

Q.F.



Industria y Comercio
SUPERINTENDENCIA

Delegatura de Propiedad Industrial
División de Nuevas Creaciones

ICT
SOLICITUD

PATENTE DE INVENCION

21 EXPEDIENTE No

04-42457

54 TITULO

NUEVA FORMULACION DE JARABE DE EPINASTINA SECO

Y ACUOSOS

51 CLASIFICACION INTERNACIONAL

A61K31/55

71 SOLICITANTE

BOEHRINGER INGELHEIM INTERNATIONAL GMBH

DOMICILIO

Ingelheim am Rhein, República Federal de Alemania,

74 APODERADO

EMILIO FERRERO

Código No 1092

22 BOGOTA, D C ,

07-05-2004

202099

SS

**Industria y Comercio**

SUPERINTENDENCIA

PETITORIO

SUPERINDUSTRIA Y COMERCIO

Radicación : 84042457 00000000

Folios: 71 ón

Fecha (MD): 2004-05-07 17:19:25

Trámite : 011 PCT-PATENT 379 FASE NNCI 411 PRESENTAC

Dependencia: 2020 DIVISION DE NUEVAS CREACIONES

**FORMULARIO UNICO DE SOLICITUD DE PATENTE
PCT
ENTRADA EN FASE NACIONAL****SOLICITUD DE:****1**☒ Patente de Invención.☐ Patente de Modelo de Utilidad.☐ Capítulo I.☒ Capítulo II.**2****SOLICITANTE
(71)**Nombre: **BOEHRINGER INGELHEIM
INTERNATIONAL GMBH**
sociedad constituida y existente bajo las
leyes de la República Federal de AlemaniaDirección: D-55216 Ingelheim am Rhein,
República Federal de Alemania
Domicilio: Ingelheim am Rhein,
República Federal de Alemania**IDENTIFICACIÓN**C.C. ☐ NIT ☐C.E. ☐ Otro ☐

Cual _____

Número _____

3**REPRESENTANTE
O APODERADO**Nombre: **EMILIO FERRERO**
Dirección: Carrera 4ª. No. 72-35
Teléfono: 347 36 11
Fax: 217 92 11
E-mail: clientes@camyp.com.
Domicilio: Bogotá, Colombia.**IDENTIFICACIÓN**C.C. ☒ NIT ☐C.E. ☐ Otro ☐

Cual _____

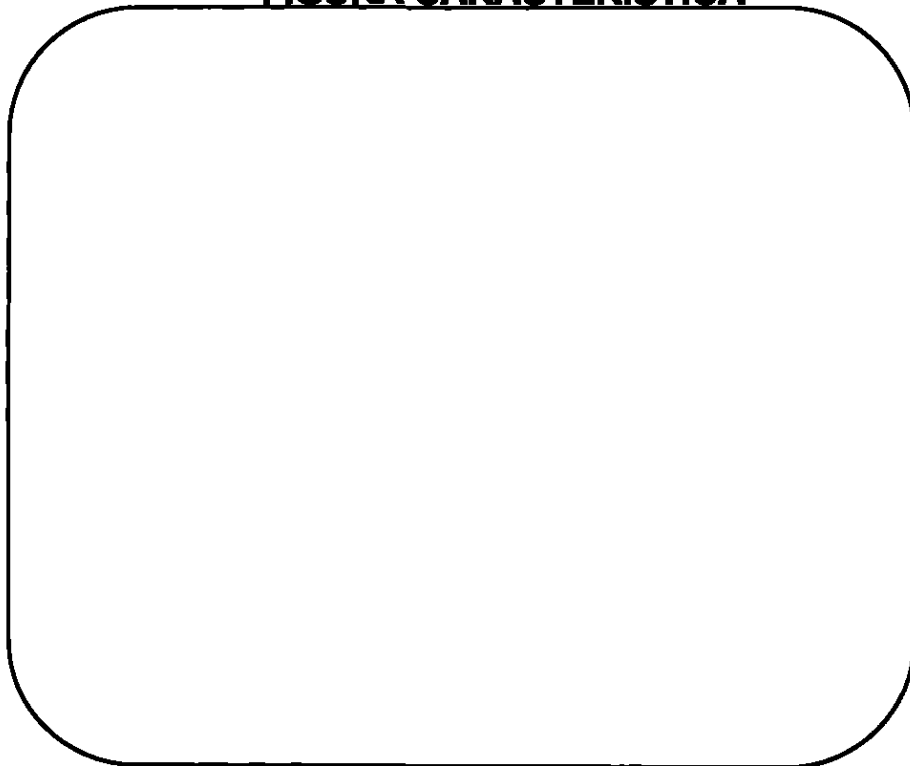
Número 438.019 T.P 31.929**4****INVENTOR (ES)
(72)**1. **Koichi WADA**
2-59-17, Shirogane, Inagawa-cho,
Kawabe-Gun, Hyogo 666-0257,
Japón3. **Toshimitsu OHKI**
4-25-40, Kanda,
Ikeda, Osaka 563-0043,
Japón2. **Manabu NAKATANI**
5-16 Matsugaoka-cho,
Kawanishi, Hyogo 666-0037,
Japón4. **Kenzo TOYOSHIMA**
7-25, Higashi-asahi-gaoka,
Ikoma, NARA 630-0254,
Japón**5****PCT (86)**Solicitud Internacional No. PCT/EP02/11250Fecha: Octubre 8 de 2002Publicación Internacional No. WO 03/037350 A1Fecha: Mayo 8 de 2003**6****Título (54)****NUEVA FORMULACIÓN DE JARABE DE EPINASTINA SECO Y ACUOSO****7****Clasificación Internacional (51) A61K 31/55****8****Prioridad****(33) País de Origen****(32) Fecha****(31) Número de Solicitud**SI ☒ NO ☐DEOctubre 26 de 2001101 52 973.2**9****C mprobante de pago No.: 04 – 28.821****Fecha: Abril 12, 2004**

10

Anex s:

- ☒ Comprobante de pago de la tasa de presentación de la solicitud por \$ 422.000.00.
- ☐ Comprobante de pago por reivindicación de prioridad.
- ☒ Documento que acredita la existencia y representación legal cuando el solicitante sea persona jurídica.
- ☒ Poderes, si fuere el caso.
- ☐ Documento de cesión del inventor al solicitante o a su causante.
- ☐ Declaraciones.
- ☒ Copia de la solicitud internacional. (Resumen, descripción, reivindicaciones, dibujos)
- ☒ Traducción de la solicitud internacional al castellano. (Resumen, descripción, reivindicaciones, dibujos)
- ☒ Copia del examen preliminar efectuado por la IPEA.
- ☒ Traducción del examen preliminar efectuado por la IPEA.
- ☐ De ser el caso, copia del contrato de acceso.
- ☐ De ser el caso, documento que acredite la licencia o autorización de uso de conocimientos tradicionales de las comunidades indígenas.
- ☐ De ser el caso, certificado de depósito del material biológico.
- ☐ Arte final 12x12
- ☐ De ser el caso, información sobre otras solicitudes de patente o títulos obtenidos en el extranjero por el mismo titular o su causante, relacionadas parcial o totalmente con la invención de esta solicitud.
- ☐ Otros

11

FIGURA CARACTERÍSTICA

12

Solicito la concesión de la patente,

NOMBRE: EMILIO FERRERO

FIRMA : 
C.C. 438.019 de Usaquén T.P. 31.929

For patents, utility models, industrial designs, trademarks, commercial names, trade emblems, slogans.

Para patentes, modelos de utilidad, diseños industriales, marcas de fábrica, nombres comerciales, enseñas, lemas comerciales.

REPRESENTACION Y PODER

REPRESENTATION AND
 POWER OF ATTORNEY

9233
 0569

I (we), the undersigned /Yo (nosotros), abajo firmado (s)
BOEHRINGER INGELHEIM INTERNATIONAL GMBH

of/domiciliado (s) en **D-55216 Ingelheim am Rhein,**
GERMANY

por el presente nombramos a GERMAN CAVELIER, tpa. 832; GONZALO PERDOMO, tpa. 831; EMILIO FERRERO, tpa. 31929; y LUZ CLEMENCIA DE PAEZ, tpa. 23555; domiciliados en la Carrera 4ª N° 72-35, Bogotá, Colombia, en obediencia a lo dispuesto en el parágrafo 1º del Artículo 543 del Código de Comercio, el primero como principal y los demás como suplentes, en su orden, como mis (nuestros) representantes en todos los asuntos de propiedad industrial con facultad para recibir notificaciones y nombrar apoderados judiciales o extrajudiciales. El primer representante suplente reemplazará al principal en caso de ausencia o impedimento temporal o definitivo de aquél. La misma regla se aplicará cuando el segundo representante suplente haya de reemplazar al primero, o el tercero al segundo. En tales casos, el representante principal, o el primero, o segundo suplente, en su caso, o ambos, declararán su intención de no ejercer la representación mediante declaración autenticada por Notario Público en Colombia, o por Notario u otro Funcionario Público, o Cónsul de Colombia, en el extranjero; y si se tratare de impedimento, con el certificado respectivo. Si alguno de los nombrados faltare definitivamente, el siguiente tomará su lugar. Cuando cesare la ausencia o impedimento del representante principal, o de su primero o segundo suplentes, en su caso, podrán ejercer la representación, en su orden, uno u otros según el caso, asumiéndola por el solo hecho de ejercerla, cesando en ese momento el ejercicio de la representación por el primero, segundo o tercer suplente en su caso.

Además, confiero (conferimos) poder a los abogados arriba nombrados, para obtener la protección de mi (nuestra) propiedad industrial y contra la competencia desleal, a cuyo efecto autorizo (amos) a los dichos apoderados para que me (nos) representen ante cualesquiera entidades o personas, ejerzan o no jurisdicción, especialmente ante las del orden administrativo, contencioso-administrativo y judicial, así como tribunales de arbitramento, en todo lo concerniente a los siguientes asuntos: a) Obtención de patentes de invención, modelos de utilidad, y diseños industriales; el registro de marcas de fábrica, colectivas, defensivas, de servicio, lemas comerciales, nombres comerciales, enseñas, variedades vegetales y denominaciones de origen; su renovación, traspaso, cambio de nombre o domicilio, cancelación voluntaria; y el registro de licencias de uso de esos derechos; b) Las acciones de competencia desleal, protección del consumidor, oposiciones u observaciones, cancelación administrativa y judicial, nulidad, medidas cautelares, concesión de licencias, la tutela, la protección de secretos industriales, y en general los juicios civiles, penales, administrativos o contencioso-administrativos relacionados con estos derechos; acciones y procesos que promovamos o se nos promuevan. Y para que en todos los asuntos arriba determinados, puedan sustituir este mandato, transigir, conciliar, admitir los hechos del proceso, desistír, cancelar, recibir, renunciar, y ratificar los actos de agentes oficiosos.

In due compliance with the terms of paragraph 1st. of article 543 of the Commercial Code, do hereby appoint GERMAN CAVELIER, tpa. 832; GONZALO PERDOMO, tpa. 831; EMILIO FERRERO, tpa. 31929; and LUZ CLEMENCIA DE PAEZ, tpa. 23555; domiciled at Carrera 4ª N° 72-35, Bogotá, Colombia, the first as principal and the others as alternates, in the order of their appointment, as our representatives for all industrial property matters with faculty to receive notifications and to appoint attorneys in and out of Court. The first alternate shall replace the principal in case of his absence or of temporal or definitive impediment. The same rule will apply when the second alternate representative is to replace the first one, or when the third is to replace the first or second alternates in their turn, or both of them, second. In such cases, the principal representative, or the first or second alternates in their turn, or both of them, shall state their intention not to act as representatives through a declaration given before a Notary Public in Colombia, or before a Notary or another Public Official or a Colombian Consul abroad; and in case of impediment, the appropriate certificate shall suffice. If any of the appointees were to be definitely absent, the following alternate shall take his place. When the absence or impediment of the principal representative, or of the first or second alternate in their turn ceases, the representation can be taken again in their sequence, by the principal, the first or second alternate depending on case, and the mere fact or its exercise will suffice. The exercise of the representation by the first, second or third alternates in their turn shall end at such time.

In addition, we grant a Power of Attorney in favor of the above-named attorneys-at-law so that they may obtain the protection of my (our) industrial property and against the unfair competition, for which purpose I (we) authorize the said attorneys to represent me (us) before authorities or persons, with or without jurisdiction, especially before administrative, administrative-contencioso-administrative and judicial, as well as before Arbitration Court, in all matters concerning the following: a) Obtainment of patents, utility models and industrial designs; the registration of trademarks, collective, defensive and service marks, slogans, commercial names, trade emblems, vegetal varieties and denominations of origin; its renewal, assignment, change of name or domicile, voluntary cancellation; and the registration of licenses of use of the above rights; b) Actions of unfair competition, protection to the consumer, oppositions or observations, administrative or Court cancellation, nullity, infringement, granting of licenses, the action for writ mandamus, the protection of trade secrets, and in general the civil, penal, and administrative suits relating to those rights; actions and suits instituted by me (us) or against me (us). And that in all the above matters they may substitute this Power of Attorney, compromise, conciliate, admit the facts of the case, desist, cancel, receive, resign, and ratify acts done by representatives without a power of attorney.

Ingelheim am Rhein, 12.12.1995

Given and signed this/Dado y firmado hoy

BOEHRINGER INGELHEIM

in/en **INTERNATIONAL GMBH**

ppa.

ppa.

Dr. Dieter Laudien

Dr. Gerhard Huber

Signature

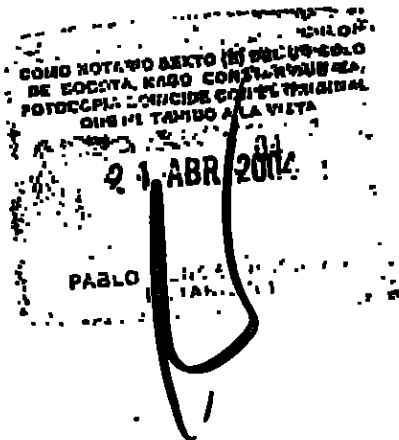
Firma

LEGALIZACION

El Señor Cónsul de Colombia debe expedir un *certificado consular* sobre (1) la existencia legal de la compañía que otorga el poder, (2) que ésta ejerce su objeto social, y (3) que las personas que otorgan el poder están autorizadas para darlo. A este efecto les solicitamos que muestren al Señor Cónsul las pruebas que acreditan esos hechos (1), (2) y (3).

LEGALIZATION

The Colombia Consul must issue a *consular certificate*, on (1) the legal existence of the company which grants Power-of-Authority, (2) that it is in actual exercise of company purposes, and (3) that the persons who execute the Power of Attorney is authorized to do so. To this effect, please show the Consul the evidence to prove the above facts (1), (2) and (3).



NOTA PARA EL SEÑOR CONSUL DE COLOMBIA: Según los artículos 65 del C. de P.C. y 480 del C. de Co., si el poderdante es una sociedad, el Señor Cónsul debe certificar que tuvo a la vista las pruebas de su existencia, que ejerce su objeto social y que quien confiere el poder es su representante.

Vorselbige, vor mir gefertigte Namensunterschriften der Herren:

1. Dr. Dieter L a u d i e n, Dipl.-Chemiker, wohnhaft in 55127 Mainz,.
2. Dr. Gerhard H u b e r, Rechtsanwalt, wohnhaft in 55411 Bingen,

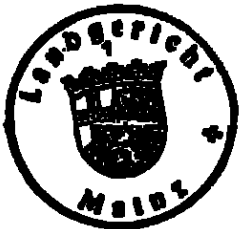
- mir bekannt -

beglaubige ich hiermit.

Gleichzeitig bescheinige ich aufgrund heutiger Einsichtnahme in das Handelsregister des Amtsgerichts Bingen, daß die Firma Boehringer Ingelheim International GmbH mit Sitz in Ingelheim am Rhein im Handelsregister des Amtsgerichts Bingen unter HR B 1063 eingetragen ist und daß die Herren Dr. Laudien und Dr. Huber als Prokuristen gemeinschaftlich zur Vertretung der Gesellschaft berechtigt sind.

Ingelheim am Rhein, den 12. Dezember 1995/hün


Notariatsverweser
anstelle des Notars
Prof. Dr. Weirich in Ingelheim



- 910 E 1 -

Die Echtheit vorstehender Unterschrift des Notariatsassessors Dr. Peter Wirth - Notariatsverweser anstelle des Notars Prof. Dr. Weirich in Ingelheim und die Echtheit des eingedruckten Dienst - ~~stempel~~ - siegels werden hierdurch bestätigt. Zugleich wird bescheinigt, daß der Vorgenannte zur Vornahme der Amtshandlung gesetzlich befugt war.

Kostenberechnung:

Gebühr für Legalisation

(Wert: DM 5.000,-)

JVKostO. v. 26.7.1957

BGBI. I S. 881

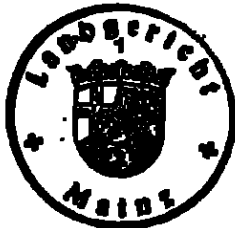
DM 50,-

12. DEZ. 1995

Mainz, den



Amtsinspektor



Mainz, den dreizehnten Dezember neunzehnhundertfünfundneunzig

Der Präsident des Landgerichts


(Dr. Hans Paul Töllerberg)



CONSULADO GENERAL DE COLOMBIA

MUNICH

Nr. 169

El Cónsul General de Colombia

CERTIFICA

Que el Dr. Hanns Paul Tüttenberg ----, quién autentica la firma del signatario en el presente documento, ejercía en la fecha allí indicada las funciones de Presidente del Tribunal Regional en Mainz.

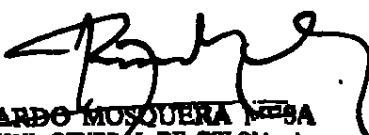
Que la firma BOEHRINGER INGELHEIM INTERNATIONAL GmbH, domiciliada en 55216 Ingelheim am Rhein, Registro Mercantil Nr. HR B 1063 del Juzgado Municipal de Bingen está constituida y ejerce su objeto social de conformidad con las leyes de la República Federal de Alemania.

Que los señores Dr. DIETER LAUDIN Y Dr. GERHARD HUBER

quien(es) firman el presente documento tiene (n) facultad legal suficiente para representar a la mencionada firma y otorgar poderes en su nombre.

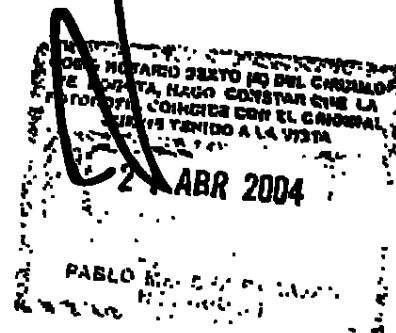
Que ha tenido a la vista la documentación que prueba lo anterior.

Munich, 18 de Diciembre de 1995


RICARDO MOSQUERA MESA
CONSUL GENERAL DE COLOMBIA

Derechos para la Nación	US \$	6.-
Fondo Rotatorio	US \$	100.-
Tasa consular	US \$ 1 x DM	1,60 = DM 169.60

PAGADO





COMO NOTARIO CERTO DE DEL CIRCULAR
DE FOLIO, HAYO CONSTAR QUE LA
FOTOCOPIA CONCORDA CON EL ORIGINAL
QUE HA TENIDO A LA VISTA

21 ABR 2004

PASLO...

MINISTERIO DE RELACIONES
EXTERIORES

Mosquera

NO SE ASUME
RESPONSABILIDAD DEL TEXTO

ENE - 11 A 11:44

OFICINA DE CALIFICACIONES
ESTADO DE BOGOTA D.C.

7-004.5133 A Q 27

TRADUCCION OFICIAL No. 5133

de un documento escrito en Alemán, el cual para su identificación se sella con el sello de la traductora, lo mismo que la presente.-

(A continuación del poder conferido a GERMAN CAVELIER, tpa. 832; GONZALO PERDOMO, tpa. 831; EMILIO FERRERO tpa, 31929; y LUZ CLEMENCIA DE PAEZ, tpa 23555; domiciliados en la Carrera 4 No. 72-35, Bogotá, Colombia, por la BOEHRINGER INGELHEIM INTERNATIONAL GMBH, domiciliada en D-55216 Ingelheim am Rhein, RFA, a través de sus representantes los Srs. Dr. Dieter Laudien y Dr. Gerhard Huber:)

Handwritten signature/initials.

Legalización

Protocolo notarial No. 2659/93 y

Certifico la autenticidad de las firmas antecedentes puestas ante mí por los señores:

1. Dr. Dieter Laudien, Dipl. Chim., domiciliado en 55127 Mainz,
2. Dr. Gerhard Huber, abogado, domiciliado en 55411 Bingen

a quienes conozco en persona.

COMO AUTENTICO EN EL CIRCULO
EL CUAL HA SIDO COMITADO LA
FOTOCOPIA CONCORDA CON EL ORIGINAL
QUE LA TENGO A LA VISTA

21 ABR 2004

PABLO GARCIA
NOTARIO

Igualmente certifico, por haber examinado en la fecha el Registro de Comercio del Juzgado Municipal de Bingen, HR B 1063, que la firma Boehringer Ingelheim International GmbH, domiciliada en Ingelheim am Rhein, está inscrita bajo el No. HR B 1063 en el Registro de Comercio del Juzgado Municipal de Bingen y que los señores Dr. Laudien y Dr. Huber, en su calidad de apoderados, están facultados para representar conjuntamente a la sociedad.

Ingelheim am Rhein, 12 de diciembre de 1995/hün

Fdo.: firma ilegible

(Hilo y oblea roja en relieve:) El notario suplente

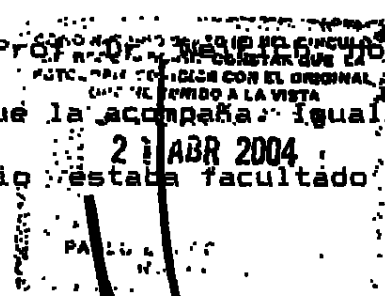
El notario suplente - Ingelheim del notario de Ingelheim

Prof. Dr. Weirich

(dos sellos redondos en tinta del Tribunal Regional de Mainz)

910 E 1

Se certifica la autenticidad de la firma antecedente del Dr. Peter Wirth, como notario suplente del Prof. Dr. Weirich, Notario de Ingelheim, y la del sello oficial que la acompaña. Igualmente se certifica que el mencionado notario estaba facultado para realizar ese acto oficial.



Mainz, trece de diciembre de mil novecientos noventa y cinco

9

El Presidente del Tribunal Regional

(E) Fdo.: firma ilegible

(Dr. Hanns Paul Tüttenberg)

Costas

Derechos de legalización
(Valor: DM 5.000,-)
JVKostO del 26 de julio 1957
Gacetas Oficial I Pag. 861
DM 20,--
Mainz, 13 de diciembre de 1995
Fdo.: firma ilegible
Inspector

EN ESPAÑOL: La legalización de las firmas antecedente por el
Consulado de Colombia en Munich bajo el No. 1849 de 10 de
diciembre de 1995, y por el Ministerio de Relaciones Exteriores
de Colombia bajo el No. 051606 de 14 de enero de 1996.
Pagados derechos y Fondo Rotatorio

COMO NOTARIO PUBLICO DEL CIRCULO DE BOGOTA, HAGO CONSTAR QUE LA FOTOCOPIA CONCORDA CON EL ORIGINAL QUE SE ME PRESENTO A LA VISTA

21 ABR 2004

ES TRADUCCION FIEL Y COMPLETA, de la cual se deja copia en los
archivos de estas oficinas para su confrontación.

Santafé de Bogotá, 6 de enero de 1996.

ALZ ARCHAUS DE BOGOTA
20.01.96
549 Minutario
13/01/96

[Firma]

COMO NOTARIO SEXTO ENCARGADO DE SANTAFE
DE BOGOTA HAGO CONSTAR QUE LA FIRMA DE

[Handwritten signature]

C. C. _____
COINCIDE CON LA REGISTRADA POR EL (ELLA)
EN ESTA NOTARIA

09 ENE 1996

SANTAFE DE BOGOTA D.C.



NO SE ASUME
RESPONSABILIDAD DEL TEXTO

1996 ENE 10 A 11:33

COMO NOTARIO SEXTO ENCARGADO DE SANTAFE DE BOGOTA HAGO CONSTAR QUE LA COPIA CONFORMA CON EL ORIGINAL
JEFES DE REGISTRO Y CANCELACIONES
SANTAFE DE BOGOTA D.C.
21 ABR 2004

MINISTERIO DE RELACIONES
EXTERIORES

[Handwritten signature]
08/19/11

CUYA FIRMA
PRESENTE
PRESENTE
LAS FUNCIONES

TELEFAX: (57) (1) 30 9850
TELEX: 49479 CAVE CO
(23)7407379 CAVE UC

CAVELIER

ABOGADOS

EDIFICIO SISKI
CARRERA 4ª, No. 72-35
BOGOTÁ 8, COLOMBIA

CORREO ELECTRONICO MUNDIAL: CAVE
TELEFONO (57) (1) 2120100
CABLES: CAVELEYES

Señor Jefe de la
DIVISION DE NUEVAS CREACIONES
Superintendencia de Industria y Comercio
E. S. D.

Poderdante: BOEHRINGER INGELHEIM INTERNATIONAL GMBH

Poder conferido el: 12-12-95.

Yo, GERMAN CAVELIER, obrando en mi calidad de apoderado principal del poderdante arriba mencionado atentamente manifiesto a Usted que sustituyo el poder que me ha sido conferido en la persona del doctor EMILIO FERRERO, Abogado con Tarjeta Profesional No. 31.929, con todas las facultades que me fueron conferidas.

Hago la anterior sustitución conforme al artículo 66 del Código de Procedimiento Civil ya que los otros sustitutos faltan en este momento.

Señor Jefe,


GERMAN CAVELIER

T.P.A. No. 832

C.C. No. 2.877.924 de Bogotá

Acepto:



EMILIO FERRERO

T.P.A. No. 31.929

C.C. No. 438.019 de Usaquén

2e-780-2

NOTARIA SEXTA DE BOGOTÁ
RECONOCIMIENTO Y PRESENTACION PERSONAL

Bogotá, D. C. 11 ENE 1996

Ante mí, PABLO XIENDEZ BARAJAS S.

NOTARIO SEXTO ENCARGADO DEL CIRCULO DE BOGOTÁ

Compareció(eron):

quien(es) exhibió(aron) la(s):

28770124
438019

y la(s) Libreta(s) Militar(es).

domiciliado(s) en Bogotá y declaró(aron) que la(s) firma(s) que
aparecen(n) en el presente documento es(son) la(s) suya(s) y
que el contenido del mismo es cierto.
En constancia se firmó esta Diligencia.

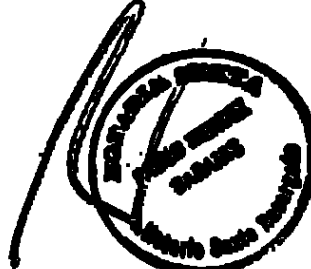
NOTA DEL CIRCULO
CONTESTAR QUE LA
CON EL ORIGINAL
A LA VISTA

21 MAR 2004

Ben Calvo

N

Emilio Franco



(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
8 May 2003 (08.05.2003)

PCT

(10) International Publication Number
WO 03/037350 A1

(51) International Patent Classification⁷: A61K 31/35,
9/00, 9/14, 9/20, 47/26, A61P 11/02, 11/06, 27/02

(74) Common Representative: BOEHRINGER INGEL-
HEIM INTERNATIONAL GMBH; Binger Str. 173,
55216 INGELHEIM (DE).

(21) International Application Number: PCT/EP02/11250

(22) International Filing Date: 8 October 2002 (08.10.2002)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
101 52 973.2 26 October 2001 (26.10.2001) DE

(71) Applicant (for all designated States except US):
BOEHRINGER INGELHEIM INTERNATIONAL
GMBH [DE/DE]; Binger Str. 173, 55216 INGELHEIM
(DE).

(81) Designated States (*national*): AE, AG, AL, AM, AT, AU,
AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU,
CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GH, GI,
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW,
MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG,
SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ,
VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (*regional*): ARIPO patent (GH, GM,
KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW),
Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM),
European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE,
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(54) Title: NEW DRY AND AQUEOUS EPINASTINE-SYRUP-FORMULATION

(57) Abstract: The present invention refers to a new formulation of epinastine in form of a powder (dry syrup) to be mixed with water prior to use. Epinastine can be used either as free base or as a pharmaceutically acceptable salt thereof. Epinastine among others is for treating allergies, pain, in particular chronic pain and inflammation caused pain, migraine, asthma, rhinitis, conjunctivitis and/or bronchitis. In particular, the formulation is for treating allergies, dermatitis, rhinitis, conjunctivitis, bronchitis and asthma.

WO 03/037350 A1

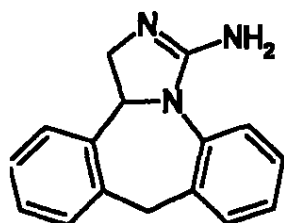
New dry and aqueous Epinastine-Syrup-Formulation

The present invention refers to a new formulation of epinastine in form of a powder (dry syrup) to be mixed with water prior to use. Epinastine among others is for
5 treating allergies, pain, in particular chronic pain and inflammation caused pain, migraine, asthma, rhinitis, conjunctivitis and/or bronchitis (f.e. EP-B-0 035 749, EP 1000623). In particular, the formulation is for treating allergies, dermatitis, rhinitis, conjunctivitis, bronchitis and asthma.

10 State of the Art

Epinastine, chemically known as 3-Amino-9,13b-dihydro-1H-dibenz-[c,f]imidazol[1,5-a]azepine and its acid addition salts are disclosed for the first time in the German Patent application P 30 08 944.2 which forms the basis for EP 0035749.

15 Chemically epinastine is represented by the following formula, which does not reflect stereochemical properties:



20 Epinastine can be used either as free base or as a pharmaceutically acceptable salt thereof. Preferably, epinastine is used as hydrochloride.

If not specified further in the context of the present invention the term epinastine is
25 used for the free base as well as for pharmaceutically acceptable salts.

Methods for its preparations can be taken from EP 0496306 or from WO 01/40229.

13

Epinastine is marketed in Japan under the brand name Alesion and most often is used due to its antihistaminic effects.

5 The state of the art prefers tablets as application form for epinastine.

However, especially for children or the elderly people, tablets are not easy to take and therefore there is a need of new formulation easily applicable by children or elderly people.

10

Summary of the present invention

It was found that a suitable formulation for such a group of customers like children and the elderly might be liquid formulations. However, it turned out that epinastine has a strong taste of bitterness.

15

As a consequence there was a need – and to solve this is one objective of the present invention - to develop a neutral or good tasting liquid formulation of epinastine and/or one of its pharmaceutically acceptable acid addition salts.

20 Another objective of the present invention is to provide a liquid epinastine-formulation which can be stored for some time without the risk of fast decreasing pharmaceutical quality.

Still another objective of the present invention is to create an easy to handle
25 epinastine-formulation for to provide a liquid. Such a liquid formulation shall also be rather a solution than a dispersion in order to improve its acceptance by the patient.

14

Description of the present invention

The present invention relates to a powder-like formulation (dry syrup) of epinastine, either in enantiomeric, racemic form or a salt thereof, which is mixed with water prior to use. To do so it is required that the powder is dissolved in water very quickly.

5

In the context of the present invention the term "powder" is used simultaneously with the term "dry syrup" which in turn stands for an essentially water-free admixture of the active form of epinastine, preferably epinastine-hydrochloride, and pharmaceutically acceptable additives and adjuvants necessary to form an aqueous, sweet tasting formulation of the active substance when mixed with water.

10

Surprisingly, it was found that aqueous formulations of epinastine-hydrochloride cause two different kinds of bad tasting in form of strong bitterness. On one hand there is a quick-acting kind of bitterness and on the other hand there is a lasting bitterness that is tasted for quite a long time.

15

Unfortunately, the bitter taste of epinastine could not be masked by the use of one conventional taste masking agent as sucrose for example.

20

In stead it was found that the taste of strong bitterness can be overcome by the combination of quick- and slow acting sweeteners and flavouring agents.

As a consequence thereof a preferred embodiment of the formulation of the present invention should comprise at least one of each kind of these masking agents.

25

For the masking of quick-acting bitterness, saccharin sodium, erythritol and/or aspartame turned out to be effective. Another suitable group of compounds comprises sugars and sugar-derived polyols such as sucrose, D-sorbitol, glycerin and D-mannitol. Preferably, the formulation comprises saccharin sodium, erythritol and/or aspartame. Most preferred is the combination of saccharin sodium, erythritol and aspartame.

30

The amount of the at least one masking agent for to mask the quick-acting bitterness depends of the agent used.

In case of saccharin sodium, it is between 0.1 % w/w and 2.0 % w/w of the powder formulation. Preferably the amount is 0.8. %

5

In case of erythritol it is between 50 % w/w and 95 % w/w of the powder formulation. Preferably the amount is 75 to 80 % w/w, most preferred it is 80% w/w.

And in case of aspartame it is between 1 % w/w and 30 % w/w of the powder
10 formulation. Preferably the amount is 5 to 15% w/w, most preferred it is 10%.

For masking the lasting bitterness glycyrrhizins were found to be highly effective. Among them glycyrrhizic acid and/or monoammonium glycyrrhizinate are the preferred ones. The most preferred one is monoammonium glycyrrhizinate.

15

The amount of monoammonium glycyrrhizinate in the powder formulation is 0.1-% w/w and 3.0 % w/w of the powder formulation. More preferred are 0.1 to 1% w/w and most preferred is 0.6%.

20 The formulation further may comprise adjuvants, among which are for example pH-adjusting agents. It is preferred to add such pH-adjusting agents to adjust the pH of the resulted liquid to a value of between 5 and 8, preferably 6 and 7. Among those agents are citric acid, succinic acid, tartaric acid, acetic acid, citrates, acetates, vitamin C, hydrochloric acid, carbonates, phosphates, disodium phosphate,
25 monosodium phosphate, sodium-, calcium-, potassium- and/or magnesium-hydroxide. Preferred are buffer substances like disodium phosphate.

Further commonly other used additives can optionally be added, too.
Among these are

30

- binding agents such as hydroxypropylcellulose, methylcellulose, hydroxypropylmethylcellulose, hydroxyethylcellulose, starch, dextrin, gelatine and polyvinylpyrrolidone, preferably hydroxypropylcellulose,
- 5 - flow agents such as hydrated silicon dioxide, light anhydrous silicic acid,
- odorizers such as sunfix orange No.22734 (commercial name, sunfix orange which is preferred contains orange flavour (30%w/w), acacia (30%w/w) and dextrin(40%w/w)), orange oil, mentha oil, eucalyptus strawberry flavour, vanilla flavour, yoghurt flavour and other flavours known in the art,
- 10 - colour pigments such as food yellow No.5, also being known as sunset yellow FCF (disodium salt of 6-hydroxy-5-(4-sulfophenylazo)-2-naphthalenesulfonic acid), the latter being preferred, ferric oxide, and other food colour pigments, f.e. the ones known in Japan as food red No.3, 102, 105 and 106, food yellow No.4 and other food colours known in the art, and/or
- 15 - preservatives such as benzoic acid, salts thereof, preferably sodium benzoate, paraoxybenzoic acids, salts thereof and other known preservatives, whereby sodium benzoate is preferred and
- effervescent agents such as bicarbonate.

20 The amount of epinastine or its salt is between 0.5 % w/w and 5 % w/w of the powder formulation. More Preferred is an amount of between 0,5 % w/w and 2 % w/w, the most preferred amount is 1 %.

The powder formulation preferably does not contain an active substance which is not
25 epinastine or a pharmaceutically acceptable salt thereof.

The active substance, preferably epinastine-hydrochloride and all the additives are mixed to a powder and then the powder is mixed with water to preferably obtain a liquid formulation. Although the liquid formulation may either be a solution,
30 suspension or a colloid, the preferred liquid formulation is a transparent and clear aqueous solution.

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It is preferred to mix the powder formulation with water to obtain a liquid having a concentration of between 250mg per 5-50ml and 2000mg per 10-100 ml , preferably the amount is between 50 mg per 10 ml and 2000mg per 10ml.

5 If epinastine-hydrochlorid is used, the amount in the context of the present invention is (about) the same as for the free base.

In order to ensure that the patient easily can prepare the liquid formulation the inventive powder formulation (dry syrup) can be delivered in certain packages. In these packages the water and the inventive powder formulation are stored separately
10 from each other. The package further allows the both components to mix in an easy way.

As a consequence thereof the present invention also relates to a kit comprising two components, a) the inventive powder formulation and b) water, both components separated from each other.
15

In the state of the art several bottles having special caps are known to solve this issue. Most often in such packages the liquid solvent can be stored in a bottle of glass, plastic, metal and so on while the cap for closing the bottle comprises a
20 chamber to take the dry powder formulation. Prior to use the patient can take of the powder of the cap and mix it with the water in the bottle. This mixing process can either be done consciously, meaning the patient actively takes the powder and puts it into the water. In other embodiments the patient can initiate the mixing process in a more automatic way by for example just screwing, pressing, shaking the cap or the
25 bottle in order to put away a barrier in the chamber containing the powder and by doing so allowing it to fall from the cap into the bottles.



Such packagings are disclosed for example in EP 0599189, EP 0344849, EP 0217425, EP 0093090, US 3802604 and others. Herewith, all of these devices are incorporated by reference. Other, similar devices might be used, too.

Besides, such package forms the dry syrup formulation can be stored in an

5 aluminium or plastic-bag or in an aluminium or plastic bottle. The such stored powder then can be used with a pre-metered amount of water, stored in another package or the freshly filled drinking water is used.

Other package systems may be used, too.

10

In the context of the present invention the powder formulation can also be pressed to tablet to be dissolved in water, for example an effervescent tablet. In such an embodiment the tablet – just as the powder formulation - may additionally comprise an effervescent agent such as bicarbonate.

15

19

Experimental**New dry and aqueous epinastine- Syrup-Formulation 0.5%.**

Powder-Formulation No.	1	2	3	4	5	6	7
epinastine hydrochloride [mg]	5	5	5	5	5	5	5
glycerin [mg]	0	0	0	0	0	0	350
sucrose [mg]	0	0	0	0	0	540	620
anhydrous citric acid [mg]	0	0	0	0	0	25	0
monoammonium glycyrrhizinate [mg]	7	0	6	6	6	0	0
saccharin sodium [mg]	0	6	4	0	5	5	0
sodium fumarate [mg]	10	10	0	10	5	0	10
disodium phosphate [mg]	0	0	0	3	15	10	0
erithritol [mg]	923	919	925	916	904	395	0
aspartame [mg]	60	60	60	60	60	25	0
sodium benzoate [mg]	0	0	0	0	0	0	15
Results							
Appearance when mixed with water*	white	clear*	white	clear*	clear*	clear*	clear*
Masking of Bitterness	good	good	good	good	very good	good	good

* the amount of water is not significant. However, 1g of powder preferably should be readily soluble in 5-50 ml of water.

5 * Clear in the meaning of transparent.

New dry and aqueous epinastine-Syrup-Formulation 1.0%

Powder-Formulation No.	8	9	10	11	12	13	14
epinastine hydrochloride [mg]	10	10	10	10	10	10	10
glycerin [mg]	0	0	0	0	0	0	350
sucrose [mg]	0	0	0	0	0	542	425
anhydrous citric acid [mg]	0	0	0	0	0	25	0
monoammonium glycyrrhizinate [mg]	10	0	10	6	6	0	0
saccharin sodium [mg]	0	10	5	0	8	0	0
sodium fumarate [mg]	20	10	0	15	5	0	10
disodium phosphate [mg]	0	0	0	10	15	0	0
erithritol [mg]	859	859	854	838	835	397	200
aspartame [mg]	100	100	100	100	100	25	0
hydroxypropylcellulose [mg]	0	20	20	20	20	0	0
hydrated silicon dioxide [mg]	1	1	1	1	1	1	0
Odorizor* [mg]	0	(1)	(1)	(1)	(1)	(1)	0
food yellow No.5** [mg]	0	(0.05)	(0.05)	(0.05)	(0.05)	(0.05)	0
sodium benzoate [mg]	0	0	0	0	0	0	5
<u>Results</u>							
Appearance when mixed with water***	white	clear [#]	white	clear [#]	clear [#]	clear [#]	clear [#]
Masking of Bitterness	good	good	good	good	very good	good	good

*sunfix orange No.22734 (commercial name) containing orange flavor (30%w/w), acacia (30%w/w) and dextrin (40%w/w).

** Another name of Food yellow no.5 is sunset yellow FCF (disodium salt of 6-hydroxy-5-(4-sulfophenylazo)-2-naphthalenesulfonic acid).

*** the amount of water is not significant, however, 1g of powder preferably should be readily soluble in 10-100 ml of water.

[#] Clear in the meaning of transparent.

Claims

1. Pharmaceutical powder formulation comprising an active agent based on epinastine and/or an acid addition salt, preferably the hydrochloride, at least two
5 kinds of sweeteners and/or flavourings and optionally further pharmaceutically acceptable adjuvants, whereby one of the at least two kinds of sweeteners and/or flavourings is for to mask the quick-acting bitterness of the active agent and the other one is for to mask the long-acting bitterness of the active agent.
- 10 2. Pharmaceutical powder formulation according to claim 1, characterised in that the at least one sweetener and/or flavouring for to mask the quick-acting bitterness is selected from saccharin sodium, erythritol, aspartame and/or sugars or other polyols such as sucrose, glycerin, D-sorbitol and D-mannitol.
- 15 3. Pharmaceutical powder formulation according to claim 1 or 2, characterised in that the at least one sweetener and/or flavouring for to mask the quick-acting bitterness is selected from saccharin sodium, erythritol and aspartame. :
4. Pharmaceutical powder formulation according to claim 1 to 3, characterised in
20 that the at least one sweetener and/or flavouring for to mask the quick-acting bitterness is a combination of saccharin sodium, erythritol and aspartame.
5. Pharmaceutical powder formulation according to any of claims 1 to 4,
characterised in that the at least one sweetener and/or flavouring for to mask the
25 long-acting bitterness is a glycyrrhizinate or glycyrrhinic acid, preferably selected from mono-, di-ammonium glycyrrhizinate, di-, tri-sodium glycyrrhizinate and/or dipotassium glycyrrhizinate, most preferably monoammonium glycyrrhizinate.

6. Pharmaceutical powder formulation according to any of claims 1 to 5,
characterised in that the formulation further comprises a pH-adjusting agent
selected from the group of citric-acid, citrates, succinic acid, tartaric acid, acetic
5 acid, acetates, vitamin C, hydrochloric acid, carbonates, sodium-, calcium-,
potassium- and/or magnesium- hydroxide, phosphates, preferably
disodiumphosphate and/or monosodium phosphate, most preferably monosodium
phosphate.
- 10 7. Pharmaceutical powder formulation according to any of claims 1 to 6,
characterised in that the formulation further comprises at least one adjuvans
selected from the group of odorizers, colour pigments, preservatives, flow agents
and/or binding agents.
- 15 8. Pharmaceutical powder formulation according to any of claims 1 to 7,
characterised in that the formulation comprises epinastine-hydrochloride in an
amount of between 0.5% w/w and 5 %w/w, saccharin sodium in an amount of
between 0.1 % w/w and 2.0 % w/w, erythritol in an amount of between 50 % w/w
and 95 % w/w, aspartame in an amount of between 1 % w/w and 30 % w/w,
20 monoammonium glycyrrhizinate in an amount of 0.1 % w/w and 3.0 % w/w and
optionally disodiumphosphate, sodium fumarate, hydroxypropylcellulose,
hydrated silicon dioxide, orange flavor, acacia, dextrin and /or disodium salt of 6-
hydroxyl-5-(4-sulfophenylazo)-2-naphthalenesulfonic acid.
- 25 9. Pharmaceutical powder formulation according to any of claims 1 to 8,
characterised in that the formulation comprises epinastine hydrochloride,
monoammonium glycyrrhizinate, saccharin sodium, sodium fumarate, erythritol,
aspartame, hydroxypropylcellulose, hydrated silicon dioxide, orange flavour,
acacia, dextrin and disodium salt of 6-hydroxyl-5-(4-sulfophenylazo)-2-
30 naphthalenesulfonic acid.

10. Pharmaceutical powder formulation according to any of claims 1 to 9, characterised in that the formulation comprises an effervescent agent.

11. Pharmaceutical tablet, comprising the ingredients of the powder formulation according to any of claims 1 to 10.

12. Liquid formulation available by mixing any of the powder formulations of claims 1 to 10 or the tablet of claims 11 with water.

10

13. Liquid formulation according to claim 12, characterised in that the formulation is a solution.

15

14. Liquid formulation according to claim 13, characterised in that the formulation is a dispersion.

15. Liquid formulation according to claim 12 or 13, characterised in that the formulation comprises a pH-adjusting agent according to claim 6 in an amount to adjust the pH to between 5 and 8, preferably to between 6 and 7.

20

16. Liquid formulation according to any of claims 12 to 15, characterised by an amount of epinastine of between 0.09 mg and 35 mg per 10 ml, preferably of between 0.4 mg and 18 mg per 10 ml.

25

17. Liquid formulation according to any of claims 12 to 15, characterised by an amount of epinastine-hydrochloride of between 0.1 mg and 40 mg per 10 ml, preferably of between 0.5 mg and 20 mg per 10 ml.

30

18. Liquid formulation according to any of claims 12 to 17, characterised in that 250 mg to 2000 mg of a powder formulation according to any of claims 1 to 9 or the tablet of claim 11 are mixed with 10 to 100 ml of water.

21/

19. Package comprising a kit of a powder formulation according to any of claims 1 to 10 or the tablet of claim 11 and separated thereof water to obtain a liquid formulation according to any of claims 12 to 18 if the powder and the water are mixed together.

20. Package according to claim 19, characterised in that the package is a bottle with a cap comprising a chamber, that can be opened easily in a manual way or by screwing or pressing the cap onto the bottle, the chamber containing a powder formulation according to any of claims 1 to 10 or the tablet of claim 11 and the bottle comprising the water.

21. Use of a powder formulation according to any of claims 1 to 10 or use of the tablet of claim 11 to mix with water to obtain a formulation according to any of claims 12 to 18.

22. Use of a formulation according to any of claims 1 to 18 for to manufacture a medical preparation for to treat allergies, pain, in particular chronic pain and inflammation caused pain, migraine, asthma, rhinitis, conjunctivitis and/or bronchitis, preferably for to treat allergies.

23. Method of treating allergies, pain, in particular chronic pain and inflammation caused pain, migraine, asthma, rhinitis, conjunctivitis and/or bronchitis, preferably for to treating allergies characterised by mixing a powder formulation according to any of claim 1 to 10 or the tablet of claim 11 with water to obtain a liquid formulation according to any of claims 12 to 18 and to apply this formulation to a patient.

24. Process for making a powder formulation according to any of claims 1 to 10 by mixing the different components together.



25. Process for making a tablet according to claim 11 by mixing the different components together and subsequent pressing thereof.

- 5 26. Process for making a liquid formulation according to any of claims 12 to 18 by mixing the powder formulation according to any of claims 1 to 10 or the tablet according to claim 11 with water.

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0	For receiving Office use only	
0-1	International Application No.	
0-2	International Filing Date	
0-3	Name of receiving Office and "PCT International Application"	
0-4	Form - PCT/RO/101 PCT Request	
0-4-1	Prepared using	PCT-EASY Version 2.92 (updated 01.06.2002)
0-5	Petition The undersigned requests that the present international application be processed according to the Patent Cooperation Treaty	ERFASST 64
0-6	Receiving Office (specified by the applicant)	European Patent Office (EPO) (RO/EP)
0-7	Applicant's or agent's file reference	1-1261-PCT
I	Title of invention	NEW DRY AND AQUEOUS EPINASTINE-SYRUP-FORMULATION
II	Applicant	
II-1	This person is:	applicant only
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II-6	State of nationality	DE
II-7	State of residence	DE
II-8	Telephone No.	06132/77-2003
II-9	Facsimile No.	06132/77-4377
III-1	Applicant and/or inventor	
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III-1-7	State of residence	JP

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III-2	Applicant and/or inventor	
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III-3-7	State of residence	JP
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III-4-2	Applicant for	US only
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III-4-6	State of nationality	JP
III-4-7	State of residence	JP
IV-1	Agent or common representative; or address for correspondence The person identified below is hereby/has been appointed to act on behalf of the applicant(s) before the competent International Authorities as:	common representative
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IV-1-3	Telephone No.	06132/77-2003
IV-1-4	Facsimile No.	06132/77-4377

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V	Designation of States	
V-1	Regional Patent (other kinds of protection or treatment, if any, are specified between parentheses after the designation(s) concerned)	AP: GH GM KE LS MW MZ SD SL SZ TZ UG ZM ZW and any other State which is a Contracting State of the Harare Protocol and of the PCT EA: AM AZ BY KG KZ MD RU TJ TM and any other State which is a Contracting State of the Eurasian Patent Convention and of the PCT EP: AT BE BG CH&LI CY CZ DE DK EE ES FI FR GB GR IE IT LU MC NL PT SE SK TR and any other State which is a Contracting State of the European Patent Convention and of the PCT OA: BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG and any other State which is a member State of OAPI and a Contracting State of the PCT
V-2	National Patent (other kinds of protection or treatment, if any, are specified between parentheses after the designation(s) concerned)	AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH&LI CN CO CR CU CZ DE DK DM DZ EC EE 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 MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW
V-5	Precautionary Designation Statement In addition to the designations made under items V-1, V-2 and V-3, the applicant also makes under Rule 4.9(b) all designations which would be permitted under the PCT except any designation(s) of the State(s) indicated under item V-6 below. The applicant declares that those additional designations are subject to confirmation and that any designation which is not confirmed before the expiration of 15 months from the priority date is to be regarded as withdrawn by the applicant at the expiration of that time limit.	
V-6	Exclusion(s) from precautionary designations	NONE
VI-1	Priority claim of earlier national application	
VI-1-1	Filing date	26 October 2001 (26.10.2001)
VI-1-2	Number	101 52 973.2
VI-1-3	Country	DE
VII-1	International Searching Authority Chosen	European Patent Office (EPO) (ISA/EP)

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VIII	Declarations	Number of declarations	
VIII-1	Declaration as to the identity of the inventor	-	
VIII-2	Declaration as to the applicant's entitlement, as at the international filing date, to apply for and be granted a patent	-	
VIII-3	Declaration as to the applicant's entitlement, as at the international filing date, to claim the priority of the earlier application	-	
VIII-4	Declaration of inventorship (only for the purposes of the designation of the United States of America)	-	
VIII-5	Declaration as to non-prejudicial disclosures or exceptions to lack of novelty	-	
IX	Check list	number of sheets	electronic file(s) attached
IX-1	Request (including declaration sheets)	5	-
IX-2	Description	9	-
IX-3	Claims	5	-
IX-4	Abstract	1	EZABST00.TXT
IX-5	Drawings	0	-
IX-7	TOTAL	20	
	Accompanying items	paper document(s) attached	electronic file(s) attached
IX-8	Fee calculation sheet	✓	-
IX-13	Priority document(s)	Item(s) VI-1	-
IX-17	PCT-EASY diskette	-	Diskette
IX-19	Figure of the drawings which should accompany the abstract		
IX-20	Language of filing of the international application	English	
X-1	Signature of applicant, agent or common representative		
X-1-1	Name	BOEHRINGER INGELHEIM INTERNATIONAL GMBH	
X-1-2	Name of signatory	Dr. Kläs	
X-1-3	Capacity	ppa	
X-2	Signature of applicant, agent or common representative		
X-2-1	Name	BOEHRINGER INGELHEIM INTERNATIONAL GMBH	
X-2-2	Name of signatory	Dr. Fuchs	
X-2-3	Capacity	i.V.	

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10-1	Date of actual receipt of the purported international application	
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1-1261-PCT

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10-2	Drawings:	
10-2-1	Received	
10-2-2	Not received	
10-3	Corrected date of actual receipt due to later but timely received papers or drawings completing the purported International application	
10-4	Date of timely receipt of the required corrections under PCT Article 11(2)	
10-5	International Searching Authority	ISA/EP
10-6	Transmittal of search copy delayed until search fee is paid	

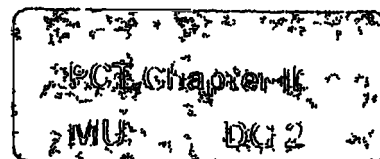
FOR INTERNATIONAL BUREAU USE ONLY

11-1	Date of receipt of the record copy by the International Bureau	
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The demand must be filed directly with the competent International Preliminary Examining Authority or, if two or more Authorities are competent, with the one chosen by the applicant. The full name or two-letter code of that Authority may be indicated by the applicant on the line below:

IPEA/ _____

PCT
DEMAND



under Article 31 of the Patent Cooperation Treaty:

The undersigned requests that the international application specified below be the subject of international preliminary examination according to the Patent Cooperation Treaty and hereby elects all eligible States (except where otherwise indicated).

For International Preliminary Examining Authority use only	
Identification of IPEA	Date of receipt of DEMAND
Box No. I IDENTIFICATION OF THE INTERNATIONAL APPLICATION	
Applicant's or agent's file reference 1/1261-PCT	
International application No. PCT/EP 02/11250	International filing date (day/month/year) 8. October 2002 (08/10/02)
(Earliest) Priority date (day/month/year) 26. October 2001 (26/10/01)	
Title of invention New dry and aqueous Epinastine-Syrup-Formulation	
Box No. II APPLICANT(S)	
Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.) BOEHRINGER INGELHEIM INTERNATIONAL GMBH 55216 Ingelheim	
Telephone No. 06132/77-2003	
Facsimile No. 06132/77-4377	
Teleprinter No.	
Applicant's registration No. with the Office	
State (that is, country) of nationality: DE	State (that is, country) of residence: DE
Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.) WADA, Koichi 2-59-17, Shirogane, Inagawa-cho Kawabe-gun Hyogo 666-0257 JP	
State (that is, country) of nationality: JP	State (that is, country) of residence: JP
Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.) NAKATANI, Manabu 5-16 Matsugaoka-cho Kawanishi, Hyogo 666-0037 JP	
State (that is, country) of nationality: JP	State (that is, country) of residence: JP
☒ Further applicants are indicated on a continuation sheet.	

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Sheet No. 2.

International application No.
PCT/EP 02/11250

Continuation of Box No. II APPLICANT(S)	
<i>If none of the following sub-boxes is used, this sheet should not be included in the demand</i>	
Name and address: <i>(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)</i> OHKI, Toshimitsu 4-25-40, Kouda Ikeda Osaka, 563-0043 JP	
State <i>(that is, country)</i> of nationality: JP	State <i>(that is, country)</i> of residence: JP
Name and address: <i>(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)</i> TOYOSHIMA, Kenzo 7-25, Higashi-asahigaoka Ikoma Nara 630-0254 JP	
State <i>(that is, country)</i> of nationality:	State <i>(that is, country)</i> of residence:
Name and address: <i>(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)</i> -	
State <i>(that is, country)</i> of nationality: -	State <i>(that is, country)</i> of residence:
Name and address: <i>(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)</i> 	
State <i>(that is, country)</i> of nationality:	State <i>(that is, country)</i> of residence:
Name and address: <i>(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)</i> 	
State <i>(that is, country)</i> of nationality:	State <i>(that is, country)</i> of residence:
☐ Further applicants are indicated on another continuation sheet.	

Box No. III AGENT OR COMMON REPRESENTATIVE; OR ADDRESS FOR CORRESPONDENCEThe following person is ☐ agent ☐ common representativeand ☐ has been appointed earlier and represents the applicant(s) also for international preliminary examination.☐ is hereby appointed and any earlier appointment of (an) agent(s)/common representative is hereby revoked.☐ is hereby appointed, specifically for the procedure before the International Preliminary Examining Authority, in addition to the agent(s)/common representative appointed earlier.Name and address: *(Family name followed by given name, for a legal entity, full official designation.
The address must include postal code and name of country.)*

Telephone No.

Facsimile No.

Teleprinter No.

Agent's registration No. with the Office

☐ Address for correspondence: Mark this check-box where no agent or common representative is/has been appointed and the space above is used instead to indicate a special address to which correspondence should be sent.**Box No. IV BASIS FOR INTERNATIONAL PRELIMINARY EXAMINATION****Statement concerning amendments:***

1. The applicant wishes the international preliminary examination to start on the basis of:

☐ the international application as originally filedthe description ☒ as originally filed☐ as amended under Article 34the claims ☒ as originally filed☐ as amended under Article 19 (together with any accompanying statement)☐ as amended under Article 34the drawings ☒ as originally filed☐ as amended under Article 342. ☐ The applicant wishes any amendment to the claims under Article 19 to be considered as reversed.3. ☐ The applicant wishes the start of the international preliminary examination to be postponed until the expiration of 20 months from the priority date unless the International Preliminary Examining Authority receives a copy of any amendments made under Article 19 or a notice from the applicant that he does not wish to make such amendments (Rule 69.1(d)). *(This check-box may be marked only where the time limit under Article 19 has not yet expired.)*

* Where no check-box is marked, international preliminary examination will start on the basis of the international application as originally filed or, where a copy of amendments to the claims under Article 19 and/or amendments of the international application under Article 34 are received by the International Preliminary Examining Authority before it has begun to draw up a written opinion or the international preliminary examination report, as so amended.

Language for the purposes of international preliminary examination: ENGLISH☒ which is the language in which the international application was filed.☐ which is the language of a translation furnished for the purposes of international search.☐ which is the language of publication of the international application.☐ which is the language of the translation (to be) furnished for the purposes of international preliminary examination.**Box No. V ELECTION OF STATES**The applicant hereby elects all eligible States *(that is, all States which have been designated and which are bound by Chapter II of the PCT)*

excluding the following States which the applicant wishes not to elect:

Box No. VI CHECK LIST

The demand is accompanied by the following elements, in the language referred to in Box No. IV, for the purposes of international preliminary examination:

- | | | |
|--|---|--------|
| 1. translation of international application | : | sheets |
| 2. amendments under Article 34 | : | sheets |
| 3. copy (or, where required, translation) of amendments under Article 19 | : | sheets |
| 4. copy (or, where required, translation) of statement under Article 19 | : | sheets |
| 5. letter | : | sheets |
| 6. other (specify) | : | sheets |

For International Preliminary Examining Authority use only

- | received | not received |
|--------------------------|--------------------------|
| ☐ | ☐ |
| ☐ | ☐ |
| ☐ | ☐ |
| ☐ | ☐ |
| ☐ | ☐ |
| ☐ | ☐ |

The demand is also accompanied by the item(s) marked below:

- | | |
|--|---|
| 1. ☒ fee calculation sheet | 5. ☐ statement explaining lack of signature |
| 2. ☐ original separate power of attorney | 6. ☐ sequence listings in computer readable form |
| 3. ☐ original general power of attorney | 7. ☐ tables in computer readable form related to sequence listings |
| 4. ☐ copy of general power of attorney; reference number, if any: | 8. ☐ other (specify): |

Box No. VII SIGNATURE OF APPLICANT, AGENT OR COMMON REPRESENTATIVE

Next to each signature, indicate the name of the person signing and the capacity in which the person signs (if such capacity is not obvious from reading the demand).

BOEHRINGER INGELHEIM INTERNATIONAL GMBH

ppa.

Dr. Kläs

i.v.

Dr. Fuchs

For International Preliminary Examining Authority use only

1. Date of actual receipt of DEMAND:

2. Adjusted date of receipt of demand due to CORRECTIONS under Rule 60.1(b):

- | | |
|--|---|
| 3. ☐ The date of receipt of the demand is AFTER the expiration of 19 months from the priority date and item 4 or 5, below, does not apply. | ☐ The applicant has been informed accordingly. |
| 4. ☐ The date of receipt of the demand is WITHIN the period of 19 months from the priority date as extended by virtue of Rule 80.5. | |
| 5. ☐ Although the date of receipt of the demand is after the expiration of 19 months from the priority date, the delay in arrival is EXCUSED pursuant to Rule 82. | |

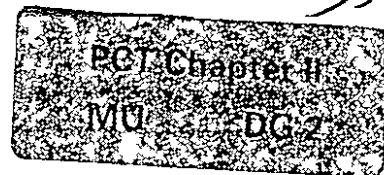
For International Bureau use only

Demand received from IPEA on:

PCT

FEE CALCULATION SHEET

Annex to the Demand



International application No. PCT/EP 02/11250	For International Preliminary Examining Authority use only
Applicant's or agent's file reference 1/1261-PCT	Date stamp of the IPEA
Applicant BOEHRINGER INGELHEIM INTERNATIONAL GMBH	
CALCULATION OF PRESCRIBED FEES	
1. Preliminary examination fee	1.530 P
2. Handling fee (<i>Applicants from certain States are entitled to a reduction of 75% of the handling fee. Where the applicant is (or all applicants are) so entitled, the amount to be entered at H is 25% of the handling fee.</i>)	159 H
3. Total of prescribed fees Add the amounts entered at P and H and enter total in the TOTAL box	1.689 €
TOTAL	
MODE OF PAYMENT	
☒ authorization to charge deposit account with the IPEA (see below)	☐ cash
☐ cheque	☐ revenue stamps
☐ postal money order	☐ coupons
☐ bank draft	☐ other (specify):
AUTHORIZATION TO CHARGE (OR CREDIT) DEPOSIT ACCOUNT <i>(This mode of payment may not be available at all IPEAs)</i>	
☒ Authorization to charge the total fees indicated above.	IPEA/ <u>EP</u>
☒ <i>(This check-box may be marked only if the conditions for deposit accounts of the IPEA so permit)</i> Authorization to charge any deficiency or credit any overpayment in the total fees indicated above.	Deposit Account No.: <u>2800.0140</u>
	Date: <u>2. May 2003</u>
	Name: <u>BOEHRINGER INGELHEIM GMBH</u>
	Signature: <u></u> <u></u> Dr. Fuchs

PCT

NOTICE INFORMING THE APPLICANT OF THE
COMMUNICATION OF THE INTERNATIONAL
APPLICATION TO THE DESIGNATED OFFICES

(PCT Rule 47.1(c), first sentence)

To:

BOEHRINGER INGELHEIM INTERNATIONAL GMBH
Binger Str. 178 Eingang CD Patents
55216 INGELHEIM
ALLEMAGNE

21. Mai 2003

SB gesehen erledigt

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IMPORTANT NOTICE

Date of mailing(day/month/year) 08 May 2003 (08.05.03)	
Applicant's or agent's file reference 1-1261-PCT	
International application No. PCT/EP02/11250	
International filing date(day/month/year) 08 October 2002 (08.10.02)	Priority date(day/month/year) 26 October 2001 (26.10.01)
Applicant BOEHRINGER INGELHEIM INTERNATIONAL GMBH	

ERFASST

1. Notice is hereby given that the International Bureau has **communicated**, as provided in Article 20, the international application to the following designated Offices on the date indicated above as the date of mailing of this notice:

KP, KR, US

In accordance with Rule 47.1(c), third sentence, those Offices will accept the present notice as conclusive evidence that the communication of the international application has duly taken place on the date of mailing indicated above and no copy of the international application is required to be furnished by the applicant to the designated Office(s).

2. The following designated Offices have waived the requirement for such a communication at this time:

AE, AG, AL, AM, AP, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EA, EC, EE, EP, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OA, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW

The communication will be made to those Offices only upon their request. Furthermore, those Offices do not require the applicant to furnish a copy of the international application (Rule 49.1(a-bis)).

3. Enclosed with this notice is a copy of the international application as published by the International Bureau on 08 May 2003 (08.05.03) under No. 03/037350

4. **TIME LIMITS for filing a demand for international preliminary examination and for entry into the national phase**

The applicable time limit for entering the national phase will, **subject to what is said in the following paragraph**, be **30 MONTHS** from the priority date, not only in respect of any elected Office if a demand for international preliminary examination is filed before the expiration of **19 months** from the priority date, but also in respect of any designated Office, in the absence of filing of such demand, where Article 22(1) as modified with effect from 1 April 2002 applies in respect of that designated Office. For further details, see *PCT Gazette* No. 44/2001 of 1 November 2001, pages 19926, 19932 and 19934, as well as the *PCT Newsletter*, October and November 2001 and February 2002 issues.

In practice, **time limits other than the 30-month time limit** will continue to apply, for various periods of time, in respect of certain designated or elected Offices. For **regular updates on the applicable time limits** (20, 21, 30 or 31 months, or other time limit), Office by Office, refer to the *PCT Gazette*, the *PCT Newsletter* and the *PCT Applicant's Guide*, Volume II, National Chapters, all available from WIPO's Internet site, at <http://www.wipo.int/pct/en/index.html>.

For filing a **demand for international preliminary examination**, see the *PCT Applicant's Guide*, Volume I/A, Chapter IX. Only an applicant who is a national or resident of a PCT Contracting State which is bound by Chapter II has the right to file a demand for international preliminary examination (at present, all PCT Contracting States are bound by Chapter II).

It is the applicant's **sole responsibility** to monitor all these time limits.

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Authorized officer

Judith Zahra

Facsimile No (41-22) 740 14 35

Telephone No (41-22) 329 01 11

30. Juni 2003

PATENT COOPERATION TREATY

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From the INTERNATIONAL BUREAU

To:

BOEHRINGER INGELHEIM INTERNATIONAL
GMBH
Binger Str. 173
55216 INGELHEIM
Germany

INFORMATION CONCERNING ELECTED
OFFICES NOTIFIED OF THEIR ELECTION

(PCT Rule 61.3)

Date of mailing (day/month/year) 12 June 2003 (12.06.03)		IMPORTANT INFORMATION	
Applicant's or agent's file reference 1-1261-PCT			
International application No. PCT/EP02/11250	International filing date (day/month/year) 08 October 2002 (08.10.02)	Priority date (day/month/year) 26 October 2001 (26.10.01)	
Applicant BOEHRINGER INGELHEIM INTERNATIONAL GMBH et al			

1. The applicant is hereby informed that the International Bureau has, according to Article 31(7), notified each of the following Offices of its election:

EP : AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR
National : AU, BG, CA, CN, DE, GB, IL, JP, KP, KR, MN, NO, PL, RO, RU, SK, US

2. The following Offices have waived the requirement for the notification of their election; the notification will be sent to them by the International Bureau only upon their request:

AP : GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW
EA : AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
OA : BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
National : AE, AG, AL, AM, AT, AZ, BA, BB, BR, BY, BZ, CH, CO, CR, CU, CZ, DK, DM, DZ, EC, EE,
ES, FI, GD, GE, GH, GM, HR, HU, ID, IN, IS, KE, KG, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG,
MK, MW, MX, MZ, NZ, OM, PH, PT, SD, SE, SG, SI, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN,
YU, ZA, ZM, ZW

3. The applicant is reminded that he must enter the "national phase" before the expiration of 30 months from the priority date before each of the Offices listed above. This must be done by paying the national fee(s) and furnishing, if prescribed, a translation of the international application (Article 39(1)(a)), as well as, where applicable, by furnishing a translation of any annexes of the international preliminary examination report (Article 36(3)(b) and Rule 74.1).

Some offices have fixed time limits expiring later than the above-mentioned time limit. For detailed information about the applicable time limits and the acts to be performed upon entry into the national phase before a particular Office, see Volume II of the PCT Applicant's Guide.

The entry into the European regional phase is postponed until 31 months from the priority date for all States designated for the purposes of obtaining a European patent.

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Facsimile No. (41-22) 338.89.70

Authorized officer:

Frédéric SONTAG (Fax 338 8970)

Telephone No. (41-22) 338 8391

PATENT COOPERATION TREATY

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From the INTERNATIONAL SEARCHING AUTHORITY

PCT

To:
BOEHRINGER INGELHEIM INTERNATIONAL
GMBH
Binger Strasse 173
D-55216 Ingelheim am Rhein
GERMANY

Eingang CD Patents

18. Dez. 2002

NOTIFICATION OF TRANSMITTAL OF
THE INTERNATIONAL SEARCH REPORT
OR THE DECLARATION

(PCT Rule 44.1)

SB	gesehen	erledigt
917		

Date of mailing
(day/month/year)

18/12/2002

sdT am
7.5.03
au 45

Applicant's or agent's file reference

1-1261-PCT

FOR FURTHER ACTION

See paragraphs 1 and 4 below

International application No.

PCT/EP 02/11250

International filing date
(day/month/year)

08/10/2002 / CG / TS

Applicant

BOEHRINGER INGELHEIM INTERNATIONAL GMBH

ZA Patents
Frist: 18.2.2003
Termin no: 18.10.03

1. ☒ The applicant is hereby notified that the International Search Report has been established and is transmitted herewith.

Filing of amendments and statement under Article 19:

The applicant is entitled, if he so wishes, to amend the claims of the International Application (see Rule 46):

When? The time limit for filing such amendments is normally 2 months from the date of transmittal of the International Search Report; however, for more details, see the notes on the accompanying sheet.

Where? Directly to the International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland
Facsimile No.: (41-22) 740.14.35

For more detailed instructions, see the notes on the accompanying sheet.

2. ☐ The applicant is hereby notified that no International Search Report will be established and that the declaration under Article 17(2)(a) to that effect is transmitted herewith.

3. ☐ With regard to the protest against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

☐ the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.

☐ no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. **Further action(s):** The applicant is reminded of the following:

Shortly after **18 months** from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90bis.1 and 90bis.3, respectively, before the completion of the technical preparations for international publication.

Within **19 months** from the priority date, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until 30 months from the priority date (in some Offices even later).

Within **20 months** from the priority date, the applicant must perform the prescribed acts for entry into the national phase before all designated Offices which have not been elected in the demand or in a later election within 19 months from the priority date or could not be elected because they are not bound by Chapter II.

Name and mailing address of the International Searching Authority



European Patent Office, P.B. 5818 Patentlaan 2
NL-2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

These Notes are intended to give the basic instructions concerning the filing of amendments under article 19. The Notes are based on the requirements of the Patent Cooperation Treaty, the Regulations and the Administrative Instructions under that Treaty. In case of discrepancy between these Notes and those requirements, the latter are applicable. For more detailed information, see also the PCT Applicant's Guide, a publication of WIPO.

In these Notes, "Article", "Rule", and "Section" refer to the provisions of the PCT, the PCT Regulations and the PCT Administrative Instructions respectively.

INSTRUCTIONS CONCERNING AMENDMENTS UNDER ARTICLE 19

The applicant has, after having received the international search report, one opportunity to amend the claims of the international application. It should however be emphasized that, since all parts of the international application (claims, description and drawings) may be amended during the international preliminary examination procedure, there is usually no need to file amendments of the claims under Article 19 except where, e.g. the applicant wants the latter to be published for the purposes of provisional protection or has another reason for amending the claims before international publication. Furthermore, it should be emphasized that provisional protection is available in some States only.

What parts of the international application may be amended?

Under Article 19, only the claims may be amended.

During the international phase, the claims may also be amended (or further amended) under Article 34 before the International Preliminary Examining Authority. The description and drawings may only be amended under Article 34 before the International Examining Authority.

Upon entry into the national phase, all parts of the international application may be amended under Article 28 or, where applicable, Article 41.

When?

Within 2 months from the date of transmittal of the international search report or 16 months from the priority date, whichever time limit expires later. It should be noted, however, that the amendments will be considered as having been received on time if they are received by the International Bureau after the expiration of the applicable time limit but before the completion of the technical preparations for international publication (Rule 46.1).

Where not to file the amendments?

The amendments may only be filed with the International Bureau and not with the receiving Office or the International Searching Authority (Rule 46.2).

Where a demand for international preliminary examination has been/is filed, see below.

How?

Either by cancelling one or more entire claims, by adding one or more new claims or by amending the text of one or more of the claims as filed.

A replacement sheet must be submitted for each sheet of the claims which, on account of an amendment or amendments, differs from the sheet originally filed.

All the claims appearing on a replacement sheet must be numbered in Arabic numerals. Where a claim is cancelled, no renumbering of the other claims is required. In all cases where claims are renumbered, they must be renumbered consecutively (Administrative Instructions, Section 205(b)).

The amendments must be made in the language in which the international application is to be published.

What documents must/may accompany the amendments?

Letter (Section 205(b)):

The amendments must be submitted with a letter.

The letter will not be published with the international application and the amended claims. It should not be confused with the "Statement under Article 19(1)" (see below, under "Statement under Article 19(1)").

The letter must be in English or French, at the choice of the applicant. However, if the language of the international application is English, the letter must be in English; if the language of the international application is French, the letter must be in French.

The letter must indicate the differences between the claims as filed and the claims as amended. It must, in particular, indicate, in connection with each claim appearing in the international application (it being understood that identical indications concerning several claims may be grouped), whether

- (i) the claim is unchanged;
- (ii) the claim is cancelled;
- (iii) the claim is new;
- (iv) the claim replaces one or more claims as filed;
- (v) the claim is the result of the division of a claim as filed.

The following examples illustrate the manner in which amendments must be explained in the accompanying letter:

1. [Where originally there were 48 claims and after amendment of some claims there are 51]:
"Claims 1 to 29, 31, 32, 34, 35, 37 to 48 replaced by amended claims bearing the same numbers; claims 30, 33 and 36 unchanged; new claims 49 to 51 added."
2. [Where originally there were 15 claims and after amendment of all claims there are 11]:
"Claims 1 to 15 replaced by amended claims 1 to 11."
3. [Where originally there were 14 claims and the amendments consist in cancelling some claims and in adding new claims]:
"Claims 1 to 6 and 14 unchanged; claims 7 to 13 cancelled; new claims 15, 16 and 17 added." or
"Claims 7 to 13 cancelled; new claims 15, 16 and 17 added; all other claims unchanged."
4. [Where various kinds of amendments are made]:
"Claims 1-10 unchanged; claims 11 to 13, 18 and 19 cancelled; claims 14, 15 and 16 replaced by amended claim 14; claim 17 subdivided into amended claims 15, 16 and 17; new claims 20 and 21 added."

"Statement under article 19(1)" (Rule 46.4)

The amendments may be accompanied by a statement explaining the amendments and indicating any impact that such amendments might have on the description and the drawings (which cannot be amended under Article 19(1)).

The statement will be published with the international application and the amended claims.

It must be in the language in which the international application is to be published.

It must be brief, not exceeding 500 words if in English or if translated into English.

It should not be confused with and does not replace the letter indicating the differences between the claims as filed and as amended. It must be filed on a separate sheet and must be identified as such by a heading, preferably by using the words "Statement under Article 19(1)."

It may not contain any disparaging comments on the international search report or the relevance of citations contained in that report. Reference to citations, relevant to a given claim, contained in the international search report may be made only in connection with an amendment of that claim.

Consequence if a demand for international preliminary examination has already been filed

If, at the time of filing any amendments under Article 19, a demand for international preliminary examination has already been submitted, the applicant must preferably, at the same time of filing the amendments with the International Bureau, also file a copy of such amendments with the International Preliminary Examining Authority (see Rule 62.2(a), first sentence).

Consequence with regard to translation of the international application for entry into the national phase

The applicant's attention is drawn to the fact that, where upon entry into the national phase, a translation of the claims as amended under Article 19 may have to be furnished to the designated/elected Offices, instead of, or in addition to, the translation of the claims as filed.

For further details on the requirements of each designated/elected Office, see Volume II of the PCT Applicant's Guide.

PATENT COOPERATION TREATY

PCT

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INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 1-1261-PCT	FOR FURTHER ACTION see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, Item 5 below.	
International application No. PCT/EP 02/ 11250	International filing date (day/month/year) 08/10/2002	(Earliest) Priority Date (day/month/year) 26/10/2001
Applicant BOEHRINGER INGELHEIM INTERNATIONAL GMBH		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 5 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

- a. With regard to the language, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

- b. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international search was carried out on the basis of the sequence listing:

☐ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☒ Certain claims were found unsearchable (See Box I).

3. ☐ Unity of invention is lacking (see Box II).

4. With regard to the title,

☒ the text is approved as submitted by the applicant.

☐ the text has been established by this Authority to read as follows:

5. With regard to the abstract,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the drawings to be published with the abstract is Figure No.

☐ as suggested by the applicant.

☐ because the applicant failed to suggest a figure.

☐ because this figure better characterizes the invention.

☒ None of the figures.

INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP 02/11250

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61K31/55 A61K9/00 A61K9/14 A61K9/20 A61K47/26
A61P11/02 A61P11/06 A61P27/02 A61P29/00

1/2

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

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, PAJ, WPI Data, MEDLINE, EMBASE, BIOSIS, PASCAL, SCISEARCH, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 1 020 193 A (DAIICHI SEIYAKU CO) 19 July 2000 (2000-07-19) page 2, line 33-36 page 3, line 51,52 claims 3,7,17,18 ---	1-26
X	EP 0 658 340 A (UNILEVER PLC ;UNILEVER NV (NL)) 21 June 1995 (1995-06-21) page 2, line 55 -page 3, line 8 ---	1
A	PATENT ABSTRACTS OF JAPAN vol. 1997, no. 06, 30 June 1997 (1997-06-30) & JP 09 052849 A (TAISHO PHARMACEUT CO LTD), 25 February 1997 (1997-02-25) abstract --- -/--	1-26



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

* Special categories of cited documents :

A document defining the general state of the art which is not considered to be of particular relevance

E earlier document but published on or after the international filing date

L document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

O document referring to an oral disclosure, use, exhibition or other means

P document published prior to the international filing date but later than the priority date claimed

T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

X document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

Y document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

& document member of the same patent family

Date of the actual completion of the international search

10 December 2002

Date of mailing of the international search report

18/12/2002

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Zimmer, B

INTERNATIONAL SEARCH REPORT

International Application No PCT/EP 02/11250	V3
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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 5 942 503 A (JUNG BIRGIT ET AL) 24 August 1999 (1999-08-24) column 6; claims 1-3 -----	1-26

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP 02/11250

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Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.: —
because they relate to subject matter not required to be searched by this Authority, namely:
Rule 39.1(iv) PCT - Method for treatment of the human or animal body by therapy Although claims 22,23 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/EP 02/11250

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Patent document cited in search report		Publication date	Patent family member(s)	Publication date
EP 1020193	A	19-07-2000	AU 9187598 A	23-04-1999
			CA 2305179 A1	08-04-1999
			EP 1020193 A1	19-07-2000
			NO 20001612 A	30-05-2000
			CN 1280506 T	17-01-2001
			WO 9916470 A1	08-04-1999
			RU 2184570 C2	10-07-2002
EP 0658340	A	21-06-1995	EP 0658340 A1	21-06-1995
JP 09052849	A	25-02-1997	NONE	
US 5942503	A	24-08-1999	DE 19542281 A1	15-05-1997
			AT 213160 T	15-02-2002
			AU 706112 B2	10-06-1999
			AU 7623096 A	05-06-1997
			BG 62511 B1	31-01-2000
			BG 102408 A	30-12-1998
			BR 9611502 A	02-03-1999
			CA 2232008 A1	22-05-1997
			CN 1202111 A	16-12-1998
			CZ 9801498 A3	14-10-1998
			DE 59608738 D1	21-03-2002
			DK 861081 T3	27-05-2002
			EE 9800158 A	15-12-1998
			WO 9717971 A1	22-05-1997
			EP 0861081 A1	02-09-1998
			ES 2171746 T3	16-09-2002
			HU 9903489 A2	28-03-2000
			JP 2000500446 T	18-01-2000
			NO 982172 A	13-05-1998
			NZ 322467 A	28-01-2000
			PL 326653 A1	12-10-1998
			PT 861081 T	28-06-2002
			SI 861081 T1	30-06-2002
			SK 61398 A3	09-09-1998
			TR 9800853 T2	21-09-1998
			ZA 9609520 A	14-05-1997

PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

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PCT

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Rule 71.1)

To:		
BOEHRINGER INGELHEIM INTERNATIONAL GMBH Binger Strasse 173 D-55216 Ingelheim am Rhein ALLEMAGNE		
Eingang CD Patents		
04. Nov. 2003		
SE	gesehen	erledigt
St	[Signature]	

Date of mailing (day/month/year)	03.11.2003
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Applicant's or agent's file reference 1-1261-PCT

IMPORTANT NOTIFICATION

International application No. PCT/EP02/11250	International filing date (day/month/year) 08.10.2002	Priority date (day/month/year) 26.10.2001
---	--	--

Applicant BOEHRINGER INGELHEIM INTERNATIONAL GMBH
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1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.
2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.

3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. REMINDER

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

The applicant's attention is drawn to Article 33(5), which provides that the criteria of novelty, inventive step and industrial applicability described in Article 33(2) to (4) merely serve the purposes of international preliminary examination and that "any Contracting State may apply additional or different criteria for the purposes of deciding whether, in that State, the claimed inventions is patentable or not" (see also Article 27(5)). Such additional criteria may relate, for example, to exemptions from patentability, requirements for enabling disclosure, clarity and support for the claims.

Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Senkel, H Tel. +49 89 2399-8071
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PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

v2

Applicant's or agent's file reference 1-1261-PCT	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/PEA416)	
International application No. PCT/EP02/1250	International filing date (day/month/year) 08.10.2002	Priority date (day/month/year) 26.10.2001
International Patent Classification (IPC) or both national classification and IPC A61K31/55		
Applicant BOEHRINGER INGELHEIM INTERNATIONAL GMBH		
1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36. 2. This REPORT consists of a total of 6 sheets, including this cover sheet. ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT). These annexes consist of a total of sheets.		
3. This report contains indications relating to the following items: I ☒ Basis of the opinion II ☐ Priority III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability IV ☐ Lack of unity of invention V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement VI ☐ Certain documents cited VII ☐ Certain defects in the international application VIII ☐ Certain observations on the International application		
Date of submission of the demand 06.05.2003	Date of completion of this report 03.11.2003	
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Zimmer, B Telephone No. +49 89 2399-8600	



**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/EP02/11250

✓

I. Basis of the report

1. With regard to the **elements** of the international application (*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 since they do not contain amendments (Rules 70.16 and 70.17)*):

Description, Pages

1-9 as originally filed

Claims, Numbers

1-26 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
☐ the language of publication of the international application (under Rule 48.3(b)).
☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
☐ filed together with the international application in computer readable form.
☐ furnished subsequently to this Authority in written form.
☐ furnished subsequently to this Authority in computer readable form.
☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
☐ the claims, Nos.:
☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. **PCT/EP02/11250**

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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. 22 and 23 regarding industrial applicability

because:

- ☒ the said international application, or the said claims Nos. 22 and 23 regarding industrial applicability 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.
☐ no international search report has been established for the said claims Nos.

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

- ☐ the written form has not been furnished or does not comply with the Standard.
☐ the computer readable form has not been furnished or does not comply with the Standard.

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	1-26
	No: Claims	
Inventive step (IS)	Yes: Claims	
	No: Claims	1-26
Industrial applicability (IA)	Yes: Claims	1-21,24-26
	No: Claims	

2. Citations and explanations

see separate sheet

Re Item III

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

Claims 22 and 23 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 (Art. 34(4)(a)(i) PCT).

Re Item V

Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Reference is made to the following documents:

D1: EP-A-1 020 193 (DAIICHI SEIYAKU CO) 19 July 2000 (2000-07-19)
D2: EP-A-0 658 340 (UNILEVER PLC ;UNILEVER NV (NL)) 21 June 1995
(1995-06-21)

2. Novelty

None of the cited prior art documents discloses a pharmaceutical formulation comprising epinastine and/or an acid addition salt and two kinds of sweeteners and/ or flavourings according to claim 1 of the present application.

Therefore, the subject-matter of independent claims 1, 11, 12, 19 and 21-26 as well as the claims depending thereupon seems to be new (Art. 33(2) PCT).

3. Inventive Step

D1, which is regarded as closest prior art discloses oral administration preparations in which the unpleasant tastes, particularly the bitterness of drugs are improved by adding a sugar alcohol selected from the group consisting of erythritol,

xylitol, mannitol and sorbitol and a sweetener such as aspartam. According to D1 exemplary drugs are acid addition salts of compounds having a basic group p.2, l. 33-36; p. 3, l. 51-52 and claims 3,7,17, 18). D1 differs from the subject-matter of the present application in that epinastine is not explicitly mentioned as a compound having a basic group.

The objective technical problem of the present application thus is the provision of liquid formulations of epinastine with a good tasting.

The solution of the problem by adding two kinds of sweeteners seems to be obvious for a person skilled in the art especially in view of D1.

Therefore, the subject-matter of independent claims 1, 11, 12, 19, 21-26 of the present application does not seem to be inventive.

The combination of saccharin or saccharin alternatives with sweetening agents such as glycyrrhizin or ammonium glycyrrhizinate for bitter taste masking is further known from D2 (p. 2, l. 55-p. 3, l. 8).

Dependent claims 2, 3, 5, 6, 10, 13-18 and 20 do not appear to contain any additional features which involve an inventive step when combined with the subject-matter of any claim to which they refer. Dependent claims are only allowable when related to a patentable independent claim (Rule 6.4 PCT).

4. Further remarks

4.1 Claims 16 and 17 are not supported by the description as required by Art. 6 PCT.

4.2 The expressions such as "preferably, most preferably" employed in claims 1, 5, 8, 16, 17 and 22 relate to preferred modes which should be claimed in dependent claims.

4.3 As the expression "incorporated by reference" is not deleted in the description (p. 7, l. 2-3) the requirements of Rules 5 and 9.1 PCT are not met.

5. For the assessment of the present claims 22 and 23 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.

Traducción

TRATADO DE COOPERACIÓN DE PATENTES
PCT
INFORME DE EXAMEN PRELIMINAR INTERNACIONAL
(Artículo 36 y Regla 70 del PCT)

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Referencia del expediente del agente o solicitante 1-1261-PCT	PARA ACTUACIONES ADICIONALES	Ver notificación de Transmisión del Reporte de Examen Preliminar (Formato PCT/IPEA416)
Solicitud internacional No. PCT/EP02	Fecha de presentación internacional (día/mes/año) 08.10.2002	Fecha de prioridad (día/mes/año) 26.10.2001
Clasificación Internacional de Patentes (IPC) o clasificación nacional e IPC A61K 31/55		
Solicitante BOEHRINGE INGELHEIM INTERNATIONAL GMBH		

1. Este informe de examen preliminar internacional ha sido preparado por esta Administración encargada del Examen Preliminar Internacional y se envía al solicitante en concordancia con el artículo 36.

2. Este **INFORME** consta de una total de 6 hojas, incluyendo la portada

☐ Este informe también se acompaña de **ANEXOS**, esto es documentos de la descripción, reivindicaciones y/o dibujos que han sido corregidos y que son la base de este informe y/o documentos que contienen rectificaciones realizadas ante esta Administración (Ver Regla 70.16 y Sección 607 de las Instrucciones Administrativas según el PCT)

Estos anexos constan de un total de _____ hojas.

3. Este informe contiene indicaciones relativas a los siguientes aspectos:

I ☒ Fundamentos del Informe

II ☐ Prioridad

III ☒ No se establece concepto relativo a la novedad, nivel inventivo y aplicación industrial

IV ☐ Carencia de unidad de la invención

V ☒ Declaración razonada según el artículo 35(2), en relación con la novedad, nivel inventivo o aplicación industrial; citaciones y explicaciones que soportan dicha declaración

VI ☐ Ciertos documentos citados

VII ☐ Ciertos defectos de la solicitud internacional

VIII ☐ Ciertas observaciones respecto a la solicitud internacional

Fecha de presentación de la demanda 06.05.2003	Fecha de terminación de este reporte 03.11.2003
Nombre y dirección de correo de la autoridad encargada del examen preliminar  Oficina Europea de Patentes D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax +49 89 2399 - 4465	Funcionario Autorizado Zimmer, B Teléfono No. +49 89 2399-8600

I. Base del informe

1. Respecto a los **elementos** de la solicitud internacional (Las hojas de reemplazo que han sido entregadas a la Oficina receptora en respuesta a la invitación bajo el Artículo 14 se refieren en este informe como "originalmente presentadas" y no se anexan a este informe ya que ellas no contienen modificaciones (Regla 70.16 y 70.17)):

La descripción, páginas

1-9 como se presentaron originalmente

Las reivindicaciones, números

1-26 como se presentaron originalmente

2. Respecto al **lenguaje**, todos los elementos marcados anteriormente estuvieron disponibles o fueron enviados a la Administración en el lenguaje en que se presentó la solicitud internacional, a menos que se indique otra cosa en este punto.

Estos elementos estuvieron disponibles o fueron enviados a esta Administración en el siguiente lenguaje _____ el cual es:

- ☐ el lenguaje de la traducción enviada para propósitos de la búsqueda internacional (bajo Regla 23.1 (b)).
☐ el lenguaje de la publicación de la solicitud internacional (bajo Regla 48.3(b)).
☐ el lenguaje de la traducción entregada con propósitos del examen preliminar internacional (bajo Regla 55.2 y/o 55.3).

3. Respecto a cualquier **secuencia de nucleótido y/o amino ácidos** divulgada en la solicitud internacional, el examen preliminar internacional se llevó a cabo con base en el listado de secuencias:

- ☐ contenido en la solicitud internacional en forma escrita
☐ presentado junto con la solicitud internacional en forma legible por computador
☐ entregado posteriormente a esta Administración en forma legible por computador
☐ La declaración de que el listado de secuencias posteriormente entregado no va más allá de lo divulgado en la solicitud internacional originalmente presentada, ha sido entregada.
☐ La declaración de que la información grabada en la forma legible por computador es idéntica al listado de secuencias escrito que se ha entregado.

4. ☐ Las modificaciones han dado como resultado la cancelación de:

- ☐ la descripción, páginas _____,
☐ las reivindicaciones, Nos. _____,
☐ los dibujos, página _____.

5. ☐ Este reporte ha sido establecido como si (parte de) las modificaciones no se hubieran realizado, ya que éstas han sido consideradas como una ampliación de lo inicialmente divulgado como se indica en la Casilla Suplementaria (Regla 70.2(c)).

(Cualquier hoja de reemplazo que contenga dichas modificaciones deberá ser referida bajo el punto 1 y anexada a este informe)

6. Observaciones adicionales, si es necesario:

III. No establecimiento de opinión con respecto a la novedad, nivel inventivo y aplicabilidad Industrial.

1. La pregunta de si la invención reivindicada parece tener novedad, nivel inventivo (que no sea obvia), o que sea aplicable industrialmente no ha sido examinada con respecto a:

- ☐ la solicitud internacional completa
☒ las reivindicaciones Nos. 22 y 23, con respecto a la aplicación Industrial

Porque

- ☒ la solicitud internacional, o las mencionadas reivindicaciones Nos. _____ se relacionan con los siguientes objetos, los cuales no requieren examen preliminar internacional (*especifique*):K

Ver Hoja Separada

- ☐ la descripción, las reivindicaciones o los dibujos (*indique los elementos particulares abajo*) o las mencionadas reivindicaciones Nos. _____ son demasiado confusas que no se puede formar ninguna opinión significativa (*especifique*):
- ☐ la descripción, o las mencionadas reivindicaciones Nos. _____ no están adecuadamente soportadas por la descripción que no se puede formar ninguna opinión significativa.
- ☐ no se ha establecido un reporte de búsqueda para las mencionadas reivindicaciones Nos. _____

2. No se pudo realizar un examen preliminar internacional significativo debido a fallas en el listado de nucleótidos y/o aminoácidos para dar cumplimiento con los estándares del Anexo C de las Instrucciones Administrativas:

- ☐ El formato escrito no ha sido suministrado o no cumple con los estándares.
- ☐ El formato de lectura por computador no ha sido suministrado o no cumple con los estándares.

V. Declaración motivada según el Artículo 35(2) en cuanto a la novedad, el nivel inventivo y la aplicación Industrial; citas y explicaciones que apoyan esta declaración.

1. Declaración

Novedad (N)	Reivindicaciones	SI	<u>1-26</u>
	Reivindicaciones	NO	_____
Nivel inventivo (NI)	Reivindicaciones	SI	_____
	Reivindicaciones	NO	<u>1-26</u>
Aplicación Industrial (AI)	Reivindicaciones	SI	<u>1-21, 24-26</u>
	Reivindicaciones	NO	_____

2. Citas y explicaciones

Ver Hoja Separada

Ítem III

No-establecimiento de opinión con respecto a la novedad, nivel inventivo y aplicabilidad Industrial.

Esta autoridad considera que la materia de reivindicaciones 22 y 23 se encuentra cubierta por lo provisto en la Regla 67.1 (iv) del PCT. Consecuentemente, no se formulará una opinión con respecto a la aplicabilidad industrial del objeto de estas reivindicaciones (Art. 34(4)(a)(i)PCT).

Ítem V

Declaración motivada según el Artículo 35(2) en cuanto a la novedad, el nivel inventivo y la aplicación Industrial; citas y explicaciones que apoyan esta declaración.

1. Se hace referencia a los siguientes documentos

D1: EP-A-1 020 193 (DAIICHI SEIYAKU CO) Julio 19, 2000 (2000-07-19)

D2: EP-A-0 658 340 (UNILEVER PLC; UNILEVER NV (NL)) Junio 21, 1995 (1995-06-21)

2. Novedad

Ninguno de los documentos citados divulga una formulación farmacéutica que comprenda epinastina y/o una sal de adición y dos clases de endulzantes y/o saborizantes de acuerdo con la reivindicación 1 de la presente solicitud.

De esta forma, el objeto de las reivindicaciones independientes 1, 11, 12, 19 y 21-26 así como las que dependen de ellas parecen ser novedosas (Art. 33(2) PCT).

3. Nivel Inventivo

D1, que se considera como el arte previo mas cercano, divulga preparaciones para administración oral en las que los sabores desagradables, particularmente el amargo de los fármacos, se mejoran por la adición de un alcohol azúcar seleccionado del grupo que consiste del eritriol, xilitol, manitol y sorbitol y un endulzante como el aspartame. De acuerdo

con D1, los fármacos ejemplo son sales de adición de compuestos que tienen un grupo básico (p. 2, l. 33-36; p.3, l. 51-52 y reivindicaciones 3, 7, 17, 18). D1 difiere del objeto de la presente solicitud en que la epinastina no está explícitamente mencionada como un compuesto que contiene el grupo básico.

El problema técnico de la presente solicitud es el de proporcionar formulaciones líquidas de epinastina con buen sabor.

Solucionar este problema adicionando dos clases de endulzantes parece ser obvia para una persona versada en la materia, especialmente al observar a D1.

De esta forma, el objeto de el objeto de las reivindicaciones independientes 1, 11, 12, 19, 21-26 de la presente solicitud no parece ser inventiva.

La combinación de la sacarina o de alternativas de la sacarina con agentes endulzantes como la glicirricina o el glicirricinato de amonio para enmascarar el sabor amargo es conocido a partir de D2 (p. 2, l. 55 – p. 3, l. 8)

Las reivindicaciones independientes 2, 3, 5, 6, 10, 13-18 y 20 no parecen contener características adicionales que representen un nivel inventivo cuando se combinan con el objeto de cualquiera de las reivindicaciones a las que se refieren. Las reivindicaciones dependientes solo son permitidas cuando se relacionan con una reivindicación independiente patentable (Regla 6.4 PCT).

4. Observaciones adicionales

- 4.1. Las reivindicaciones 16 y 17 no están soportadas por la descripción como lo requiere el Art. 6 del PCT.**
- 4.2. Las expresiones tales como "preferiblemente, mas preferiblemente" empleadas en las reivindicaciones 1, 5, 8, 16 17 y 22 se relacionan con modalidades preferidas las cuales deben ser reivindicadas como reivindicaciones dependientes.**
- 4.3. La expresión "Incorporado por referencia" no ha sido borrada de la descripción (p. 7, l. 2-3) no se cumplen los requerimientos de las Reglas 5 y 9.1 del PCT.**

5. No existe un criterio unificado de los Estados Contratantes del PCT para determinar la aplicabilidad industrial de las reivindicaciones 22 y 23.

La patentabilidad también puede ser dependiente de la formulación de las reivindicaciones. La EPO, por ejemplo, no reconoce la aplicabilidad industrial del objeto de las reivindicaciones de uso de un compuesto en un medicamento, pero permite, sin embargo, las reivindicaciones de un compuesto conocido para un primer uso en un tratamiento médico y el uso de dicho compuesto para la manufactura de un medicamento para un nuevo tratamiento médico.

PRP/WPCL9255/ID-000235

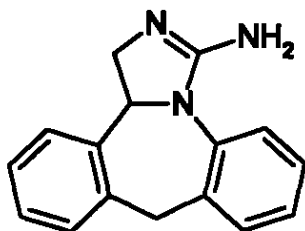
Nueva formulación de jarabe de epinastina seco y acuoso.

La presente invención se refiere a una nueva formulación de epinastina en forma de polvo (jarabe seco) para ser mezclada con agua antes de usarse. Entre otras cosas, la epinastina se emplea en el tratamiento de alergias, dolor, en particular el dolor crónico y el dolor producido por una inflamación, la migraña, el asma, la rinitis, la conjuntivitis y/o la bronquitis (por ejemplo, véanse los documentos EP-B-0 035 749, EP 1000623). En particular, la formulación es para el tratamiento de alergias, dermatitis, rinitis, conjuntivitis, bronquitis y asma.

Estado de la técnica.

La epinastina, conocida químicamente como 3-amino-9,13b-dihidro-1H-dibenzo-[c,f]imidazol[1,5-a]azepina, y sus sales de adición de ácido, se describe por primera vez en la solicitud de patente alemana P 30 08 944.2, que forma la base para el documento EP 0035749.

Químicamente, la epinastina se representa por la fórmula siguiente, que no refleja las propiedades estereoquímicas:



La epinastina puede usarse como base libre o como sal de la misma aceptable farmacéuticamente. Preferentemente, la epinastina se usa como hidrocloreuro.

Si no se especifica con más detalle en el contexto de la presente invención, el término epinastina se usa para la base libre, así como para las sales aceptables farmacéuticamente.

Los métodos para su preparación pueden tomarse de los documentos EP 0496306 o WO 01/40229.

La epinastina se comercializa en Japón bajo el nombre de marca Alesion® y lo más frecuente es que se use por sus efectos antihistamínicos.

El estado de la técnica prefiere los comprimidos como forma de aplicación para la epinastina.

Sin embargo, especialmente para niños o ancianos, los comprimidos no son fáciles de tomar y por tanto existe la necesidad de nuevas formulaciones fácilmente aplicables para niños y ancianos.

Sumario de la presente invención.

Se encontró que una formulación adecuada para un grupo de usuarios tal como los niños y los ancianos, podrían ser formulaciones líquidas. Sin embargo, resultó
5 que la epinastina tiene un intenso sabor amargo.

En consecuencia, existía la necesidad (y resolver esto era un objetivo de la presente invención) de desarrollar una formulación líquida de epinastina y/o una de
10 sus sales de adición de ácido aceptable farmacéuticamente, de sabor neutro o agradable.

Otro objetivo de la presente invención es proporcionar una formulación líquida de epinastina que pueda ser almacenada durante algún tiempo sin riesgo de que disminuya rápidamente su calidad farmacéutica.
15

Otro objetivo más de la presente invención es crear una formulación de epinastina fácil de manejar para proporcionar un líquido. Tal formulación de líquido debe ser además una solución mejor que una dispersión, para mejorar su aceptación por el paciente.
20

Descripción de la presente invención.

La presente invención se refiere a una formulación de tipo polvo (jarabe seco) de epinastina, bien sea en
25 forma enantiómera, racémica, o una sal de las mismas, que se mezcla con agua antes de usarla. Para ello se requiere que el polvo se disuelva en agua muy rápidamente.

En el contexto de la presente invención, el término "polvo" se usa al mismo tiempo que la expresión "jarabe seco", que a su vez quiere decir una mezcla esencialmente libre de agua de la forma activa de epinastina, preferentemente hidrocloreto de epinastina, y aditivos y coadyuvantes aceptables farmacéuticamente, necesarios para formar una formulación acuosa de la sustancia activa de sabor dulce cuando se mezcla con agua.
30
35

Sorprendentemente, se encontró que las formulaciones acuosas de hidrocloreto de epinastina producen dos tipos con mal sabor en forma de un intenso amargor. Por una parte, hay un tipo de amargor de acción rápida y por otra parte hay un amargor duradero que se aprecia durante un tiempo bastante prolongado.
40

Desgraciadamente, el sabor amargo de la epinastina no pudo enmascararse mediante el uso de un agente de enmascaramiento de sabores convencional, como la sacarosa, por ejemplo.
45

En cambio, se encontró que el intenso sabor amargo

puede superarse mediante la combinación de agentes edulcorantes y saborizantes de acción rápida y lenta.

Como consecuencia, una realización preferida de la formulación de la presente invención debía comprender al menos uno de cada tipo de estos agentes de enmascaramiento.

Para enmascarar el amargor de acción rápida, la sacarina sódica, el eritritol y/o el aspartamo resultaron ser efectivos. Otro grupo de compuestos adecuados comprende azúcares y polioles derivados del azúcar tales como sacarosa, D-sorbitol, glicerina y D-manitol. Preferentemente, la formulación comprende sacarina sódica, eritritol y/o aspartamo. Lo más preferido es la combinación de sacarina sódica, eritritol y aspartamo.

La cantidad del al menos un agente de enmascaramiento para enmascarar el amargor de acción rápida depende del agente usado. En el caso de la sacarina sódica, está entre 0,1 % p/p y 2,0% p/p de la formulación en polvo. Preferentemente la cantidad es de 0,8%.

En el caso del eritritol, está entre 50% y 95% p/p de la formulación en polvo. Preferentemente la cantidad es de 75 a 80% p/p, y lo más preferentemente es 80% p/p.

Y en el caso del aspartamo, está entre 1% p/p y 30% p/p de la formulación en polvo. Preferentemente la cantidad es de 5 a 15% p/p, y lo más preferentemente es 10%.

Para enmascarar el amargor duradero, se encontró que los glicirricinatos eran altamente eficaces. Entre ellos, los preferidos son el ácido glicirricínico y/o el glicirricinato monoamónico. El más preferido es el glicirricinato monoamónico.

La cantidad de glicirricinato monoamónico en la formulación de polvo es de 0,1% p/p a 3,0% p/p de la formulación en polvo. Más preferida es de 0,1 a 1% p/p, y la más preferida es 0,6%.

La formulación puede comprender además coadyuvantes, entre los cuales están, por ejemplo, agentes de ajuste del pH. Se prefiere añadir tales agentes de ajuste del pH para ajustar el pH del líquido resultante en un valor entre 5 y 8, preferentemente entre 6 y 7. Entre esos agentes se encuentran el ácido cítrico, ácido succínico, ácido tartárico, ácido acético, citratos, acetatos, vitamina C, ácido clorhídrico, carbonatos, fosfatos, fosfato disódico, fosfato monosódico, hidróxido sódico, cálcico, potásico y/o magnésico. Se prefieren sustancias tampón como el fosfato disódico.

También pueden añadirse opcionalmente otros aditivos

usados habitualmente. Entre ellos se encuentran:

- agentes aglutinantes tales como hidroxipropilcelulosa, metilcelulosa, hidroxipropilmetilcelulosa, hidroxietilcelulosa, almidón, dextrina, gelatina y polivinilpirrolidona, preferentemente hidroxipropilcelulosa,
 - agentes antiapelmazantes tales como dióxido de silicio hidratado, ácido silícico anhidro ligero,
 - sustancias odorizantes tales como naranja "sunfix" n° 22734 (nombre comercial, el naranja sunfix que se prefiere contiene sabor de naranja (30% p/p), acacia (30% p/p) y dextrina (40% p/p)), aceite de naranja, aceite de menta, sabor de fresa de eucalipto, sabor de vainilla, sabor de yogurt y otros sabores conocidos en la técnica,
 - pigmentos colorantes tales como amarillo alimentario n° 5, también conocido como amarillo ocaso FCF (sal disódica del ácido 6-hidroxi-5-(4-sulfofenilazo)-2-naftalenosulfónico), prefiriéndose este último, óxido férrico y otros pigmentos colorantes alimentarios, p. ej. los conocidos en Japón como rojo alimentario n° 3, 102, 105 y 106, amarillo alimentario n° 4 y otros colorantes alimentarios conocidos en la técnica, y/o
 - conservantes tales como ácido benzoico, sus sales, preferentemente benzoato sódico, ácidos paraoxibenzoicos, sus sales, y otros conservantes conocidos, de los que se prefiere el benzoato sódico, y
 - agentes efervescentes tales como bicarbonato.
- La cantidad de epinastina o su sal está entre 0,5% p/p y 5% p/p de la formulación en polvo. Es más preferida una cantidad entre 0,5% p/p y 2% p/p; la cantidad más preferida es 1%.

Preferentemente la formulación en polvo no contiene una sustancia activa que no sea epinastina o una sal de la misma aceptable farmacéuticamente.

La sustancia activa, preferentemente hidrocloreto de epinastina, y todos los aditivos se mezclan formando un polvo y después el polvo se mezcla con agua para obtener preferentemente una formulación líquida. Aunque la formulación líquida puede ser una solución, una suspensión o un coloide, la formulación líquida preferida es una solución acuosa clara y transparente.

Se prefiere mezclar la formulación de polvo con agua para obtener un líquido que tiene una concentración entre 250 mg po 5-50 ml y 2000 mg por 10-100 ml, preferentemen-

te la cantidad está entre 50 mg por 10 ml y 2000 mg por 10 ml. Si se usa hidrocloreuro de epinastina, la cantidad en el contexto de la presente invención es (aproximadamente) la misma que para la base libre.

5 Para asegurarse de que el paciente puede preparar fácilmente la formulación líquida, la formulación en polvo de la invención (jarabe seco) puede ser suministrada en determinados envases. En estos envases, el agua y la formulación en polvo de la invención se almacenan por separado. El envase permite además mezclar los dos componentes de una manera fácil.

 Como consecuencia de ello, la presente invención se refiere también a un estuche que comprende dos componentes: a) la formulación de polvo de la invención y b) 15 agua, estando separados ambos componentes.

 En el estado de la técnica, se conocen diversos frascos que tienen tapones especiales para resolver esta cuestión. Lo más frecuentemente, en tales envases el disolvente líquido puede ser guardado en un frasco de vidrio, material plástico, metal, etc., mientras que el tapón para cerrar el frasco comprende una cámara para tomar la formulación en polvo seco. Antes de usarlo, el paciente puede tomar el polvo del tapón y mezclarlo con el agua en el frasco. Este proceso de mezcla puede hacerse conscientemente, lo que significa que el paciente toma el polvo activamente y lo pone en el agua. En otras realizaciones, el paciente puede iniciar el proceso de mezcla de una forma más automática, por ejemplo enroscando, apretando, agitando el tapón o el frasco con el fin de eliminar una barrera en la cámara que contiene el polvo, y, al hacerlo, dejar que caiga desde el tapón a los frascos. 20 25 30

 Tales envases se describen porejemplo en los documentos EP 0599189, EP 0344849, EP 0217425, EP 0093090, US 3802604 y otros. Todos estos dispositivos se incorporan al presente texto como referencia. También podrían usarse otros dispositivos similares. 35

 Además de tales formas de envase, la formulación de jarabe seco pueden guardarse en una bolsa de aluminio o material plástico o en un frasco de aluminio o material plástico. Tal polvo almacenado puede entonces usarse con una cantidad de agua previamente medida, almacenarse en otro envase, o se usa el agua potable recién introducida. 40

 También pueden usarse otros sistemas de envase.

 En el contexto de la presente invención, la formulación de polvo puede también prensarse en comprimidos para disolver en agua, por ejemplo un comprimido efervescente. 45

En tal realización, el comprimido (como la formulación en polvo) puede comprender adicionalmente un agente efervescente tal como bicarbonato.

5 Parte experimental

Nueva formulación de jarabe de epinastina seco y acuoso al 0,5%.

Polvo-Formulación No.	1	2	3	4	5	6	7
hidrocloruro de epinastina [mg]	5	5	5	5	5	5	5
glicerina [mg]	0	0	0	0	0	0	350
sacarosa [mg]	0	0	0	0	0	540	620
ácido cítrico anhidro [mg]	0	0	0	0	0	25	0
glicirricinato monoamónico [mg]	7	0	6	6	6	0	0
sacarina sódica [mg]	0	6	4	0	5	5	0
fumarato sódico [mg]	10	10	0	10	5	0	10
fosfato disódico [mg]	0	0	0	3	15	10	0
eritritol [mg]	923	919	925	916	904	395	0
aspartamo [mg]	60	60	60	60	60	25	0
benzoato sódico [mg]	0	0	0	0	0	0	15
Resultados							
Aspecto cuando se mezcla con agua*	blanco	claro [#]	blanco	claro [#]	claro [#]	claro [#]	claro [#]
Enmascaramiento del amargor	bueno	bueno	bueno	bueno	muy bueno	bueno	bueno

- 10 * La cantidad de agua no es significativa. Sin embargo, preferentemente 1 g de polvo debe ser fácilmente soluble en 5-50 ml de agua.

Claro en el sentido de transparente.

Nueva formulación de jarabe de epinastina seco y acuoso al 1,0%.

Polvo-Formulación No	8	9	10	11	12	13	14
hidrocloruro de epinastina [mg]	10	10	10	10	10	10	10
glicerina [mg]	0	0	0	0	0	0	350
sacarosa [mg]	0	0	0	0	0	542	425
ácido cítrico anhidro [mg]	0	0	0	0	0	25	0
glicirricinato monoamónico [mg]	10	0	10	6	6	0	0
sacarina sódica [mg]	0	10	5	0	8	0	0
fumarato sódico [mg]	20	10	0	15	5	0	10
fosfato disódico [mg]	0	0	0	10	15	0	0
eritritol [mg]	859	859	854	838	835	397	200
aspartamo [mg]	100	100	100	100	100	25	0
hidroxipropilcelulosa [mg]	0	20	20	20	20	0	0
dióxido de silicio hidratado (mg)	1	1	1	1	1	1	0
Odorizante* (mg)	0	(1)	(1)	(1)	(1)	(1)	0
amarillo alimentario No. 5** (mg)	0	(0,05)	(0,05)	(0,05)	(0,05)	(0,05)	0
benzoato sódico (mg)	0	0	0	0	0	0	5
Resultados							
Aspecto cuando se mezcla con agua*	blanco	claro [#]	blanco	claro [#]	claro [#]	claro [#]	claro [#]
Enmascaramiento del amargor	bueno	bueno	bueno	bueno	muy bueno	bueno	bueno

5 *naranja sunfix No. 22734 (nombre comercial) que contiene sabor de naranja (30% p/p), acacia (30%p/p) y dextrina (40% p/p).

10 ** Otro nombre del amarillo alimentario no.5 es amarillo ocaso FCF (salt disódica del ácido 6-hidroxi-5-(4-sulfofenilazo)-2-naftalenosulfónico.

*** La cantidad de agua no es significativa. Sin embargo, preferentemente 1 g de polvo debe ser fácilmente soluble en 5-50 ml de agua.

Claro en el sentido de transparente.

REIVINDICACIONES

1ª. Formulación farmacéutica en polvo, que comprende un agente activo basado en epinastina y/o una sal de adición de ácido, preferentemente el hidrocloruro, al menos dos tipos de edulcorantes y/o saborizantes, y opcionalmente otros coadyuvantes aceptables farmacéuticamente, en la que uno de los al menos dos tipos de edulcorantes y/o saborizantes es para enmascarar el amargor de acción rápida del agente activo y el otro es para enmascarar el amargor de acción prolongada del agente activo.

2ª. Formulación farmacéutica en polvo según la reivindicación 1ª, caracterizada porque el al menos un edulcorante y/o saborizante para enmascarar el amargor de acción rápida se elige entre sacarina sódica, eritritol, aspartamo y/o azúcares u otros polioles tales como sacarosa, glicerina, D-sorbitol y D-manitol.

3ª. Formulación farmacéutica en polvo según las reivindicaciones 1ª o 2ª, caracterizada porque el al menos un edulcorante y/o saborizante para enmascarar el amargor de acción rápida se elige entre sacarina sódica, eritritol y aspartamo.

4ª. Formulación farmacéutica en polvo según las reivindicaciones 1ª a 3ª, caracterizada porque el al menos un edulcorante y/o saborizante para enmascarar el amargor de acción rápida es una combinación de sacarina sódica, eritritol y aspartamo.

5ª. Formulación farmacéutica en polvo según cualquiera de las reivindicaciones 1ª a 4ª, caracterizada porque el al menos un edulcorante y/o saborizante para enmascarar el amargor de acción prolongada es un glicirricinato o ácido glicirricínico, preferentemente elegido entre glicirricinato mono- o di-amónico, glicirricinato di- o tri-sódico y/o glicirricinato potásico, lo más preferentemente glicirricinato monoamónico.

6ª. Formulación farmacéutica en polvo según cualquiera de las reivindicaciones 1ª a 5ª, caracterizada porque la formulación comprende además un agente de ajuste del pH elegido entre el grupo de ácido cítrico, citratos, ácido succínico, ácido tartárico, ácido acético, acetatos, vitamina C, ácido clorhídrico, carbonatos,

hidróxido sódico, cálcico, potásico y/o magnésico, fosfatos, preferentemente fosfato monosódico y/o fosfato disódico, lo más preferentemente fosfato monosódico.

5 7ª. Formulación farmacéutica en polvo según cualquiera de las reivindicaciones 1ª a 6ª, caracterizada porque la formulación comprende además al menos un coadyuvante elegido entre el grupo de sustancias odorizantes, colorantes, conservantes, agentes antiapelmazantes y/o
10 otros agentes aglutinantes.

 8ª. Formulación farmacéutica en polvo según cualquiera de las reivindicaciones 1ª a 7ª, caracterizada porque la formulación comprende hidrocloruro de epinastina
15 na en una cantidad entre 0,5% p/p y 5% p/p, sacarina sódica en una cantidad entre 0,1% p/p y 2,0% p/p, eritritol en una cantidad entre 50% p/p y 95% p/p, aspartamo en una cantidad entre 1% p/p y 30% p/p, glicirricinato momoamónico en una cantidad entre 0,1% p/p y 3,0% p/p y opcio-
20 nalmente fosfato disódico, fumarato sódico, hidroxipropilcelulosa, dióxido de silicio hidratado, sabor de naranja, acacia, dextrina y/o sal disódica del ácido 6-hidroxi-5-(4-sulfofenilazo)-2-naftalenosulfónico.

25 9ª. Formulación farmacéutica en polvo según cualquiera de las reivindicaciones 1ª a 8ª, caracterizada porque la formulación comprende hidrocloruro de epinastina, glicirricinato momoamónico, sacarina sódica, fumarato sódico, eritritol, aspartamo, hidroxipropilcelulosa, di-
30 óxido de silicio hidratado, sabor de naranja, acacia, dextrina y sal disódica del ácido 6-hidroxi-5-(4-sulfofenilazo)-2-naftalenosulfónico.

 10ª. Formulación farmacéutica en polvo según cualquiera de las reivindicaciones 1ª a 9ª, caracterizada porque la formulación comprende un agente efervescente.

 11ª. Comprimido farmacéutico que comprende los ingredientes de la formulación en polvo según cualquiera de
40 las reivindicaciones 1ª a 10ª.

 12ª. Formulación líquida disponible mezclando con agua cualquiera de las formulaciones en polvo según las reivindicaciones 1ª a 10ª o el comprimido según la rei-
45 vindicación 11ª.

13^a. Formulaci3n l3quida seg3n la reivindicaci3n 12^a, caracterizada porque la formulaci3n es una soluci3n.

14^a. Formulaci3n l3quida seg3n la reivindicaci3n 13^a, caracterizada porque la formulaci3n es una dispersi3n.

15^a. Formulaci3n l3quida seg3n la reivindicaci3n 12^a o 13^a, caracterizada porque la formulaci3n comprende un agente de ajuste del pH seg3n la reivindicaci3n 6^a en una cantidad adecuada para ajustar el pH entre 5 y 8, preferentemente entre 6 y 7.

16^a. Formulaci3n l3quida seg3n cualquiera de las reivindicaciones 12^a a 15^a, caracterizada por una cantidad de epinastina entre 0,09 mg y 35 mg por 10 ml, preferentemente entre 0,4 mg y 18 mg por 10 ml.

17^a. Formulaci3n l3quida seg3n cualquiera de las reivindicaciones 12^a a 15^a, caracterizada por una cantidad de hidroc loruro de epinastina entre 0,1 mg y 40 mg por 10 ml, preferentemente entre 0,5 mg y 20 mg por 10 ml.

18^a. Formulaci3n l3quida seg3n cualquiera de las reivindicaciones 12^a a 17^a, caracterizada porque se mezclan de 250 mg a 2000 mg de una formulaci3n en polvo seg3n cualquiera de las reivindicaciones 1^a a 9^a o el comprimido seg3n la reivindicaci3n 11^a, con 10 a 100 ml de agua.

19^a. Un envase que comprende un estuche de una formulaci3n en polvo seg3n cualquiera de las reivindicaciones 1^a a 10^a o el comprimido seg3n la reivindicaci3n 11^a, y, separada de la misma, agua, para obtener una formulaci3n l3quida seg3n cualquiera de las reivindicaciones 12^a a 18^a si se mezclan el polvo y el agua.

20^a. Un envase seg3n la reivindicaci3n 19^a, caracterizado porque el envase es un frasco con un tap3n que comprende una c3mara, que puede ser abierta f3cilmente de una forma manual o enroscando o apretando el tap3n sobre el frasco, conteniendo la c3mara una formulaci3n en polvo seg3n cualquiera de las reivindicaciones 1^a a 10^a o el comprimido seg3n la reivindicaci3n 11^a, y comprendiendo el frasco agua.

21^a. El uso de una formulación en polvo según cualquiera de las reivindicaciones 1^a a 10^a o el uso del comprimido según la reivindicación 11^a, para mezclar con
5 agua y obtener una formulación según cualquiera de las reivindicaciones 12^a a 18^a.

22^a. El uso de una formulación según cualquiera de las reivindicaciones 1^a a 18^a para la elaboración de un
10 preparado médico para tratar alergias, dolor, en particular dolor crónico y dolor producido por una inflamación, migraña, asma, rinitis, conjuntivitis y/o bronquitis, preferentemente para tratar alergias.

15 23^a. Método para tratar alergias, dolor, en particular dolor crónico y el dolor producido por una inflamación, migraña, asma, rinitis, conjuntivitis y/o bronquitis, preferentemente para tratar alergias, caracterizado por mezclar con agua una formulación en polvo según cualquiera de las reivindicaciones 1^a a 10^a o el comprimido
20 según la reivindicación 11^a, para obtener una formulación líquida según cualquiera de las reivindicaciones 12^a a 18^a, y aplicar esta formulación a un paciente.

25 24^a. Un procedimiento para preparar una formulación en polvo según cualquiera de las reivindicaciones 1^a a 10^a mezclando entre sí los distintos componentes.

25^a. Un procedimiento para preparar un comprimido
30 según la reivindicación 11^a, mezclando los distintos componentes, y subsiguientemente prensándolos.

26^a. Un procedimiento para preparar una formulación líquida según cualquiera de las reivindicaciones 12^a a
35 18^a mezclando la formulación en polvo según cualquiera de las reivindicaciones 1^a a 10^a o el comprimido según la reivindicación 11^a con agua.

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Resumen

La presente invención se refiere a una nueva formulación de epinastina en forma de polvo (jarabe seco) para ser mezclada con agua antes de usarse. La epinastina puede usarse como base libre o bien como sal de la misma aceptable farmacéuticamente. La epinastina, entre otras cosas, se aplica al tratamiento de alergias, dolor, en particular el dolor crónico y el dolor producido por una inflamación, la migraña, el asma, la rinitis, la conjuntivitis y/o la bronquitis. En particular, la formulación es para el tratamiento de alergias, dermatitis, rinitis, conjuntivitis, bronquitis y asma.

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COLO 09255-841-006-1
PRP/WPCL9255/ID-000230

NIT : 800176089-

SUPERINDUSTRIA Y COMERCIO

Radicacion : 94942457 90000000

Folios: 71

Fecha (AND): 2004-05-07 17:19:26

Tramite : 811 PCT-PATENT 379 FASE NACI 411 PRESENTAC

Dependencia: 2020 DIVISION DE NUEVAS CREACIONES

RECIBO OFICIAL DE CAJA : 04 - 28,821
FECHA : ABRIL 12 DE 2004

CONSIGNACION

DEPOSITANTE	TIPO PAGO	BANCO	CUENTA	No. PAGO	FECHA PGO	Vr. PAGO
CAVELIER ABOGADOS	CONSIGNACION	BANCO POPULAR	050-00110-6	22156877	12/04/2004	53,734,000.00

CONCEPTO

CANT. CONTABILISTICO	CONCEPTO	TOTAL CONCEPTO
1 30005-01-01 SOLICITUDES	7 TRAMITES DE SOL. DE DISENOS INDUS	422,000.
	TOTAL :	422,000.00

SUM: CUATROCIENTOS VEINTIDOS MIL PESOS

RESPONSABLE : 

RECIBO DE CAJA APLICADO AL EXPEDIENTE No. _____

Cdo 09255-841-006-1

X²⁰ 712

SUPERINDUSTRIA Y COMERCIO
Radicación : 04042457 00000000 Folios: 71
Fecha (MD) 2004-05-07 17:19:25
Trámite 011 PCT-PATENT 379 FASE NACI 411 PRESENTA
Dependencia 2020 DIVISION DE NUEVAS CREACIONES

REQUISITOS NECESARIOS PARA PRESENTACION Y AGILIZACION DEL TRAMITE

	USUARIO	RADICADOR
PATENTE DE INVENCION	()	()
MODELO DE UTILIDAD	()	()
Indicación de que se solicita la concesión de una patente	()	()
Datos de identificación del solicitante o de la persona que se presenta la solicitud.	()	()
Descripción de la invención.	()	()
Dibujos de ser estos pertinentes.	()	()
Comprobante de Pago de las tasas establecidas.	()	()
COMPLETA ()	INCOMPLETA ()	()
DISEÑO INDUSTRIAL ()		
- Indicación de que se solicita el registro de Diseño Industrial	()	()
- Datos de identificación del solicitante o de la persona que presenta la solicitud	()	()
- Representación gráfica o fotográfica del Diseño Industrial o muestra del Material que incorpora el diseño	()	()
Comprobante de pago de las tasas establecidas	()	()
COMPLETA ()	INCOMPLETA ()	()
ESQUEMA DE TRAZADO ()		
- Indicación de que solicita el registro de un Esquema de trazado	()	()
- Datos de identificación del solicitante o de la persona que presenta La solicitud	()	()
Representación gráfica del esquema de trazado	()	()
Comprobante de pago de las tasas establecidas	()	()
COMPLETA ()	INCOMPLETA ()	()

Firma Responsable

Clavda M Nava

Fecha

2020
Bogotá D C

Doctor(a)
EMILIO FERRERO
Apoderado
BOEHRINGER INGELHEIM INTERNATIONAL GMBH.

Oficio N°
05563

ASUNTO:

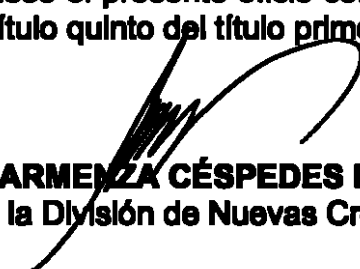
Radicación N°	04-042457
Solicitud internacional	PCT/EP02/11250
Fecha Inicio fase nacional	26/05/2004
Trámite	011
Evento	379
Actuación	416
Folios	001

Como resultado del examen de forma, realizado con fundamento en el artículo 38 de la Decisión 486 de la Comisión de la Comunidad Andina, artículo 27 del Tratado de Cooperación en Materia de Patentes (PCT), regla 51 bis del Reglamento y Circular Única de la Superintendencia de Industria y Comercio, se le comunica que:

- La solicitud no contiene copia del documento en que consta la cesión del derecho de patente del inventor al solicitante o a su causante (Art. 26-k Decisión 486).

En cumplimiento de lo dispuesto por el artículo 39 de la Decisión 486, se le requiere para que dentro del término de dos meses siguientes a la fecha de notificación del presente oficio, complete los requisitos anteriormente enunciados. En caso de no dar cumplimiento al presente requerimiento, la solicitud se considerará abandonada y perderá su prelación.

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


ALIX CARMENZA CÉSPEDES DE VERGEL
Jefe de la División de Nuevas Creaciones.

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

17 de Julio 2004

202044

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