAPS S.A.
3. Recibo de caja del respectivo pago de tasa.
4. Copias de los documentos:
 - D1: WO2005062722 publicada el 14 de julio de 2005.

6. NOTIFICACIONES

Para efectos de notificaciones que debe hacer su Despacho, informo que mi representada y la suscrita recibiremos notificaciones en la Secretaría de su Despacho o en mis oficinas situadas en la Carrera 13 N° 119-95, Of. 104 de esta ciudad de Bogotá.

Señor director,



ELIANA ISAURA MORENO BOHÓRQUEZ

C.C. 51'975.664 de Bogotá

T.P.A. 83823 del C.S. de la J.

ANEXO 1

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

(19) World Intellectual Property
Organization
International Bureau(43) International Publication Date
14 July 2005 (14.07.2005)

PCT

(10) International Publication Number
WO 2005/062722 A2

(51) International Patent Classification: Not classified

(21) International Application Number:
PCT/IN2004/000362MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG,
PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM,
TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM,
ZW.(22) International Filing Date:
22 November 2004 (22.11.2004)

(25) Filing Language: English

(26) Publication Language: English

(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, LU, MC, 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).(30) Priority Data:
1204/MUM/2003
21 November 2003 (21.11.2003) IN

Declarations under Rule 4.17:

- as to the identity of the inventor (Rule 4.17(i)) for all designations
- as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii)) for all designations
- as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii)) for all designations
- as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii)) for all designations
- as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii)) for all designations
- as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii)) for all designations
- as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii)) for all designations
- of inventorship (Rule 4.17(iv)) for US only

(71) Applicant (for all designated States except US): SUN
PHARMACEUTICAL INDUSTRIES LIMITED
[IN/IN]; Acme Plaza, Andheri-Kurla Road, Andheri
(East), Mumbai 400059 (IN).

(71) Applicants and

(72) Inventors: MUNGRE, Ashish, Prabhakar [IN/IN]; Sun
Pharmaceutical Industries Limited, 17/B, Mahal Industrial
Estate, Off Mahakali Caves Road, Andheri (East), Mumbai
400093 (IN). NABAR, Manisha, Saiprasad [IN/IN]; Sun
Pharmaceutical Industries Limited, 17/B, Mahal Industrial
Estate, Off Mahakali Caves Road, Andheri (East), Mumbai
400093 (IN).

Published:

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

(81) Designated States (unless otherwise indicated, for every
kind of national protection available): AE, AG, AL, AM,
AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN,
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI,
GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE,
KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD,For two-letter codes and other abbreviations, refer to the "Guid-
ance Notes on Codes and Abbreviations" appearing at the begin-
ning of each regular issue of the PCT Gazette.

(54) Title: ORAL PHARMACEUTICAL COMPOSITION

(57) Abstract: The present invention provides an immediate release oral pharmaceutical composition comprising a therapeutically effective amount of fexofenadine or its pharmaceutically acceptable salts, a dissolution enhancing amount of a thermomelting binding agent and pharmaceutically acceptable excipients.

WO 2005/062722 A2

ORAL PHARMACEUTICAL COMPOSITION

FIELD OF THE INVENTION

The present invention relates to an immediate release oral pharmaceutical composition of an antihistamine. Particularly, the present invention relates to an oral pharmaceutical composition of a piperidinoalkanol compound.

BACKGROUND OF THE INVENTION

Fexofenadine hydrochloride is a piperidinoalkanol compound with the chemical name $(\pm)$ -4-[1-hydroxy-4-[4-(hydroxydiphenylmethyl)-1-piperidinyl]butyl]- α,α -dimethylbenzeneacetic acid hydrochloride. Fexofenadine is a histamine H_1 -receptor antagonist useful as an antihistamine, anti-allergy agent and bronchodilator. It is indicated for the relief of symptoms associated with seasonal allergic rhinitis in adults and children 6 years of age and older. It is also indicated for treatment of uncomplicated skin manifestations of chronic idiopathic urticaria in adults and children 6 years of age and older. The recommended dose of fexofenadine for treatment of allergic rhinitis in adults is 60 mg twice daily or 180 mg once daily. The recommended dose of fexofenadine for treatment of chronic idiopathic urticaria in adults is 60 mg twice daily.

Fexofenadine hydrochloride is commercially available in the United States of America as Allegra[®] capsules and Allegra tablets.

United States Patent Number 4,929,605 (priority date Oct 7, 1987, assigned to Merrell Dow) claims a composition comprising piperidinoalkanol compound, 0.1-6% w/w of a non-ionic or cationic surfactant, and 2-50% w/w of a pharmaceutically acceptable carbonate salt. These immediate release compositions have been reported to have acceptable in-vitro dissolution characteristics and efficient bioavailability. The surfactant used may be expected to improve the wetting of the hydrophobic piperidinoalkanols, and the carbonate salt used may be expected to provide efficient disintegration of the dosage form in the gastrointestinal milieu, thereby ensuring that a greater surface area of the piperidinoalkanol compound is made available for absorption.

United States Patent Numbers 5,738,872, 5,855,912, 5,932,247 and 6,113,942 (priority date Feb 28, 1995, assigned to Hoechst Marion Roussel, Inc) relate to a pharmaceutical composition of a piperidinoalkanol compound like fexofenadine prepared by a wet granulation process comprising a diluent, a disintegrant and a solution of a binding agent. The

patents focus on improving the bioavailability of the piperidinoalkanol compounds by using wet granulation.

United States Patent Application Number 20030203020A1 (priority date Feb 28, 1995,
5 assigned to Hoechst Marion Roussel, Inc) relates to a composition of piperidinoalkanol
compounds obtained using specific excipients, and using piperidinoalkanol compound having
a specific surface area greater than $1\text{m}^2/\text{g}$. The compositions described and exemplified in this
application use the method of wet granulation. The large surface area and the process of wet
granulation may be expected to improve bioavailability of the piperidinoalkanol compounds.
10 However, use of solvents may cause change in the polymorphic form of the piperidinoalkanol
and may adversely affect its bioavailability.

United States Patent Number 5,290,569 (priority date Apr 12, 1990, assigned to Shionogi and
Co.) relates to orally administrable coated granules. The patent claims a composition
15 comprising granules obtained by mixing polyethylene glycol and a drug, followed by coating
of the granules with a mixture of polyethylene glycol and a hydrophobic thermomelting
material, the coated granules being obtained by the process of melt granulation, without the
use of solvents. The granules are coated to a thickness such that the site and/or time for
disintegration or dissolution can be properly regulated. The compositions therefore provide
20 modified release of the drug contained therein. The patent does not suggest or teach
immediate release oral compositions that can be obtained by the process of melt granulation.

United States Patent Number 5,476,667 (priority date Oct 16, 1990, assigned to Kabi
Pharmacia) claims a method for obtaining pellets by the process of melt granulation, the
25 process being designed to obtain pellets comprising a high dose of the drug. However, the
patent does not disclose or exemplify granules of piperidinoalkanol compounds that may be
obtained by melt granulation.

United States Patent Application Number 20020160050A1 (priority date Sep 28, 1999,
30 assigned to Lundbeck) claims melt granulated substantially homogenous composition
comprising one or more hydrophilic cellulose ether polymers, a hydrophilic melt binder and a
drug. The compositions provide modified release of the drug contained therein, since the
cellulose ether used acts as binder or matrix system that regulates release of the drug.

35 United States Patent Application Number 20030228368A1 (priority date Sep 28, 2001,
assigned to Johnson and Johnson) claims an edible solid composition comprising 25-40%
w/w of at least one non-aqueous carrier which has a melting temperature less than about 45

degrees C, and about 15-60% w/w of at least one thermoplastic material which has a melting temperature greater than 50 degrees C. The compositions are obtained by placing a mixture of the non-aqueous carrier material, the thermoplastic material and a drug in a mold, heating the mold to 50-100 degrees C, and cooling it to 0-25 degrees C.

5

United States Patent Number 6,723,348 (priority date Nov 16, 2001, assigned to Ethypharm) relates to orodispersible tablets of fexofenadine, which are able to disintegrate in the buccal cavity upon contact with saliva by formation of an easy-to-swallow suspension, in less than 60 seconds containing; fexofenadine, or one of its pharmaceutically acceptable salt, in the form of coated granules, and a mixture of excipients comprising at least one disintegrating agent, a soluble diluent agent and a lubricant. The formulation of this invention is prepared by direct compression of the coated granules of fexofenadine and the mentioned excipients. The patent does not relate to conventional tablet compositions that are meant to be swallowed and which disintegrate in the gastrointestinal tract.

15

Piperidinoalkanol compounds like fexofenadine are hydrophobic in nature and have low water solubility. Direct compression is a method of choice for the manufacture of tablets because it involves minimum number of steps. However, we have observed that use of direct compression for preparation of compositions of fexofenadine cause problems such as capping and sticking. We have also observed that tablets made using dry granulation process do not release fexofenadine at a desirable rate. The use of wet granulation processes may cause a change in the polymorphic form of the piperidinoalkanol, and may adversely affect its bioavailability. We have surprisingly found that the problems of the prior art can be avoided by the use of melt granulation process, so that the hydrophobic piperidinoalkanol compounds are in intimate contact with the thermomelting binding agent used. The use of the process of melt granulation as per the present invention avoids micronisation of the piperidinoalkanol compounds to increase their surface area, avoids use of surfactants and other means such as large amounts of disintegrating agents, avoids use of solvents that may have a deleterious effect on the stability of the piperidinoalkanol compounds, and at the same time provides a process that is feasible and industrially applicable.

25

30

OBJECTS OF THE INVENTION

It is an object of the present invention to provide an immediate release oral pharmaceutical composition of a piperidinoalkanol compound by melt granulation process.

35

It is yet another object of the present invention to provide an immediate release oral pharmaceutical composition of fexofenadine or its pharmaceutically acceptable salts by melt

granulation, such that the composition provides therapeutically effective levels of fexofenadine.

SUMMARY OF THE INVENTION

- 5 The present invention provides an immediate release oral pharmaceutical composition comprising a therapeutically effective amount of fexofenadine or its pharmaceutically acceptable salts, a dissolution enhancing amount of a thermomelting binding agent and pharmaceutically acceptable excipients.

10 DETAILED DESCRIPTION OF THE INVENTION

- Melt granulation is a known process and involves mechanically working a particulate substance mixed with a thermomelting binder which has a melting point of 40-100°C, so as to form granules. During the process of manufacture, the thermomelting binding agent melts and adheres to the surface of the particulate drug. The process thus causes adhering of the
15 particles to form granules, which are then processed by methods conventional in the art to obtain pharmaceutical compositions.

- The thermomelting binding agent is present in the oral composition of the present invention in a dissolution enhancing amount. The term "dissolution enhancing amount" as used herein
20 means that the rate of dissolution of fexofenadine or its pharmaceutically acceptable salt in the presence of the thermomelting binding agent is greater than the rate of dissolution in the absence of the thermomelting binding agent. The amount of the thermomelting binding agent used depends on the agent used and the properties of the agent used. The thermomelting binding agent may be any suitable substance with a melting point less than about 150°C. The
25 thermomelting binding agents used in the composition of this invention typically include hydrophobic agents, hydrophilic agents or mixtures thereof. The term "hydrophobic agent" as used herein means a substance that has a hydrophilic-lipophilic balance of less than 10, and the term "hydrophilic agent" as used herein means a substance that has a hydrophilic-lipophilic balance of greater than 10. It excludes such hydrophobic agents that in any amounts
30 will not function to enhance dissolution of fexofenadine or its pharmaceutically acceptable salt. However, the use of the term "hydrophobic agent" is not restricted to surfactants, i.e. amphiphilic compounds that have both hydrophobic and hydrophilic properties, but hydrophobic agents such as hydrogenated vegetable oils are also useful as the thermomelting binding agent of the present invention which is capable of enhancing dissolution of
35 fexofenadine or its pharmaceutically acceptable salt. Hydrophobic agents that are not capable by themselves of enhancing the dissolution of fexofenadine or its pharmaceutically acceptable salt, may be used in admixture with a suitable agent such that the mixture acts as a

thermomelting binding agent capable of enhancing dissolution. Generally, the thermomelting binding agent may be used in an amount ranging from about 5% to about 95% by weight of the composition. In preferred embodiments, the thermomelting binding agent is used in an amount ranging from about 15% to about 75% by weight of the composition, more preferably in an amount ranging from about 30% to about 60% by weight of the composition, such that the composition provides an immediate release of fexofenadine or its pharmaceutically acceptable salt.

Examples of thermomelting binding agents that may be used in the oral pharmaceutical composition of the present invention include, but are not limited to, hydrophilic agents like polyethylene glycols having an average molecular weight of not less than about 400, preferably of not less than about 1,000, more preferably from about 2,000 to 20,000, polyethylene glycol derivatives, saccharides like D-glucose, maltose, fructose and the like, sugar alcohols like xylitol, D-mannitol, D-sorbitol and the like, surfactants like sorbitan, Pluronic F68 and the like and hydrophobic agents like straight-chain saturated hydrocarbons, fats and oils like cocoa butter, beef tallow, lard, hydrogenated soybean oil, and the like, animal and plant waxes like yellow beeswax, white beeswax and the like, higher fatty acids like stearic acid and the like, higher alcohols like stearyl alcohol and the like, hydrogenated plant oils like hydrogenated castor oil, hydrogenated rapeseed oil, hydrogenated cottonseed oil (Lubritab), polishing wax (a mixture of carnauba wax and paraffin), Presirol (a mixture of glycerol mono-, di- and tripalmitates), sorbitan esters, polyglycolglyceride, polyoxyethylene stearate, glycerol esters such as glyceryl monostearate (Geleol) and glyceryl distearate (Precirol); polyoxyethylene alkyl ethers such as lauroylmacrogol glyceride (Gelucire); polyoxyethylene-polyoxypropylene block copolymers such as poloxamer and the like, and mixtures thereof. It is preferred that the thermomelting binding agent has a melting point less than 100°C. In one embodiment of the present invention, xylitol is used as the thermomelting binding agent.

The pharmaceutically acceptable excipients that may be used in the present invention typically include one or more surfactants, disintegrants, binders, wicking agents, lubricants, fillers and the like. Examples of surfactants or wetting agents that may be used in the present invention include, but are not limited to, sodium lauryl sulfate, sorbitan fatty acid esters, polyoxyethylene stearates, polyoxyethylene fatty acid esters, poloxamers, polyoxyethylene ethers, sodium docusate, polyethoxylated castor oil and the like. Examples of disintegrants that may be used in the oral pharmaceutical composition of the present invention include, but are not limited to, starch, cellulose derivatives, gums, crosslinked polymers and the like. Binders that may be used include one or more of starch, gelatin, sugars, cellulose derivatives,

polyvinylpyrrolidone and the like. Examples of wicking agents include colloidal silicon dioxide, kaolin, titanium dioxide, fumed silicon dioxide, niacinamide, sodium lauryl sulfate, m-pyrrol, vinylpyrrolidone polymers such as povidone, or crosslinked polyvinylpyrrolidone such as crospovidone; cellulose and cellulose derivatives such as microcrystalline cellulose, methylcellulose, ethylcellulose, hydroxypropylcellulose, hydroxypropyl cellulose, carboxyalkyl celluloses or crosslinked carboxyalkylcelluloses and their alkali salts; sodium starch glycolate, starch and starch derivatives, ion-exchange resins and the like and mixtures thereof. Fillers that may be used in the present invention include, but are not limited to, lactose, mannitol, calcium carbonate, dicalcium phosphate, starch, microcrystalline cellulose, and the like and mixtures thereof. Examples of lubricants include talc, magnesium stearate, calcium stearate, aluminium stearate, stearic acid, hydrogenated vegetable oils, colloidal silicon dioxide, polyethylene glycol, cellulose derivatives such as carboxyalkyl cellulose and its alkali salts, and mixtures thereof. The pharmaceutical excipients are used in amounts conventionally used in the pharmaceutical art and known to a person of skill in the art.

The oral pharmaceutical composition of the present invention is prepared by the process of melt granulation, wherein the piperidinoalkanol such as fexofenadine or its pharmaceutically acceptable salt is mixed with the thermomelting binding agent and other pharmaceutically acceptable excipients and heated in a jacketed vessel at a suitable temperature so as to obtain a molten mass. Alternatively, the thermomelting binding agent may be heated so as to obtain a molten mass and the piperidinoalkanol may be added to it later. This mass is then passed through a sieve to obtain granules, which are cooled and lubricated. The lubricated mass is then either compressed to obtain tablets, or is filled in empty gelatin capsules. In yet another process, the granules of the drug obtained from the molten mass may be mixed with placebo granules comprising conventional pharmaceutical excipients, and compressed to obtain tablets. Compressed tablets may optionally be coated with a film coat for providing aesthetic appeal and/or for masking the taste of the piperidinoalkanol. Coating may be carried out using conventional methods and agents known to a person of skill in the pharmaceutical art.

The oral pharmaceutical composition of the present invention has essentially the same bioavailability as that provided by commercially available compositions of fexofenadine whose New Drug Application (NDA) received approval of the United States Food and Drug Administration (USFDA). The phrase "essentially the same bioavailability" as used herein means that if a pharmaceutical composition comprising fexofenadine or its pharmaceutically acceptable salt and a pharmaceutically acceptable carrier is tested in a crossover study (usually comprising a cohort of at least 10 or more human subjects), the average Area Under the Curve (AUC) and/or the C_{max} for each crossover group is at least 80% of the

(corresponding) average AUC and/or C_{max} observed when the same cohort of subjects is dosed with the fexofenadine formulation whose NDA received approval of USFDA. Use of AUCs, C_{max} and crossover studies is, of course well understood in the art. It may also be noted that the NDA product is approved for marketing on the basis of its therapeutic efficacy and safety demonstrated in human studies. The therapeutic efficacy and safety parameter may change if there is a change in bioavailability and thus once the NDA is approved, then it continues to be manufactured in a reproducible manner to provide the same bioavailability as the originally approved product. If there is a change in the manufacturing process, then the NDA holder must submit to the USFDA data demonstrating that the bioavailability of the product obtained using the new process is the same as that of the originally approved product. If there is any change in bioavailability of the product such that the therapeutic efficacy of the drug is affected, then the NDA holder will no longer be able to market the product using the approval received on the original product, and will instead need to file a NDA for the new product to obtain USFDA approval for it.

In preferred embodiments, the pharmaceutical compositions of the present invention are bioequivalent to commercially available preparations of fexofenadine. Approval of a generic version (Abbreviated New Drug Application, ANDA) of a proprietary drug (NDA) by the USFDA, as mentioned above, requires demonstration of "chemical equivalence" (similar quantities and availability of the active ingredient in proprietary and generic formulations), and "bioequivalence" (defined by absorption parameters generally falling between 80% and 125% of those obtained with the proprietary agent under the same testing conditions). Hence, a generic drug formulation to be approved by the USFDA, has to be bioequivalent to the reference listed drug or the proprietary formulation. The present invention provides a pharmaceutical composition for the treatment of histamine-mediated conditions that releases fexofenadine in a manner to provide desirable blood level profile of fexofenadine that provides efficacy in the treatment of histamine-mediated conditions. For example, when administered as a single dose in fasted state to healthy human subjects it provides area under the plasma concentration-time curve (AUC) which is comparable to that provided by the pharmaceutical composition of fexofenadine commercially available in the United States of America in May 2003. Alternatively, it provides peak plasma levels (C_{max}) that are comparable with those provided by the pharmaceutical composition of fexofenadine commercially available in the United States of America in May 2003. Herein, the term comparable means that 90 percent confidence intervals for the ratio of the population geometric means between the pharmaceutical composition of the present invention and the fexofenadine composition commercially available in the United States of America, namely Allegra[®], based on log-transformed data, is contained in the limits of 70-135 percent for AUC

and C_{max} . More preferred embodiments of the present invention are bioequivalent to fexofenadine composition commercially available in the United States of America. Bioequivalence may be determined according to USFDA guidelines and criteria.

- 5 The examples that follow are provided as illustrations and do not limit the scope of the present invention.

Comparative Example 1

- Oral pharmaceutical composition in the form of tablets comprising fexofenadine
10 hydrochloride was prepared as per Table 1 below.

Table 1

Ingredients	Quantity (mg/tablet)	Percent by weight
Fexofenadine Hydrochloride	180.0	30.0
Lactose, direct compression grade (DCL 21)	300.0	50.0
Silicified microcrystalline cellulose (Prosolv SMCC 90)	105.0	17.5
Sodium lauryl sulfate	6.0	1.0
Colloidal silicon dioxide	3.0	0.5
Magnesium stearate	6.0	1.0
Core tablet weight	600.0	

- Fexofenadine hydrochloride was mixed with direct compression grade lactose, Prosol
SMCC 90, sodium lauryl sulfate, colloidal silicon dioxide and magnesium stearate and
15 blended to obtain a mixture. The blend obtained had a poor flow, causing problems during compression. The tablets obtained had a high disintegration time.

Comparative Example 2

- Oral pharmaceutical composition in the form of tablets comprising fexofenadine
hydrochloride was prepared as per Table 2 below.

20

Table 2

Ingredients	Quantity (mg/tablet)	Percent by weight
Fexofenadine Hydrochloride	180.0	26.47
Dibasic calcium phosphate	302.0	44.14
Silicified microcrystalline cellulose (Prosolv SMCC 90)	80.0	11.76
Microcrystalline cellulose (Avicel PH 102)	100.0	14.71
Sodium lauryl sulfate	6.0	0.88
Colloidal silicon dioxide	6.0	0.88
Magnesium stearate	6.0	0.88

- Fexofenadine hydrochloride was mixed with dibasic calcium phosphate, Prosolv SMCC 90, microcrystalline cellulose, sodium lauryl sulfate, colloidal silicon dioxide and magnesium stearate and blended to obtain a mixture. The mixture obtained was compressed to obtained tablets. The tablets thus obtained were subjected to dissolution testing using United States Pharmacopoeia dissolution apparatus, type II, at a speed of 50 rpm. The dissolution medium used was 1800ml of 0.001M HCl. The dissolution was compared with that of Allegra® tablets. The results are recorded in Table 3 below.

Table 3

Time (mins)	Percent drug released	
	Allegra® tablets (180mg)	Composition of Comparative Example 2
10	84	35
20	91	44
30	95	48
45	96	52
60	98	56

- As is seen in Table 3 above, the release of fexofenadine hydrochloride from the tablets of comparative example 2 was not comparable to that from Allegra® tablets.

Example 1

- The oral pharmaceutical composition of the present invention was obtained as per the method given in Table 4 below.

Table 4

Ingredients	Quantity (mg/tablet)	Percent by weight
Core tablet		
Fexofenadine Hydrochloride	180.0	30.0
Xylitol 300	240.0	40.0
Polyvinyl pyrrolidone (PVP K30)	10.0	1.66
Sodium Lauryl Sulphate	4.0	0.66
Extragranular		
Microcrystalline Cellulose (Avicel PH 200)	120.0	20.0
Sodium Lauryl Sulphate	4.0	0.66
Colloidal Silicon Dioxide	3.0	0.5
Sodium Starch Glycolate	24.0	4.0
Talc	9.0	1.5
Magnesium Stearate	6.0	1.0

Fexofenadine hydrochloride used had a particle size such that 90% of the particles are about 25 microns in diameter. Xylitol, PVP K30 and sodium lauryl sulfate were sifted through a sieve #40 ASTM (ASTM stands for American Society for Testing and Materials) and mixed together in a polybag. The above blend and Fexofenadine hydrochloride were taken in a stainless steel vessel and mixed well. The blend was heated in a stainless steel vessel using water bath maintained at 75-85°C and mixed continuously till a granular mass was obtained. The hot granulated mass was cooled to approximately 70°C with stirring and passed through ASTM 8# sieve. The granules were cooled for 7 hours. The cooled granules were then sifted through ASTM 20# sieve. The granules were blended with Avicel PH 200, sodium lauryl sulfate, colloidal silicon dioxide, sodium starch glycolate and talc. The blend was lubricated with magnesium stearate and compressed into tablets at 600 mg tablet weight. Core tablets were coated using Opadry 035B6773 (Brown).

The dissolution profile of the composition of the example 1 was compared with the Allegra® tablets. The dissolution apparatus used was USP Type II at 50 rpm and the dissolution medium was 1800 ml of 0.001 M HCl. The results are given in table 5 below.

Table 5

Time (mins)	Percent drug released	
	Allegra® tablets (180mg)	Composition of Example 1
10	84	44
20	91	76
30	95	83
45	96	86
60	98	87

20

Examples 2 -- 10

The oral pharmaceutical compositions of the present invention were obtained as per the method given in Table 6 and Table 7 below.

25

Table 6

Ingredients	Quantity (mg/tablet)
Intragranular	
Fexofenadine hydrochloride	180.0
Binding agent (see Table 7)	
Placebo granules (Lactose monohydrate, corn starch and PVP K-30)	320.2
Extragranular	
Sodium Lauryl Sulphate	6.0
Colloidal Silicon Dioxide	3.0
Sodium Starch Glycolate	24.0
Talc	12.0
Magnesium Stearate	4.8
Core tablet weight	600.0

Table 7

Example number	Binding agent	Quantity (mg/tablet)
2	Polyethylene glycol (PEG 4000)	50.0
3	Polyethylene glycol (PEG 4000) Polyvinylpyrrolidone (PVP K-30)	40.0 10.0
4	Polyethylene glycol (PEG 8000)	50.0
5	Polyethylene glycol (PEG 8000) Polyvinylpyrrolidone (PVP K-30)	40.0 10.0
6	Poloxamer 188	50.0
7	Geleol (glyceryl monostearate)	50.0
8	Precirol ATO 5 (glyceryl distearate)	50.0
9	Lubritab (hydrogenated cotton seed oil)	50.0
10	Gelucire 44/10 (Lauroyl macrogol 32 glyceride)	50.0

- 5 Holt melt granulation of fexofenadine hydrochloride and the binding agent was carried out as mentioned in example 1 above. Placebo granules comprising lactose monohydrate, corn starch and PVP K-30 were prepared by conventional wet granulation process and mixed with the melt-granulated product in amounts as specified in Table 6 above. The granules thus obtained were mixed with the extragranular excipients mentioned in Table 6 and compressed to obtain tablets.

The dissolution profile of the compositions of the examples 2-10 was compared with the Allegra[®] tablets (180mg). The dissolution apparatus used was USP Type II at 50 rpm and the dissolution medium was 1800 ml of 0.001 M HCl. The results are given in table 8 below.

Table 8

Time (mins)	Percent drug released									
	Allegra®	Ex 2	Ex 3	Ex 4	Ex 5	Ex 6	Ex 7	Ex 8	Ex 9	Ex 10
10	84	69	72	67	75	80	49	54	48	75
20	91	78	79	75	82	88	66	78	78	86
30	95	81	82	80	85	91	72	82	85	88
45	96	87	87	86	88	92	76	85	89	88
60	98	89	90	88	88	92	81	87	91	89

Example 11

The oral pharmaceutical composition of the present invention was obtained as per the method

5 given below in Table 9.

Table 9

Ingredients	Quantity (mg/tablet)
Intragranular	
Fexofenadine hydrochloride	180.0
Xylitol	180.0
Placebo granules (Lactose monohydrate, corn starch and PVP K-30)	190.2
Extragranular	
Sodium Lauryl Sulphate	6.0
Colloidal Silicon Dioxide	3.0
Sodium Starch Glycolate	24.0
Talc	12.0
Magnesium Stearate	4.8
Core tablet weight	600.0

Holt melt granulation of fexofenadine hydrochloride and xylitol was carried out as mentioned in example 1. Placebo granules comprising lactose monohydrate, corn starch and PVP K-30 were prepared by conventional wet granulation process and mixed with the melt-granulated product. The granules thus obtained were mixed with the extragranular excipients and compressed to obtain tablets. The dissolution profile of the composition of the tablets thus obtained was compared with the Allegra® tablets. The dissolution apparatus used was USP Type II at 50 rpm and the dissolution medium was 1800 ml of 0.001 M HCl. The results are given in table 10 below.

15

Table 10

Time (mins)	Percent drug released	
	Allegra® tablets (180mg)	Composition of Example 11
10	84	44
20	91	77
30	95	85
45	96	89
60	98	91

Example 12

The oral pharmaceutical composition of the present invention was obtained as per the method given below in Table 11.

Table 11

Ingredients	Quantity (mg/tablet)
Intragranular	
Fexofenadine hydrochloride	180.0
Xylitol 300	300.0
Polyvinylpyrrolidone (PVP K30)	12.0
Sodium lauryl sulfate	4.0
Extragranular	
Pregelatinized starch (Starch 1500)	60.0
Microcrystalline cellulose (Avicel PH 200)	51.7
Sodium lauryl sulfate	4.0
Colloidal silicon dioxide	4.5
Sodium starch glycolate	24.0
Talc	13.2
Magnesium stearate	6.6
Coating	
Opadry 85F56975 Brown	19.8
Core tablet weight	679.8

5

Fexofenadine hydrochloride having a particle size such that d_{90} is about 25 microns is used for this composition. Xylitol, PVP K30 and sodium lauryl sulfate were sifted through ASTM #40 and mixed in a polybag. Fexofenadine hydrochloride was then added to this mixture. The blend thus obtained was heated in a stainless steel vessel using a water bath maintained at 80±10°C, and mixed continuously to obtain a granular mass. The mass was cooled to room temperature for about 2 hours, followed by sifting of the granules through ASTM #20. The granules were then mixed with Avicel PH 200, starch 1500, sodium lauryl sulfate, colloidal silicon dioxide, sodium starch glycolate, talc and magnesium stearate. This mixture was then compressed to obtain tablet cores that were then coated with Opadry to a weight gain of about 3% by weight of the core.

10

The dissolution profile of the coated tablets thus obtained was compared with the Allegra® tablets. The dissolution apparatus used was USP Type II at 50 rpm and the dissolution medium was 1800 ml of 0.001 M HCl. The results are given in table 12 below.

20

Table 12

Time (mins)	Percent drug released	
	Allegra® tablets (180mg)	Composition of Example 12
10	84	47
20	91	80
30	95	89
45	96	93
60	98	97

Example 13

The bioavailability of the pharmaceutical composition of fexofenadine hydrochloride (Example 12) of the present invention and that of commercially available fexofenadine hydrochloride tablets, Allegra® (180 mg fexofenadine hydrochloride, Aventis, Inc., USA), were studied. A single-dose, open label, randomized, comparative and two-way crossover study, with a seven-day washout period, was undertaken for the same.

The pharmacokinetic assessment was based on the plasma levels of fexofenadine hydrochloride measured by blood sampling. Blood samples were obtained before dosing and at the following times after administration of both the reference and test medications: 0.5, 1.0, 1.5, 1.75, 2.0, 2.25, 2.5, 2.75, 3.0, 3.5, 4.0, 6.0, 8.0, 12.0, 16.0 and 24.0 hours.

Eleven healthy male volunteers were enrolled for the study and all of them completed the two-way crossover study. The subjects were fasted overnight before dosing and for 4 hours thereafter. Drinking water was prohibited 2 hours before dosing and 2 hours thereafter, but was allowed ad lib at all other times. Standard meals were provided at 4, 8 and 12 hours after dosing, and at appropriate times thereafter. Meal plans were identical for both the periods.

Subjects received a single tablet of fexofenadine hydrochloride (180 mg, Example 12) with 240ml of drinking water at ambient temperature as the test medication, and a single oral dose of Allegra® (180 mg fexofenadine hydrochloride) also with 240ml of drinking water at ambient temperature as the reference medication.

The plasma concentration of fexofenadine hydrochloride was determined for samples collected at different time points and averaged over the eleven volunteers. The data is given in Table 13 below.

Table 13

Time (hrs)	Plasma concentration (ng/ml)	
	Reference (Allegra® 180 mg)	Test (Fexofenadine hydrochloride, 180 mg, Example 12)
0	0	0
0.5	291.07	166.37
1.0	517.27	444.36
1.5	524.0	561.82
1.75	543.46	564.18
2.0	510.64	563.27
2.25	518.64	543.55
2.50	562.36	571.27
2.75	525.91	567.20
3.0	523.46	543.27
3.5	464.36	456.46
4.0	441.73	434.36
6.0	319.64	326.83
8.0	190.92	175.84
12.0	68.05	69.41
16.0	36.44	35.80
24.0	14.51	15.69

The pharmacokinetic parameters calculated using the Win Nonlin software are given in Table

5 14 below.

Table 14

Parameter	Units	Ln-transformed				
		Least Square Means		Ratio (%T/R)	90% confidence Intervals on the ratio	
		Reference (Allegra® 180mg)	Test (fexofenadine hydrochloride, 180 mg, Example 11)		Lower	Upper
C _{max}	ng/ml	656.36	687.64	109.43	93.96	120.60
AUC _{0-t}	ng.hr/ml	4007.41	3928.07	103.72	84.43	115.99
AUC _{0-inf}	ng.hr/ml	4116.98	4042.89	98.20	84.72	116.22
T _{max}	hr	2.30	2.57	111.88		

Thus, the pharmaceutical composition of example 12 was found to be bioequivalent to Allegra®.

10

While the invention has been described by reference to specific embodiments, this was done for purposes of illustration only and should not be construed to limit the spirit or the scope of the invention.

15

CLAIMS

1. An immediate release oral pharmaceutical composition comprising a therapeutically effective amount of fexofenadine or its pharmaceutically acceptable salts, a dissolution
5 enhancing amount of a thermomelting binding agent and pharmaceutically acceptable excipients.
2. An immediate release oral pharmaceutical composition as claimed in claim 1, wherein the thermomelting binding agent is selected from a hydrophilic agent, a hydrophobic agent and mixtures thereof.
- 10 3. An immediate release oral pharmaceutical composition as claimed in claim 2, wherein the hydrophilic agent is selected from the group comprising polyethylene glycols and derivatives thereof, saccharides, sugar alcohols, hydrophilic surfactants and mixtures thereof.
- 15 4. An immediate release oral pharmaceutical composition as claimed in claim 2, wherein the hydrophobic agent is selected from the group comprising waxes, higher fatty acids, higher fatty alcohols, straight-chain saturated hydrocarbons, fats, hydrogenated vegetable oils, glycerol esters, polyoxyethylene alkyl ethers, polyoxyethylene-polyoxypropylene block copolymers, and mixtures thereof.
5. An immediate release oral pharmaceutical composition as claimed in claim 2, wherein the
20 hydrophilic agent is a sugar alcohol selected from xylitol, mannitol, sorbitol and mixtures thereof.
6. An immediate release oral pharmaceutical composition as claimed in claim 2, wherein the thermomelting binding agent is used in an amount ranging from about 5% to about 95% by weight of the composition.
- 25 7. An immediate release oral pharmaceutical composition as claimed in claim 5, wherein the thermomelting agent is xylitol.
8. An immediate release oral pharmaceutical composition as claimed in claim 7, wherein xylitol is present in an amount ranging from about 30% to about 60% by weight of the composition.
- 30 9. An immediate release oral pharmaceutical composition as claimed in claim 1, wherein the pharmaceutically acceptable excipients is selected from one or more of surfactants, disintegrants, binders, wicking agents, lubricants and fillers.
10. An immediate release oral pharmaceutical composition as claimed in claim 1, wherein the
35 composition has essentially the same bioavailability as commercially available fexofenadine composition whose New Drug Application received approval of United States Food and Drug Administration.



PODER ESPECIAL

Yo, WALTER TANAKA TATEKAWA, mayor de edad y vecino de la ciudad de Barranquilla (Colombia), identificado como aparece al pie de mi firma, quien en el presente documento actúa en calidad de Representante Legal de la sociedad PROCAPS S.A. sociedad legalmente constituida y domiciliada en la ciudad de Barranquilla (Colombia), por el presente documento otorgo a la doctora ELIANA ISAURA MORENO BOHORQUEZ, abogada en ejercicio, identificada como aparece al pie de su firma, con tarjeta profesional No. 83823 del C.S. de la J., poder especial, amplio y suficiente, para formular oposiciones u observaciones a la solicitud de patente No. 13 296682, titulada "COMPOSICIÓN FARMACÉUTICA QUE COMPRENDE FEXOFENADINA", cuyo titular es AVENTIS PHARMACEUTICALS, INC. publicada en la gaceta No. 683 del 10 de enero de 2014.

Nuestro apoderado queda facultado, de manera expresa, para realizar todo tipo de actos necesarios para llevar a cabo el trámite de la oposición, incluyendo, sin limitación, preparar y presentar solicitudes, hacer declaraciones, pagar tasas, contribuciones e impuestos, recabar los títulos o certificados. Asimismo quedan autorizados para impugnar administrativamente todo lo que fuere resuelto en el expediente a que se hace expresa referencia en el presente poder, con todas las facultades generales y específicas que fuera requerido para ella.

De la misma manera, además de las facultades que le confiere la naturaleza del presente mandato, se encuentran facultados para recibir, desistir, transigir, sustituir, y reasumir el presente poder, incoar acciones, interponer recursos y demás facultades conferidas por la ley.

Dado y Firmado en Barranquilla (Colombia) a los 2 días del mes de Abril de 2014.

APROBADO

02 ABR 2014

PROCAPS S.A.

PROCAPS S.A.

C.C. N° 16'251.923

NIT: 890.106.527-5

Representante Legal

Acepto:

ELIANA ISAURA MORENO BOHÓRQUEZ

C.C. 51.975.664

T.P. 83823 del C.S.J

Señor Director,
DIRECCIÓN DE NUEVAS CREACIONES
Superintendencia de Industria y Comercio
E. S. D.

Referencia : Expediente N° 13 296682
Asunto : Oposición a la solicitud de patente de Invención titulada
"COMPOSICIÓN FARMACÉUTICA QUE COMPRENDE
FEXOFENADINA"
Solicitante : AVENTIS PHARMACEUTICALS, INC.
Opositora : PROCAPS S.A.

Publicada en la Gaceta de la Propiedad Industrial
N° 683 del 10 de enero de 2014

Yo, *ELIANA ISAURA MORENO BOHÓRQUEZ*, abogada en ejercicio, identificada como aparece al pie de su firma, con tarjeta profesional No. 83823 del Consejo Superior de la Judicatura, en mi condición de apoderada de la sociedad PROCAPS S.A. conformada bajo las leyes de la República de Colombia y domiciliada en la ciudad de Barranquilla, Colombia, atentamente manifiesto que estando dentro del término de ley y por orden expresa de mi representada, presento oposición a la concesión del registro de la Patente de Invención titulada "COMPOSICIÓN FARMACÉUTICA QUE COMPRENDE FEXOFENADINA", cuyo titular AVENTIS PHARMACEUTICALS, INC., y pido a Usted declarar fundada esta oposición y en consecuencia negar el registro de la patente solicitada.

1. INTERÉS PARA ACTUAR

Conforme a lo dispuesto en el artículo 42 de la Decisión 486 de 2000 de la CAN, estando dentro del término estipulado por la ley, manifiesto el legítimo interés de nuestra representada para oponerse al registro de la patente de la referencia, atendiendo a que la solicitud pretendida no cumple con los requisitos dispuestos en la ley como se analizará más adelante y de ser concedida afectaría directamente la comercialización de algunos productos de mi representada, que contienen, en particular *FEXOFENADINA*. Por lo tanto, solicito respetuosamente a ese Despacho se sirva tener en cuenta la presente oposición dentro del trámite administrativo que se surte en esta Superintendencia.

2. FUNDAMENTOS DE HECHOS

- 2.1. La solicitud objeto de la presente fue presentada el 19 de diciembre de 2013, reivindicando prioridad bajo las solicitudes IN2011CH01727 del 2011-05-20; US201161499856P del 2011-06-22; y, EP20110305923 del 2011-07-13; y fue publicada en Colombia, en la Gaceta de la Propiedad Industrial N° 683 del 10 de enero de 2014, cuya publicación internacional corresponde a la WO2012159960 del 2012-11-29.
- 2.2. La solicitud colombiana 13 296682 objeto de la presente oposición se refiere a una formulación farmacéutica de hidrocloreto de fexofenadina en un sistema de disolvente adecuada como una composición líquida de relleno. En otro aspecto, la invención también se refiere a un proceso para la preparación de dicha formulación farmacéutica y al uso de dicha composición para la preparación de un fármaco para el tratamiento de reacciones alérgicas en un paciente.
- 2.3. En primera instancia, se debe advertir que las reivindicaciones se refieren a usos y métodos de tratamiento y no sólo a la composición farmacológica o a un método de fabricación mediante la cual se obtenga un producto tangible y según la legislación, decisión 486 de la Comunidad Andina de Naciones, Artículo 14.-

“Los Países Miembros otorgarán patentes para las invenciones, sean de producto o de procedimiento (...)”, los usos no están contemplados como patentables; y, Artículo 20.- “No serán patentables (...) d) los métodos terapéuticos o quirúrgicos para el tratamiento humano o animal, así como los métodos de diagnóstico aplicados a los seres humanos o a animales”. Solo serán patentables los productos o procedimientos. Por lo tanto a luz de la norma, dicha materia referente métodos de tratamiento no sería patentable.

2.4. Ahora bien, con base en el artículo 14 de la Decisión 486 de la CAN consagra lo siguiente: *“Los países miembros otorgarán patentes para las invenciones, sean de producto o procedimiento, en todos los campos de la tecnología, siempre que sean nuevas, tengan nivel inventivo y sean susceptibles de aplicación industrial”.* Así las cosas, las invenciones objeto de patente deben ser nuevas y tener nivel inventivo. Bien, pues antes de la fecha de prioridad de esta solicitud se encuentran los siguientes documentos que afecta la patentabilidad de la presente solicitud:

- D1: WO2005062722 publicada el 14 de julio de 2005.

2.5. Ahora bien, el documento D1, proporciona una composición farmacéutica de liberación inmediata oral que comprende una cantidad terapéuticamente eficaz de fexofenadina o sus sales farmacéuticamente aceptables para mejorar la disolución de un agente de unión termofundible y excipientes farmacéuticamente aceptables. Esta anterioridad D1, particularmente en la página 1 líneas 9 a 18, página 4 líneas 10 a 29, página 5 líneas 1 a 7 y líneas 14 a 32, así como los ejemplos 1 a 4, describe una composición oral que comprende clorhidrato de fexofenadina y una mezcla de tensioactivos hidrófilos e hidrófobos en cantidades superiores a 60 p%. El surfactante hidrófilo no iónico puede ser polisorbato 80 - "sorbitán". Los ejemplos 1 a 4 de esta anterioridad D1, ilustran todas las concentraciones del ingrediente activo hasta 30p%. Como tal, esta anterioridad D1, también revela una composición que incluye hidrocloreto de fexofenadina en combinación con surfactantes con buenas propiedades de velocidad de liberación. En las reivindicaciones 1 y 2, dicha anterioridad D1, define una

composición farmacéutica de liberación inmediata oral que comprende una cantidad terapéuticamente eficaz de fexofenadina o sus sales farmacéuticamente aceptables, una cantidad para mejorar la disolución de un agente de unión termofundible y excipientes farmacéuticamente aceptables, en el que el agente se selecciona de un agente hidrofílico, un agente hidrófobo y/o mezclas de los mismos. Como se evidencia, la materia pretendida ya se había divulgado con anterioridad en el documento D1. Por lo tanto, este documento objeto de oposición a la luz del documento D1 carece evidentemente de NOVEDAD.

2.6. En consecuencia y de acuerdo a lo descrito anteriormente, se deriva que la solicitud colombiana 13 296682 no puede pretender un monopolio por patente toda vez que lo que pretende no cumple con dos de los tres requisitos necesarios para su protección.

2.7. Que por consiguiente, respecto a la solicitud pretendida se tiene que:

2.8.1 CARENCIA DE NOVEDAD. Según la decisión 486 de la Comunidad Andina de Naciones, Artículo 16.- *“Una invención se considerará nueva cuando no está comprendida en el estado de la técnica. El estado de la técnica comprenderá todo lo que haya sido accesible al público por una descripción escrita u oral, utilización, comercialización o cualquier otro medio antes de la fecha de presentación de la solicitud de patente o, en su caso, de la prioridad reconocida.”.* A la fecha de prioridad, el 20 de mayo de 2011, ya era conocido, pues como se demostró, era parte del arte anterior con base en los documento D1, una formulación farmacéutica de hidrocloreuro de fexofenadina en un sistema de disolvente adecuada como una composición líquida de relleno, sobre el cual busca protección en el capítulo reivindicatorio.

2.8.2 CARENCIA DE APLICACIÓN INDUSTRIAL La Decisión 486 de la CAN consagra en su artículo 14 lo siguiente: *“Los países miembros otorgarán patentes para las invenciones, sean de producto o procedimiento, en todos los campos de la tecnología, siempre que sean nuevas, tengan nivel inventivo y sean*

susceptibles de aplicación industrial". La presente solicitud carece de aplicación Industrial ya que como se demostró anteriormente, algunas cláusulas reclaman un método de tratamiento y estos no son aplicables industrialmente porque primero no se obtiene un producto o proceso; y segundo no es reproducible o repetible a escala industrial. Por lo tanto, el objeto de la presente invención referido a métodos de tratamiento, no cumple con el requisito de la aplicación industrial.

2.9 Dado lo anterior, es posible deducir que la solicitud y lo reivindicado no es objeto de patentabilidad pues es contrario a lo que dicta la Decisión 486 de la Comunidad Andina de Naciones, Artículo 14.- *"Los Países Miembros otorgarán patentes para las invenciones, sean de producto o de procedimiento, en todos los campos de la tecnología, siempre que sean nuevas, tengan nivel inventivo y sean susceptibles de aplicación industrial."* La solicitud pretendida no cumple con dos de los tres requisitos de patentabilidad.

2.10 Por todo lo anterior, atentamente solicito a usted que se sirva declarar fundada *"COMPOSICIÓN FARMACÉUTICA QUE COMPRENDE FEXOFENADINA"*, cuyo titular AVENTIS PHARMACEUTICALS, INC., solicitud Colombiana que apareció publicada en la Gaceta de la Propiedad Industrial N° 683 del 10 de enero de 2014.

3. PRUEBAS

De conformidad con lo dispuesto por las normas vigentes, solicito a usted tener como prueba en este asunto los siguientes:

- D1: WO2005062722 publicada el 14 de julio de 2005.

4. FUNDAMENTO DE DERECHO

Fundamento esta observación en las normas legales siguientes:

- 4.1. Artículo 45 de la Decisión 486 de la Comisión del Acuerdo de Cartagena.
- 4.2. En las demás normas concordantes.

5. ANEXOS

Para los efectos correspondientes anexo al presente escrito los siguientes documentos:

1. Poder para actuar en el presente.
 2. Documento que acredita al representante legal de PROCAPS S.A.
 3. Recibo de caja del respectivo pago de tasa.
 4. Copias de los documentos:
- D1: WO2005062722 publicada el 14 de julio de 2005.

6. NOTIFICACIONES

Para efectos de notificaciones que debe hacer su Despacho, informo que mi representada y la suscrita recibiremos notificaciones en la Secretaría de su Despacho o en mis oficinas situadas en la Carrera 13 N° 119-95, Of. 104 de esta ciudad de Bogotá.

Señor director,

ELIANA ISAURA MORENO BOHÓRQUEZ

C.C. 51'975.664 de Bogotá

T.P.A. 83823 del C.S. de la J.