Industria y Comercio

SUPERINTENDENCIA

Delegatura de Propiedad Industrial

Division de Nuevas Creaciones

PCT

SOLICITUD

PATENTE DE INVENCION

21 **EXPEDIENTE No** 04-67463

54 **TITULO** COMPOSICIONES FARMACEUTICAS DE AGONISTA PARCIAL DE 5HT4

51 **CLASIFICACION INTERNACIONAL** A61K 31/404

71 **SOLICITANTE** NOVARTIS AG

DOMICILIO Basilea, Suiza

74 **APODERADO** JIMENA ESCOBAR URIBE

22 **BOGOTA, D C ,** Julio 24, 2004

SS

(FORMA P 10)

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Industria y Comercio
SUPERINTENDENCIA

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PCT
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1 SOLICITUD DE:

[X] Patente de Invención [ ] Patente de Modelo de Utilidad

[ ] Capitulo I [X] Capitulo II

2 SOLICITANTE (71)	Nombre: **NOVARTIS AG** Dirección: Lichtstrasse 35, CH -4056 Basilea, Suiza Nacionalidad o Domicilio: Basilea, Suiza. Lugar de Constitución : Suiza Teléfono: 41613241111 Fax: 416 13227532 E-mail	**IDENTIFICACIÓN** C.C. [ ] NIT [ ] C.E. [ ] Otro [ ] Número
3 REPRESENTANTE O APODERADO (74)	Nombre: JIMENA ESCOBAR URIBE Dirección: Cra. 11A No. 94-76 (Of. 305) Teléfono: 6 162051/61 Fax: 6 161889 E-mail: tm-patent@escobaruribe.com	**IDENTIFICACIÓN** C.C. [X] NIT [ ] C.E. [ ] Otro [ ] Número 39.779.452T.P 68228
4 INVENTOR (ES) (72)	Nombre: **VER ANEXOS** Dirección: Nacionalidad o domicilio:	

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6 TITULO (54) COMPOSICIONES FARMACÉUTICAS DE AGONISTA PARCIAL DE 5HT$_4$

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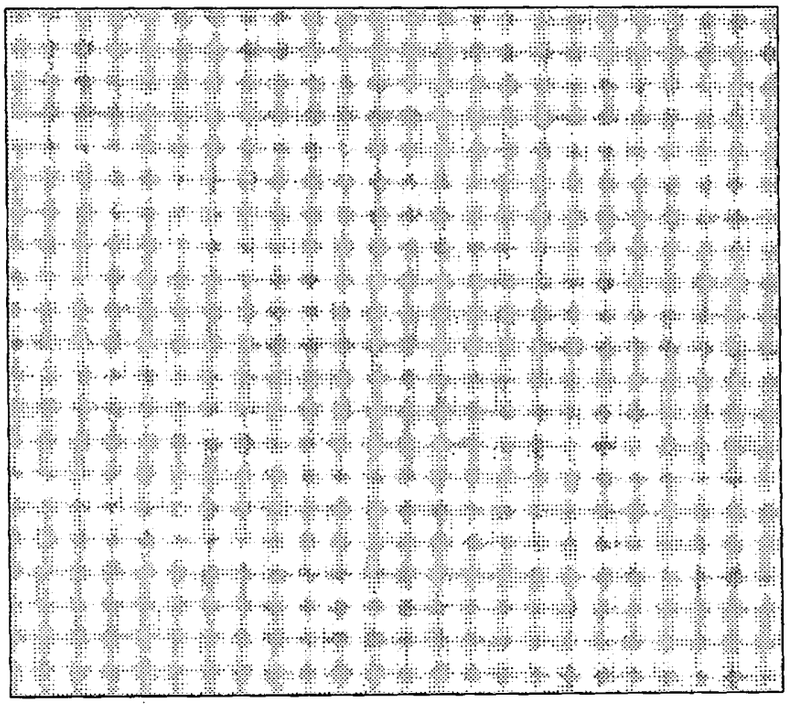
9 Comprobante de pago No. 04 - 53,383 **Fecha** Julio 7, 2004

10 **ANEXOS**

- [x] Comprobante de pago de la tasa de presentación de la solicitud
- [x] Documento que acredita la existencia y representación legal cuando el solicitante sea persona Prot. 17.398
- [x] Poderes si fuere el caso **Protocolo No. 17.398**
- [ ] Documento de cesión del inventor al solicitante o a su causante
- [ ] Declaraciones
- [ ] Copia de la solicitud internacional. (Resumen, descripción, reivindicaciones, dibujos)
- [x] Traducción de la solicitud internacional al castellano. (Resumen, descripción, reivindicaciones, dibujos)
- [x] Copia del examen preliminar internacional efectuado por la Autoridad Internacional de Examen Preliminar (IPEA).
- [ ] Traducción del examen preliminar internacional efectuado por la IPEA
- [ ] De ser el caso copia de 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 deposito del material biológico
- [ ] Arte final 12 X 12 .
- [ ] 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.
- [ ] De ser el caso, modificaciones efectuadas a la solicitud internacional
- [ ] Otros "Opinión escrita"

11 **FIGURA CARACTERÍSTICA**



12 **Solicito la concesión de la patente**

NOMBRE: JIMENA ESCOBAR URIBE

FIRMA:

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***** C O N S I G N A C I O N *****

DEPOSITANTE	TIPO PAGO	BANCO	CUENTA	No. PAGO	FECHA PGO	Vr. PAGO
ESCOBAR URIBE ASOCIADOS	CONSIGNACION	BANCO POPULAR	050-00110-6	4992977	06/07/2004	15,227,500.00

***** C O N C E P T O *****

CANT.	RENTISTICO	CONCEPTO	TOTAL CONCEPTO
1	50005-01-01 SOLICITUDES	1 TRAMITES DE SOL. DE PATENTE DE IN	422,000.00
		TOTAL : $	422,000.00

SON: CUATROCIENTOS VEINTIDOS MIL PESOS

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ANEXOS

INVENTORES

1) **AUBERT, Jérome**
(4 rue de la Feculerie, F-45150 Jargeau Francia)

2) **VITZLING, Christian**
(39 rue de Pommard F-75012 Paris Francia)

Solicito expresamente a nombre de la sociedad **NOVARTIS AG**, sociedad constituida de conformidad con las leyes de Suiza, domiciliada en Lichtstrasse 35, CH-4056 Basilea, Suiza, el otorgamiento de Patente para la invención titulada " **COMPOSICIONES FARMACÉUTICAS DE AGONISTA PARCIAL DE $5HT_4$**"

Clase A61K 31/404

JIMENA ESCOBAR URIBE
C C 39 779 452 de Usaquen
T P 68 228

RESUMEN

Una composición farmacéutica sólida para administración oral la cual comprende tegaserod en forma de base o de sal en una cantidad de hasta el 10 por ciento en peso un agente de volumen en una cantidad del 70 al 90 por ciento en peso un desintegrante en una cantidad menor al 15 por ciento en peso un abrillantador y un lubricante

COMPOSICIONES FARMACEUTICAS DE AGONISTA PARCIAL DE $5HT_4$

Campo de la Invención

La presente invención se refiere a composiciones farmacéuticas en particular a composiciones para administrar un agonista parcial del receptor 5 HT_4 como agente activo Más particularmente la presente invención se refiere a composiciones farmacéuticas para administrar tegaserod y a procedimientos para fabricar estas composiciones

Antecedentes de la Invención

Se conoce el Tegaserod (3-(5 metoxi 1H-indol 3 il metilen) N pentilcarbazimidamida) o una sal farmacéuticamente aceptable del mismo de la Patente Europea Numero EP 505322 y bajo las marcas comerciales ZELMAC y ZELNORM La Solicitud del TCP Publicada Numero WO 00/10526 describe composiciones de tegaserod por ejemplo composiciones farmacéuticas orales sólidas y su uso en incontinencia anal

A pesar de los méritos de las composiciones mencionadas anteriormente sigue existiendo una necesidad de composiciones más económicas y estables que se puedan formular de manera efectiva

Compendio de la Invención

En un aspecto esta invención proporciona una composición

farmacéutica sólida para administración oral la cual comprende

un agonista parcial de 5-HT_4 en forma de base o de sal en una cantidad de hasta el 10 por ciento en peso

un diluyente en una cantidad del 70 al 90 por ciento en peso y

un desintegrante en una cantidad menor al 15 por ciento en peso

en donde las cantidades en peso se basan en el peso total de la composición

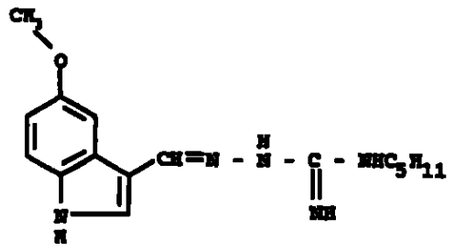
Se entiende que el término desintegrante significa una sustancia o mezcla de sustancias que facilita la desintegración de la composición después de la administración con objeto de que el ingrediente activo se libere desde la composición tan eficientemente como sea posible para permitir su disolución rápida (ver por ejemplo Remington s Pharmaceutical Science 18ª edición (1990) The Theory and Practice of Industrial Pharmacy Lachman y colaboradores Lea y Febiger (1970))

El agente activo utilizado en las composiciones de acuerdo con la presente invención es un agente activo serotonérgico que actua sobre el sistema gastrointestinal como agonista parcial del receptor 5-HT_4 Es poco soluble y sensible al ácido De preferencia el agente activo está en forma de sal por ejemplo maleato de hidrógeno o clorhidrato o en forma libre

Los agonistas parciales del receptor 5 HT_4 son utiles en la prevención y tratamiento de desórdenes de la movilidad gastrointestinal por ejemplo Síndrome de Intestino Irritable (IBS)

Enfermedad de Reflujo Gastro-Esofágico (GERD) Dispepsia Funcional (FD) Ileo Post Operativo (POI) gastroparesis diabética y estreñimiento crónico

Un agente preferido es tegaserod un agonista parcial de 5 HT_4 de la fórmula



o la forma de sal farmacéuticamente aceptable del mismo por ejemplo la sal de maleato de hidrógeno (posteriormente en la presente hml) El tegaserod tiene una solubilidad de aproximadamente el 0 02 por ciento a 25°C en agua y es sensible al ácido Hemos encontrado que se puede producir composiciones del mismo que proporcionan una buena absorción aun en el estómago

En una modalidad la composición de la invención comprende menos del 15 por ciento por ejemplo menos del 14 por ciento de preferencia el 12 por ciento o menos por ejemplo aproximadamente el 10 por ciento o menos por ejemplo del 5 al 10 por ciento en peso de desintegrante basándose en el peso total de la composición Hemos observado que el uso de este contenido tan bajo de desintegrante mejora el índice de disolución

El diluyente puede comprender lactosa manitol sucrosa sulfato de calcio fosfato de calcio o celulosa microcristalina (MCC

USP (Avicel^{MR} PH-102 FMC Corp) El diluyente puede estar presente en una cantidad del 50 al 90 por ciento de preferencia del 70 al 90 por ciento más preferiblemente del 75 al 85 por ciento De preferencia el diluyente es lactosa más preferiblemente como monohidrato de □ lactosa y/o como material amorfo (Spray dried lactose^{MR} Formost Corp)

Como desintegrante la composición de la presente invención puede comprender

- crospovidona (por ejemplo con un peso molecular >10^6 Dáltones) por ejemplo Polyplasdone XL® Kollidon CL Polyplasdone XL-10®
- almidón pregelatinizado (por ejemplo con un Peso Molecular de 30 000 a 120 000 Dáltones) por ejemplo almidón 1500^{MR} (Colorcon Reino Unido)

De preferencia el desintegrante es crospovidona que de preferencia es insoluble en agua De manera ideal el desintegrante exhibe rápidamente una alta capilaridad o una capacidad de hidratación pronunciada con poca tendencia a la formación de gel

El tamaño de partículas del desintegrante puede ser de aproximadamente 1 a aproximadamente 500 micras Una distribución de tamaños de partículas preferida es de 10 a 400 por ejemplo menos de 400 micras por ejemplo para Polyplasdone XL® menos de 80 micras por ejemplo menos de 74 micras para por ejemplo Polyplasdone XL 10® aproximadamente el 50 por ciento mayores de 50 micras y máximo el 1 por ciento mayores de 250 micras en los

tamaños para por ejemplo Kollidon CL® Una crospovidona preferida es Polyplasdone XL® por ejemplo con una densidad de aproximadamente 0 213 gramos/centímetro cubico (a granel) ó de 0 273 gramos/centímetro cúbico (comprimida)

El contenido de crospovidona preferido de la composición es de aproximadamente el 8 por ciento a aproximadamente el 14 por ciento más preferiblemente de aproximadamente el 9 por ciento a aproximadamente el 12 por ciento en peso

La composición de la presente invención puede comprender además un abrillantador por ejemplo dióxido de silicio coloidal (Aerosil Degussa) Se puede utilizar de aproximadamente el 0 05 por ciento a aproximadamente el 1 por ciento en peso de abrillantador por ejemplo aproximadamente el 0 1 por ciento de Aerosil o similar

La composición además puede comprender uno o más lubricantes por ejemplo en una cantidad dentro del rango del 3 al 8 por ciento por ejemplo del 5 al 7 por ciento en peso de la composición

Los ejemplos de estos lubricantes incluyen

- Estearato de magnesio (Faci)

  benzoato de sodio

  mono ácido graso de glicerilo por ejemplo con un peso molecular de 200 a 800 Dáltones por ejemplo monoestearato de glicerilo (por ejemplo Danisco Reino Unido)

- behenato de glicerilo (por ejemplo CompritolATO888^{MR}

Gattefossé Francia

éster palmitoesteárico de glicerilo (por ejemplo Precirol[MR] Gattefossé Francia)

polioxietilenglicol (PEG BASF)

- aceite de semilla de algodón hidrogenado (Lubitrab Edward Mendell Co Inc)

aceite de semilla de ricino (Cutina HR Henkel)

En una modalidad preferida el lubricante es behenato de glicerilo Hemos observado que el uso de behenato de glicerilo mejora las propiedades de lubricación elimina la adhesión de tabletas y ayuda a estabilizar la composición Además no hay impacto o hay un impacto insignificante sobre el tegaserod en un índice de disolución *in vitro* y desintegración de tableta de la composición De preferencia la cantidad de behenato de glicerilo utilizada es de aproximadamente el 6 por ciento en peso

Típicamente el behenato de glicerilo comprende mezclas de behenato de glicerilo y dibehenato de glicerilo Para los propósitos de la presente descripción el término behenato de glicerilo se utiliza para indicar mezclas de behenato de glicerilo y dibehenato de glicerilo y también cada componente de manera separada es decir behenato de glicerilo o dibehenato de glicerilo por ejemplo en línea con la nomenclatura utilizada en la monografía USP24/NF19

La composición de la invención puede comprender uno o más aglutinantes por ejemplo en una cantidad en el rango del 1 al 10 por ciento por ejemplo del 2 al 8 por ciento por ejemplo de

aproximadamente el 5 por ciento en peso En particular se pueden utilizar los siguientes aglutinantes

hidroxipropilmetilcelulosa (HPMC2910 Pharma-coat603^{MR} Shin Etsu Chemical Co Ltd)

- copolividona (Kollidon^{MR} VA64 BASF)
- almidón de papa almidón de trigo almidón de maíz por ejemplo con un peso molecular de 30 000 a 120 000

o una mezcla de los mismos De preferencia se utiliza de aproximadamente el 1 por ciento a aproximadamente el 10 por ciento por ejemplo de aproximadamente el 4 por ciento a aproximadamente el 6 por ciento en peso de hidroxipropilmetilcelulosa como aglutinante De acuerdo con la invención hemos observado que la presencia de hidroxipropilmetilcelulosa mejora la disolución del tegaserod aun en la presencia de una cantidad baja de desintegrante

Otros excipientes convencionales que pueden estar presentes de manera opcional en la composición de la invención incluyen conservadores estabilizantes antiadherentes o acondicionadores de flujo o abrillantadores de silice por ejemplo dióxido de silicio (por ejemplo Syloid® Aerosil®) así como los colores FD&C tales como óxidos férricos

Otros excipientes dados a conocer en la literatura como por ejemplo en Lexicon der Hilftoffe de Fiedler 4ª Edición ECV Aulendorf 1996 y Handbook of Pharmaceutical Excipients Wade y Weller Editores (1994) los contenidos de los cuales se incorporan a

la presente como referencia se pueden utilizar en las composiciones farmacéuticas de acuerdo con la invención

Una composición preferida de la invención puede comprender de aproximadamente el 0 5 al 15 por ciento en peso de tegaserod menos del 15 por ciento en peso del desintegrante por ejemplo crospovidona del 3 al 7 por ciento en peso de lubricante por ejemplo behenato de glicerilo del 50 al 90 por ciento en peso de diluyente por ejemplo lactosa del 0 1 por ciento al 1 por ciento en peso de abrillantador y de manera opcional del 1 al 10 por ciento de aglutinante por ejemplo hidroxipropilmetilcelulosa (HPMC)

Las composiciones de esta invención pueden estar libres o sustancialmente libres de tensoactivo

En un aspecto adicional la presente invención proporciona una composición oral por ejemplo una tableta que comprende el agente activo tegaserod

Las dosificaciones diarias requeridas en la práctica del método de la presente invención variarán dependiendo por ejemplo del modo de administración y de la severidad de las condiciones a tratar Una dosis diaria indicada está en el rango de aproximadamente 1 a aproximadamente 30 miligramos por ejemplo de 2 a 24 miligramos del agente activo para su uso oral administrada de manera conveniente una vez o en dosis divididas

En una modalidad la presente invención proporciona una tableta de forma redonda con un diámetro de 6 a 10 milímetros de preferencia de 7 milímetros

En un aspecto adicional la presente invención proporciona un procedimiento para la producción de las composiciones de la invención Las composiciones de la invención se pueden preparar procesando el agente activo con excipientes La composición de la invención se puede formar en tabletas mediante procedimientos que involucran granulación en especial bajo condiciones secas De manera ventajosa la composición de la invención se puede formar en tabletas mediante compresión directa Se contemplan los siguientes procedimientos A B y C

Procedimiento A

La composición de la invención se puede obtener mediante

(i) preparar una mezcla de tegaserod diluyente y lubricante

(ii) tamizar la mezcla

(iii) agregar el desintegrante abrillantador lubricante y de manera opcional aglutinante y mezclar la mezcla tamizada del paso (ii) y

(iv) formar tabletas mediante compresión directa

Se puede agregar parte del lubricante en la mezcla del paso (i) el resto en la mezcla final del paso (iii) o se puede agregar la cantidad total del lubricante en la mezcla final del paso (iii)

Las mezclas en polvo del paso iii) se comprimen ya sea en una prensa de una sola perforadora (Korsh EKO) en una prensa giratoria de 6 estaciones (Korsh PH106) en una prensa giratoria de 17

estaciones (Korsh PH 230) ó en una prensa giratoria de 43 estaciones (Fette PT2090)

Todos los componentes se pueden mezclar entre sí tamizarse y mezclarse de nuevo Luego se forman las tabletas mediante compresión directa

Procedimiento B

Las composiciones de la invención se pueden obtener mediante

(i) preparar una mezcla de Tegaserod y diluyente

(ii) tamizar la mezcla

(iii) agregar el desintegrante abrillantador y de manera opcional aglutinante y mezclar la mezcla tamizada del paso (ii) y

(iv) agregar el lubricante mediante lubricación por rociado cuando se forman las tabletas mediante compresión directa

De manera conveniente se puede utilizar una prensa giratoria de 43 estaciones (Fette PT 2090) con un sistema de rociado de estearato de magnesio para llevar a cabo el paso (iv)

Los componentes se pueden mezclar entre sí tamizarse y mezclarse de nuevo Se agrega el lubricante mediante lubricación por rociado cuando se forman las tabletas mediante compresión directa

Procedimiento C

En otra modalidad las composiciones de la invención se pueden

obtener mediante

(i) preparar una mezcla de Tegaserod diluyente desintegrante abrillantador y de manera opcional aglutinante

(ii) compactar la mezcla del paso (i) mediante compactación con rodillo

(iii) moler la mezcla del paso (ii) y

(iv) formar las tabletas mediante compresión o agregar el lubricante mediante lubricación por rociado cuando se forman las tabletas mediante compresión directa

Las tabletas se pueden formar comprimiendo el polvo resultante en una prensa de una sola perforadora (Korsh EKO) en una prensa giratoria de 6 estaciones (Korsh PH106) en una prensa giratoria de 17 estaciones (Korsh PH 230) o en una prensa giratoria de 43 estaciones (Fette PT2090) con el sistema de rociado de estearato de magnesio

La siguiente es una descripción a manera de ejemplo solamente de las composiciones y procedimientos de la invención

Ejemplo 1

Se prepara una tableta de 6 miligramos utilizando el método de compresión directa

Componente	Cantidad (tableta de 125 miligramos) porcentaje peso/peso
Maleato de tegaserod	6 65
Lactosa secada por pulverización	82 85
Crospovidona	6 00
Aérosil	0 50
behenato de glicerilo	4 00

Se forma una mezcla mezclando maleato de tegaserod lactosa crospovidona aérosil y behenato de glicerilo Esta mezcla se tamiza y la mezcla de nuevo se mezcla Las mezclas en polvo resultantes se comprimen utilizando una prensa giratoria de 17 estaciones (Korsh PH 230) equipada con perforadoras superiores redondas de 7 milímetros

Ejemplo 2

Se prepara una tableta de 6 miligramos utilizando el método de compresión directa

Componente	Cantidad (tableta de 125 miligramos) porcentaje peso/peso
Maleato de tegaserod	6 65
Lactosa secada por pulverización	72 25
Hidroxipropilmetilcelulosa	5
Crospovidona	10 00
Aérosil	0 10
behenato de glicerilo	6 00

Se forma una premezcla mezclando maleato de tegaserod hidroxipropilmetilcelulosa una parte de behenato de glicerilo y una parte de lactosa Esta premezcla se mezcla con los excipientes restantes excepto el behenato de glicerilo Esta mezcla se lubrica con la parte restante de behenato de glicerilo

La mezcla final se comprime utilizando una prensa giratoria (Korsh PH 343 ó Fette PT2090) equipada con perforadoras superiores redondas de 7 milímetros

Ejemplo 3

Se prepara una tableta de 6 miligramos utilizando el método de compresión directa con lubricación por rociado *in situ*

Componente	Cantidad (tableta de 125 miligramos) porcentaje peso/peso
Maleato de tegaserod	6 65
Lactosa secada por pulverización	84 85
HPMC	3 00
Crospovidona	5 00
Aérosil	0 50
Estearato de magnesio	< 0 3

Se forma una mezcla mezclando maleato de tegaserod lactosa crospovidona aérosil y compritol Esta mezcla y la mezcla se vuelven a mezclar Se agrega el lubricante de estearato de magnesio mediante lubricación por rociado Se comprimen las mezclas en polvo resultantes utilizando una prensa giratoria de 43

estaciones (Fette PT 2090) equipada con perforadoras superiores redondas de 7 milímetros

Ejemplo 4

Se prepara una tableta de 6 miligramos utilizando compactación con rodillo

Componente	Cantidad (tableta de 125 miligramos) porcentaje peso/peso
Maleato de tegaserod	6 65
Lactosa secada por pulverización	76 85
Crospovidona	10 00
Aérosil	0 50
Behenato de glicerilo	6 00

Las composiciones se preparan mezclando maleato de tegaserod lactosa crospovidona aérosil y behenato de glicerilo Esta mezcla se compacta por compactación con rodillo y se muele Se forman las tabletas por compresión

La presente invención proporciona de esta manera una composición farmacéutica oral sólida que comprende un agonista parcial del receptor 5-HT_4 y una cantidad de desintegrante más baja que la utilizada hasta ahora

Ejemplo Comparativo

Las composiciones de la presente invención normalmente

tienen las siguientes ventajas comparadas a las composiciones descritas en la Publicación Internacional Numero WO 00/10526

A Las tabletas fabricadas de acuerdo con la presente invención son menos higroscópicas que las tabletas fabricadas de acuerdo con la Publicación Internacional Numero WO 00/10526 (procedimiento de granulación humeda)

Las tabletas (6 miligramos de tegaserod) se fabrican como se describe en el Ejemplo 2 anterior y también como se describe en el Ejemplo 3 de la Publicación Internacional Número WO 00/10526 Las tabletas de ambos lotes se exponen a una atmósfera con humedad relativa al 60 por ciento a 25 C durante un período de 72 horas Se mide el incremento de peso de las tabletas y se calcula el incremento del porcentaje en peso debido a la absorción de vapor de agua Los resultados obtenidos se presentan a continuación

Tipo de Tableta	Recuperación de agua en porcentaje en peso después de la exposición de tabletas de 6 miligramos no protegidas a 25°C/60% de humedad relativa durante 72 horas
Ejemplo 2 de la presente invención compresión directa	aproximadamente 2 por ciento
Ejemplo 3 de WO 00/10526 (granulación húmeda)	aproximadamente 5 por ciento

B - Las tabletas fabricadas de acuerdo con la presente invención (por ejemplo el Ejemplo 2 compresión directa) tienen perfiles de disolución de tegaserod similares a los de las tabletas

fabricadas de acuerdo con la Publicación Internacional Numero WO 00/10526 (procedimiento de granulación húmeda)

Las tabletas (6 miligramos de tegaserod) preparadas de acuerdo con el Ejemplo 2 de la presente solicitud y de acuerdo con el Ejemplo 3 de la Publicación Internacional Numero WO 00/10526 se suspenden en alícuotas de 900 mililitros de reguladores acuosos a diferentes pHs y en agua del grifo con agitación mediante aspas giratorias (50 rpm) Se calcula el porcentaje de disolución de tegaserod después del tratamiento de suspensión durante 30 minutos para cada tipo de tableta para cada régimen de tratamiento Los resultados obtenidos se dan más adelante

Tableta de 6 miligramos porcentaje de tegaserod disuelto después de 30 minutos (aspas giratorias 50 rpm)

Tipo de Tableta	Regulador USP, pH de 4 5 (900 ml)	Regulador USP, pH de 6 5 (900 ml)	Regulador USP, pH de 7 5 (900 ml)	Agua (500 ml)
Ejemplo 2 de la presente invención compresión directa	19 4	94 8	91 6	96 4
Ejemplo 3 de WO 00/10526	19 9	98 1	95 7	99 0

C El procedimiento de fabricación descrito en la presente invención es más simple corto y barato que el procedimiento descrito en la Publicación Internacional Numero WO 00/10526 (granulación humeda)

Esta invención proporciona composiciones de tegaserod con

menos componentes que los conocidos hasta ahora y un procedimiento de secado simple sin granulación Las formulaciones de la presente invención son menos higroscópicas superan los problemas de adhesión y proporcionan una disolución completa o sustancialmente completa dentro de 30 minutos

REIVINDICACIONES

1 Una composición farmacéutica sólida para administración oral la cual comprende

un agonista parcial de 5-HT_4 en forma de base o de sal en una cantidad de hasta el 10 por ciento en peso

un diluyente en una cantidad del 70 al 90 por ciento en peso

un desintegrante en una cantidad menor al 15 por ciento en peso y

en donde las cantidades en peso se basan en el peso total de la composición

2 Una composición de acuerdo con la reivindicación 1 en donde el agonista parcial de 5-HT_4 es tegaserod

3 Una composición de acuerdo con la reivindicación 1 ó 2 la cual además comprende un abrillantador

4 Una composición de acuerdo con cualquiera de las reivindicaciones precedentes la cual además comprende un lubricante

5 Una composición de acuerdo con cualquiera de las reivindicaciones precedentes la cual además comprende un aglutinante

6 Una composición de acuerdo con cualquiera de las reivindicaciones 2 5 en donde el tegaserod está en la forma de la sal de maleato

7 Una composición de acuerdo con cualquiera de las reivindicaciones precedentes en donde se selecciona el diluyente a partir del grupo que consiste en lactosa manitol sacarosa fosfato de calcio o celulosa microcristalina

8 Una composición de acuerdo con cualquiera de las reivindicaciones precedentes en donde el diluyente es lactosa

9 Una composición de acuerdo con cualquiera de las reivindicaciones precedentes en donde el desintegrante está presente en una cantidad del 12 por ciento o menos en peso basándose en el peso total de la composición

10 Una composición de acuerdo con cualquiera de las reivindicaciones precedentes en donde el desintegrante es crospovidona

11 Una composición farmacéutica de acuerdo con cualquiera de las reivindicaciones 4 a 10 en donde el lubricante está presente en una cantidad del 3 al 7 por ciento basándose en el peso total de la composición

12 Una composición farmacéutica de acuerdo con cualquiera de las reivindicaciones 4 a 11 en donde el lubricante es monoestearato de glicerol o behenato de glicerol

13 Una composición farmacéutica de acuerdo con cualquiera de las reivindicaciones 3 a 12 en donde el abrillantador es dióxido de sílice coloidal

14 Una composición farmacéutica de acuerdo con cualquiera de las reivindicaciones 3 a 13 en donde el aglutinante es celulosa

de hidroxipropilmetilo

15 Un procedimiento para la producción de una composición de acuerdo con cualquiera de las reivindicaciones precedentes cuyo procedimiento se lleva a cabo bajo condiciones sustancialmente secas utilizando granulación

16 Un procedimiento para la producción de una composición de acuerdo con cualquiera de las reivindicaciones precedentes cuyo procedimiento comprende

(i) preparar una mezcla de agonista parcial de 5 HT_4 por ejemplo tegaserod diluyente y lubricante

(ii) tamizar la mezcla

(iii) agregar el desintegrante abrillantador y opcionalmente aglutinante y mezclar la mezcla tamizada del paso (ii) y

(iv) formar tabletas mediante compresión directa

17 Un procedimiento para la producción de una composición de acuerdo con la reivindicación 16 en donde los componentes se mezclan con tegaserod se tamizan y se mezclan de nuevo antes de formar las tabletas

18 Un procedimiento para la producción de una composición de acuerdo con cualquiera de las reivindicaciones 1 a 14 cuyo procedimiento comprende

(i) preparar una mezcla de agonista parcial de 5-TH_4 por ejemplo tegaserod y diluyente

(ii) tamizar la mezcla

(iii) agregar el desintegrante abrillantador y de manera

opcional aglutinante y mezclar la mezcla tamizada del paso (ii)

(iv) agregar el lubricante mediante lubricación por rociado cuando se forman tabletas mediante compresión directa

19 Un procedimiento para la producción de una composición de acuerdo con la reivindicación 18 en donde todos los componentes se mezclan con tegaserod se tamizan y se mezclan de nuevo antes de formar tabletas

20 Un procedimiento para la producción de una composición de acuerdo con cualquiera de las reivindicaciones 1 a 14 cuyo procedimiento comprende

(i) preparar una mezcla de agonista parcial de 5 HT_4 por ejemplo tegaserod diluyente desintegrante abrillantador y de manera opcional aglutinante

(ii) compactar la premezcla del paso (i) mediante compactación con rodillo

(iii) moler la mezcla del paso (ii) y

(iv) formar tabletas mediante compresión

21 Una composición farmacéutica sólida para administración oral la cual consiste en o consiste esencialmente en

tegaserod en forma de base o de sal en una cantidad de hasta el 10 por ciento en peso

un diluyente en una cantidad del 70 al 90 por ciento en peso

un desintegrante en una cantidad menor al 15 por ciento en peso

un abrillantador y un lubricante

en donde las cantidades son en peso basándose en el peso total de la composición

22 Una composición farmacéutica sólida para administración oral la cual consiste en o consiste esencialmente en

tegaserod en forma de base o de sal en una cantidad de hasta el 10 por ciento en peso

un diluyente en una cantidad del 70 al 90 por ciento en peso

un desintegrante en una cantidad menor al 15 por ciento en peso

un aglutinante un abrillantador y un lubricante

en donde las cantidades son en peso basándose en el peso total de la composición

2686/P 28

PCT

REQUEST

The undersigned requests that the present international application be processed according to the Patent Cooperation Treaty

For receiving Office use only

International Application No.: PCT/EP 02/14674 ✓

International Filing Date: (20.12.02) 20 DEC 2002 ✓

Name of receiving Office and "PCT International Application": EUROPEAN PATENT OFFICE PCT INTERNATIONAL APPLICATION

Applicant's or agent's file reference (if desired) (12 characters maximum): 4-32293A

Box No. I TITLE OF INVENTION

5-HT$_4$ PARTIAL AGONIST PHARMACEUTICAL COMPOSITIONS

Box No. II APPLICANT ☐ This person is also inventor

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. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)

Novartis AG ✓
Lichtstrasse 35
4056 Basel
CH

Telephone No.: +41 61 324 11 11
Facsimile No.: +41 61 322 75 32
Teleprinter No.:
Applicant's registration No. with the Office:

State (that is, country) of nationality: CH
State (that is, country) of residence: CH

This person is applicant for the purposes of: ☐ all designated States ☐ all designated States except the United States of America ☐ the United States of America only ☒ the States indicated in the Supplemental Box

Box No. III FURTHER APPLICANT(S) AND/OR (FURTHER) INVENTOR(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. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)

Novartis Pharma GmbH
Brunner Strasse 59
1230 Vienna
AT

This person is:
☒ applicant only
☐ applicant and inventor
☐ inventor only (If this check-box is marked, do not fill in below.)

Applicant's registration No. with the Office:

State (that is, country) of nationality: AT
State (that is, country) of residence: AT

This person is applicant for the purposes of: ☐ all designated States ☐ all designated States except the United States of America ☐ the United States of America only ☒ the States indicated in the Supplemental Box

☒ Further applicants and/or (further) inventors are indicated on a continuation sheet.

Box No. IV 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: ☒ agent ☐ common representative

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.)

GROS Florent
Novartis AG
Corporate Intellectual Property
Patent & Trademark Department
4002 Basel
CH

Telephone No.: +41 61 324 11 11
Facsimile No.: +41 61 322 75 32
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.

Continuation of Box No. III FURTHER APPLICANT(S) AND/OR (FURTHER) INVENTOR(S)

If none of the following sub-boxes is used, this sheet should not be included in the request.

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. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)*

AUBERT, Jérome
4 rue de la Fécularie
45150 Jargeau
FR

This person is:
- ☐ applicant only
- ☒ applicant and inventor
- ☐ inventor only *(If this check-box is marked, do not fill in below.)*

Applicant's registration No with the Office

State *(that is, country)* **of nationality:** FR

State *(that is country)* **of residence:** FR

This person is applicant for the purposes of: ☐ all designated States ☐ all designated States except the United States of America ☒ the United States of America only ☐ the States indicated in the Supplemental Box

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. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)*

VITZLING Christian
39 rue de Pommard
75012 Paris
FR

This person is:
- ☐ applicant only
- ☒ applicant and inventor
- ☐ inventor only *(If this check-box is marked, do not fill in below.)*

Applicant's registration No. with the Office

State *(that is, country)* **of nationality:** FR

State *(that is country)* **of residence:** FR

This person is applicant for the purposes of: ☐ all designated States ☐ all designated States except the United States of America ☒ the United States of America only ☐ the States indicated in the Supplemental Box

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. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)*

This person is:
- ☐ applicant only
- ☐ applicant and inventor
- ☐ inventor only *(If this check-box is marked, do not fill in below.)*

Applicant's registration No. with the Office

State *(that is, country)* **of nationality:**

State *(that is, country)* **of residence:**

This person is applicant for the purposes of: ☐ all designated States ☐ all designated States except the United States of America ☐ the United States of America only ☐ the States indicated in the Supplemental Box

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. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)*

This person is:
- ☐ applicant only
- ☐ applicant and inventor
- ☐ inventor only *(If this check-box is marked, do not fill in below.)*

Applicant's registration No. with the Office

State *(that is, country)* **of nationality:**

State *(that is, country)* **of residence:**

This person is applicant for the purposes of: ☐ all designated States ☐ all designated States except the United States of America ☐ the United States of America only ☐ the States indicated in the Supplemental Box

☐ Further applicants and/or (further) inventors are indicated on another continuation sheet.

Box No. V DESIGNATION OF STATES *Mark the applicable check-boxes below at least one must be marked.*

The following designations are hereby made under Rule 4 9(a)

Regional Patent

☐ **AP** **ARIPO Patent** GH Ghana GM Gambia KE Kenya LS Lesotho MW Malawi MZ Mozambique SD Sudan SL Sierra Leone, SZ Swaziland, TZ United Republic of Tanzania, UG Uganda, ZM Zambia, ZW Zimbabwe, and any other State which is a Contracting State of the Harare Protocol and of the PCT *(if other kind of protection or treatment desired, specify on dotted line)*

☒ **EA** **Eurasian Patent** AM Armenia, AZ Azerbaijan, BY Belarus, KG Kyrgyzstan, KZ Kazakhstan, MD Republic of Moldova, RU Russian Federation, TJ Tajikistan, TM Turkmenistan, and any other State which is a Contracting State of the Eurasian Patent Convention and of the PCT

☒ **EP** **European Patent** AT Austria, BE Belgium, BG Bulgaria, CH & LI Switzerland and Liechtenstein, CY Cyprus, CZ Czech Republic, DE Germany DK Denmark, EE Estonia, ES Spain, FI Finland, FR France GB United Kingdom, GR Greece, IE Ireland, IT Italy LU Luxembourg, MC Monaco, NL Netherlands, PT Portugal, SE Sweden, SK Slovakia, TR Turkey and any other State which is a Contracting State of the European Patent Convention and of the PCT

☐ **OA** **OAPI Patent** BF Burkina Faso, BJ Benin CF Central African Republic, CG Congo, CI Côte d Ivoire, CM Cameroon, GA Gabon, GN Guinea, GQ Equatorial Guinea, GW Guinea-Bissau, ML Mali, MR Mauritania, NE Niger SN Senegal TD Chad, TG Togo, and any other State which is a member State of OAPI and a Contracting State of the PCT *(if other kind of protection or treatment desired, specify on dotted line)*

National Patent *(if other kind of protection or treatment desired, specify on dotted line)*

☒ AE United Arab Emirates
☒ AG Antigua and Barbuda
☒ AL Albania
☒ AM Armenia
☒ AT Austria
☒ AU Australia
☒ AZ Azerbaijan
☒ BA Bosnia and Herzegovina
☒ BB Barbados
☒ BG Bulgaria
☒ BR Brazil
☒ BY Belarus
☒ BZ Belize
☒ CA Canada
☒ CH & LI Switzerland and Liechtenstein
☒ CN China
☒ CO Colombia
☒ CR Costa Rica
☒ CU Cuba
☒ CZ Czech Republic
☒ DE Germany
☒ DK Denmark
☒ DM Dominica
☒ DZ Algeria
☒ EC Ecuador
☒ EE Estonia
☒ ES Spain
☒ FI Finland
☒ GB United Kingdom
☒ GD Grenada
☒ GE Georgia
☒ GH Ghana
☐ GM Gambia
☒ HR Croatia
☒ HU Hungary
☒ ID Indonesia
☒ IL Israel
☒ IN India
☒ IS Iceland
☒ JP Japan
☒ KE Kenya
☒ KG Kyrgyzstan
☒ KP Democratic People s Republic of Korea
☒ KR Republic of Korea
☒ KZ Kazakhstan
☒ LC Saint Lucia
☒ LK Sri Lanka
☐ LR Liberia
☐ LS Lesotho
☒ LT Lithuania
☒ LU Luxembourg
☒ LV Latvia
☒ MA Morocco
☒ MD Republic of Moldova
☐ MG Madagascar
☒ MK The former Yugoslav Republic of Macedonia
☒ MN Mongolia
☐ MW Malawi
☒ MX Mexico
☐ MZ Mozambique
☒ NO Norway
☒ NZ New Zealand
☒ OM Oman
☒ PH Philippines
☒ PL Poland
☒ PT Portugal
☒ RO Romania
☒ RU Russian Federation
☐ SD Sudan
☒ SE Sweden
☒ SG Singapore
☒ SI Slovenia
☒ SK Slovakia
☐ SL Sierra Leone
☒ TJ Tajikistan
☒ TM Turkmenistan
☒ TN Tunisia
☒ TR Turkey
☒ TT Trinidad and Tobago
☐ TZ United Republic of Tanzania
☒ UA Ukraine
☐ UG Uganda
☒ US United States of America
☒ UZ Uzbekistan
☒ VN Viet Nam
☒ YU Yugoslavia
☒ ZA South Africa
☐ ZM Zambia
☒ ZW Zimbabwe

Check-boxes below reserved for designating States which have become party to the PCT after issuance of this sheet:

☒ VC Saint Vincent and the Grenadines ☐ ☐
☒ SC Seychelles ☐ ☐

Precautionary Designation Statement: In addition to the designations made above, the applicant also makes under Rule 4 9(b) all other designations which would be permitted under the PCT except any designation(s) indicated in the Supplemental Box as being excluded from the scope of this statement 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. *(Confirmation (including fees) must reach the receiving Office within the 15-month time limit.)*

Supplemental Box *If the Supplemental Box is not used, this sheet should not be included in the request.*

1 *If, in any of the Boxes, except Boxes Nos. VIII(i) to (v) for which a special continuation box is provided, the space is insufficient to furnish all the information, in such case, write "Continuation of Box No. " (indicate the number of the Box) and furnish the information in the same manner as required according to the captions of the Box in which the space was insufficient, in particular*

(i) *If more than two persons are to be indicated as applicants and/or inventors and no "continuation sheet" is available, in such case, write "Continuation of Box No. III" and indicate for each additional person the same type of information as required in Box No. III. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.*

(ii) *If, in Box No. II or in any of the sub-boxes of Box No. III, the indication "the States indicated in the Supplemental Box" is checked: in such case, write "Continuation of Box No. II" or "Continuation of Box No. III" or "Continuation of Boxes No. II and No. III" (as the case may be), indicate the name of the applicant(s) involved and, next to (each) such name, the State(s) (and/or where applicable, ARIPO, Eurasian, European or OAPI patent) for the purposes of which the named person is applicant.*

(iii) *If, in Box No. II or in any of the sub-boxes of Box No. III, the inventor or the inventor/applicant is not inventor for the purposes of all designated States or for the purposes of the United States of America, in such case, write "Continuation of Box No. II" or "Continuation of Box No. III" or "Continuation of Boxes No. II and No. III" (as the case may be), indicate the name of the inventor(s) and, next to (each) such name, the State(s) (and/or where applicable, ARIPO, Eurasian, European or OAPI patent) for the purposes of which the named person is inventor*

(iv) *If, in addition to the agent(s) indicated in Box No. IV there are further agents, in such case, write "Continuation of Box No. IV" and indicate for each further agent the same type of information as required in Box No. IV*

(v) *If, in Box No. V the name of any State (or OAPI) is accompanied by the indication "patent of addition," or "certificate of addition," or if, in Box No. V the name of the United States of America is accompanied by an indication "continuation" or "continuation-in-part" in such case, write "Continuation of Box No. V" and the name of each State involved (or OAPI), and after the name of each such State (or OAPI), the number of the parent title or parent application and the date of grant of the parent title or filing of the parent application.*

(vi) *If in Box No. VI, there are more than five earlier applications whose priority is claimed, in such case, write "Continuation of Box No. VI" and indicate for each additional earlier application the same type of information as required in Box No. VI*

2 *If, with regard to the precautionary designation statement contained in Box No. V the applicant wishes to exclude any State(s) from the scope of that statement, in such case, write "Designation(s) excluded from precautionary designation statement" and indicate the name or two-letter code of each State so excluded.*

Continuation of Box No II
Novartis AG is applicant for all designated States with the exception of AT (Austria) and US (USA)

Continuation of Box No III
Novartis Pharma GmbH is applicant for AT (Austria) only

Box No. VI PRIORITY CLAIM

The priority of the following earlier application(s) is hereby claimed.

Filing date of earlier application (day/month/year)	Number of earlier application	Where earlier application is:		
		national application country or Member of WTO	regional application * regional Office	international application receiving Office
Item (1) 21 December 2001 (21 12 01)	01403339 3		EP	
Item (2)				
Item (3)				
Item (4)				
Item (5)				

☐ Further priority claims are indicated in the Supplemental Box.

The receiving Office is requested to prepare and transmit to the International Bureau a certified copy of the earlier application(s) *(only if the earlier application was filed with the Office which for the purpose of this international application is the receiving Office)* identified above as

☐ all items ☐ item (1) ☐ item (2) ☐ item (3) ☐ item (4) ☐ item (5) ☐ other, see Supplemental Box

** Where the earlier application is an ARIPO application, indicate at least one country party to the Paris Convention for the Protection of Industrial Property or one Member of the World Trade Organization for which that earlier application was filed (Rule 4.10(b)(ii))*

Box No. VII INTERNATIONAL SEARCHING AUTHORITY

Choice of International Searching Authority (ISA) *(if two or more International Searching Authorities are competent to carry out the international search, indicate the Authority chosen, the two-letter code may be used)*

ISA /

Request to use results of earlier search reference to that search *(if an earlier search has been carried out by or requested from the International Searching Authority).*

Date *(day/month/year)*	Number	Country *(or regional Office)*
17 04.2002	01403339	EP

Box No. VIII DECLARATIONS

The following declarations are contained in Boxes Nos. VIII (i) to (v) *(mark the applicable check-boxes below and indicate in the right column the number of each type of declaration)*

Number of declarations

☐ Box No. VIII (i) Declaration as to the identity of the inventor

☐ Box No. VIII (ii) Declaration as to the applicant's entitlement, as at the international filing date, to apply for and be granted a patent

☐ Box No VIII (iii) Declaration as to the applicant's entitlement, as at the international filing date, to claim the priority of the earlier application

☐ Box No. VIII (iv) Declaration of inventorship (only for the purposes of the designation of the United States of America)

☐ Box No VIII (v) Declaration as to non-prejudicial disclosures or exceptions to lack of novelty

Box No. IX CHECK LIST; LANGUAGE OF FILING

This international application contains		This international application is accompanied by the following item(s) *(mark the applicable check-boxes below and indicate in right column the number of each item).*	Number of items
(a) the following number of sheets in paper form			
request (including declaration sheets)	6	1 ☒ fee calculation sheet	1
description (excluding sequence listing part)	11	2 ☐ original separate power of attorney	
claims	3	3 ☐ original general power of attorney	
abstract	1	4 ☒ copy of general power of attorney; reference number if any: AV 38671 + AV 46171	2
drawings	0	5 ☐ statement explaining lack of signature	
Sub-total number of sheets	21	6. ☐ priority document(s) identified in Box No VI as item(s): 1)	
sequence listing part of description *(actual number of sheets if filed in paper form, whether or not also filed in computer readable form, see (b) below)*	0	7 ☐ translation of international application into *(language)*	
Total number of sheets	21	8 ☐ separate indications concerning deposited microorganism or other biological material	
(b) sequence listing part of description filed in computer readable form		9 ☐ sequence listing in computer readable form (indicate also type and number of carriers (diskette, CD-ROM, CD-R or other))	
(i) ☐ only (under Section 801(a)(i))		(i) ☐ copy submitted for the purposes of international search under Rule 13*ter* only (and not as part of the international application)	
(ii) ☐ in addition to being filed in paper form (under Section 801(a)(ii))		(ii) ☐ *(only where check-box (b)(i) or (b)(ii) is marked in left column)* additional copies including, where applicable, the copy for the purposes of international search under Rule 13*ter*	
Type and number of carriers (diskette, CD-ROM, CD-R or other) on which the sequence listing part is contained *(additional copies to be indicated under item 9(ii), in right column)*		(iii) ☐ together with relevant statement as to the identity of the copy or copies with the sequence listing part mentioned in left column	
		10 ☐ other *(specify)*	
Figure of the drawings which should accompany the abstract:		Language of filing of the international application. English	

Box No. X 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 request).

In the name of the applicants
The representative

13.12.2002

GROS Florent AV 38671 + 46171

For receiving Office use only

1 Date of actual receipt of the purported international application. (20. 12. 02) 20 DEC 2002		2 Drawings. ☐ received ☐ not received.
3 Corrected date of actual receipt due to later but timely received papers or drawings completing the purported international application.		
4. Date of timely receipt of the required corrections under PCT Article 11(2):		
5 International Searching Authority (if two or more are competent): ISA /	6. ☐ Transmittal of search copy delayed until search fee is paid	

For International Bureau use only

Date of receipt of the record copy by the International Bureau:

Aktenexemplar
PCT 1A | 1C | DW

Novartis AG
Corporate Intellectual Property
CH-4002 Basel
Switzerland
Tel +41 61 324 38 86
Fax +41 61 322 75 32

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NOVARTIS

Europaisches Patentamt
D-80298 München

Your Ref. | Our Ref.

January 31, 2003 | ER

Case 4-32293A

☐ European Patent Application No
☒ International Patent Application No. PCT/EP 02/14674

Please find enclosed
☐ priority document(s) No(s)
☒ 1 Power(s) of Attorney

Yours very truly

In the name of the applicant
The representative

GROS, Florent, GA 36671

Enclosures. 1 Power of Attorney

PCT

POWER OF ATTORNEY

(for an International Application filed under the Patent Cooperation Treaty)

(PCT Rule 90.4)

The undersigned applicants

Jérome AUBERT

Christian VITZLING

hereby appoint

GROS, Florent
Novartis AG
Corporate Intellectual Property
Patent & Trademark Department
4002 Basel
CH

as ☒ agent ☐ common representative

to represent the undersigned before all the competent International Authorities in connection with the International Application identified below

Title of the invention **5-HT$_4$ PARTIAL AGONIST PHARMACEUTICAL COMPOSITIONS**

Applicant's file reference **4-32293A**

International Application number (if already available) **PCT/EP 02/14674**

filed with the European Patent Office as Receiving Office and to make or receive payments on behalf of the undersigned

Signature of the applicants Date

Jérome Aubert — 14 01 03
Jérome AUBERT

Christian Vitzling — 15.11 02
Christian VITZLING

PC 04/02

Aktenexemplar
PCT 1A | 1C | DW

Novartis AG
Corporate Intellectual Property
CH-4002 Basel
Switzerland
Tel: +41 61 324 38 86
Fax: +41 61 322 75 32

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NOVARTIS

Europäisches Patentamt
D-80298 München

February 6, 2003

Your Ref

Our Ref
ER

Case: 4-32293A

☐ European Patent Application No.
☒ International Patent Application No PCT/EP 02/14674

Please find enclosed
☒ 1 priority document(s) No(s) EP 01403339.3
☐ Power(s) of Attorney
☐ Declaration of Inventor

Yours very truly

In the name of the applicant
The representative

GROS, Florent, GA 36671

Enclosure: 1 Priority document No EP 01403339 3

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

(19) World Intellectual Property Organization
International Bureau

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PCT

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(30) Priority Data:
01403339 3 21 December 2001 (21 12.2001) EP

(71) Applicant *(for all designated States except AT US)* NOVARTIS AG [CH/CH] Lichtstrasse 35 CH-4056 Basel (CH).

(71) Applicant *(for AT only)* NOVARTIS PHARMA GMBH [AT/AT] Brunner Strasse 59, A 1230 Vienna (AT).

(72) Inventors, and

(75) Inventors/Applicants *(for US only)*: AUBERT, Jérome [FR/FR] 4 rue de la Féculerie, F-45150 Jargeau (FR). VITZLING, Christian [FR/FR] 39 rue de Pommard, F 75012 Paris (FR).

(74) Agent GROS, Florent Novartis AG Corporate Intellectual Property Patent & Trademark Department, CH-4002 Basel (CH)

(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, GE, GH HR, HU ID IL, IN IS, JP KE, KG KP KR, KZ, LC, LK, LT LU LV MA, MD, MK, MN MX, NO, NZ, OM, PH PL, PT RO, RU SC, SE, SG SK, TJ TM TN TR, TT UA, US, UZ, VC VN YU ZA, ZW

(84) Designated States *(regional)*: Eurasian patent (AM AZ, BY KG KZ, MD, RU TJ TM), European patent (AT BE, BG CH, CY CZ, DE, DK, EE, ES, FI, FR, GB GR, IE, IT LU MC, NL, PT SE, SI, SK, TR).

Published.

— *with international search report*

— *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments*

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

WO 03/053432 A1

(54) Title: 5HT$_4$ PARTIAL AGONIST PHARMACEUTICAL COMPOSITIONS

(57) Abstract: A solid pharmaceutical composition for oral administration comprising tegaserod in base or salt form in an amount of up to 10% by weight a bulking agent in an amount of 70 to 90% by weight a disintegrant in an amount of less than 15% by weight a glidant and a lubricant.

23 06 2003 VT
4-32293A PATENT COOPERATION TREATY
Adrian Spillmann EP02/14674

Corporate Intellectual Property
22 April 2003
APPL | M/D | F/L | PS | Copy

PCT

From the INTERNATIONAL SEARCHING AUTHORITY

To:
NOVARTIS AG
Corporate Intellectual Property
Attn Gros, Florent
Patent & Trademark Department
CH-4002 Basel
SWITZERLAND

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL SEARCH REPORT OR THE DECLARATION

(PCT Rule 44.1)

Applicant's or agent's file reference: 4-32293A	Date of mailing (day/month/year): 23/04/2003
International application No.: PCT/EP 02/ 14674	FOR FURTHER ACTION See paragraphs 1 and 4 below
Applicant: NOVARTIS AG	International filing date (day/month/year): 20/12/2002

1 [X] 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 30 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	Authorized officer
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	Jaap Hurenkamp

Form PCT/ISA/220 (July 1998)

NOTES TO FORM PCT/IBA/220

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.

NOTES TO FORM PCT/ISA/220 (continued)

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 appplication 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

Consequences 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.

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PATENT CO PERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference	FOR FURTHER ACTION	see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below
4-32293A		
International application No.	International filing date (day/month/year)	(Earliest) Priority Date (day/month/year)
PCT/EP 02/ 14674	20/12/2002	21/12/2001
Applicant		
NOVARTIS AG		

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.

[X] 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. [X] Certain claims were found unsearchable (See Box I)

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

4. With regard to the title,

[X] 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,

[X] 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.

[ ] None of the figures.

[ ] because the applicant failed to suggest a figure.

[ ] because this figure better characterizes the invention.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP 02/14674

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61K31/404 A61K9/20

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, BIOSIS, PAJ, WPI Data, 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	WO 00 57857 A (YUHAN CORP) 5 October 2000 (2000-10-05) page 6, line 5 - line 9 page 6 -page 7, example 6 page 15, claims 1-3	1,3-5, 7-11, 13-16
X	WO 00 10526 A (NOVARTIS ERFIND VERWALT GMBH ,NOVARTIS AG (CH), ZUEGER OTHMAR (CH)) 2 March 2000 (2000-03-02) cited in the application page 2, paragraph 4 page 18 -page 20, examples 1,2 page 25 -page 26, claims 1,2,6-11	1-13,20

☐ 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	Date of mailing of the international search report
9 April 2003	23/04/2003

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
VON EGGELKRAUT, S

Form PCT/ISA/210 (second sheet) (July 1992)

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I 2

Claims searched completely
2,6,17,19,21,22

Claims searched incompletely
1,3-5,7-16,18,20

Reasoning

Present claims 1,3-5,7-16,18,20 relate to a product defined by reference to a property, namely the activity as 5-HT4 partial agonist The claims cover all products having this property, whereas the application provides support within the meaning of Article 84 EPC and disclosure within the meaning of Article 83 EPC for only a very limited number of such products In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible Independent of the above reasoning, the claims also lack clarity (Article 84 EPC) An attempt is made to define the product by refernce to a result to be achieved Again, this lack of clarity in the present case is such as to render a meaningful seach over the whole of the claimed scope impossible, Consequently, th search has been carried out for those parts of the claims which appear to be clear, supported and disclosed, namely those parts relating to the 5-HT4 partial agonist tegaserod claimed in claims 2,6,17,19,21,22 and to the concept of "5-HT4 agonists"

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66 1(e) PCT) The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP 02/14674

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:

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:

see FURTHER INFORMATION sheet PCT/ISA/210

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.

INTERNATI NAL SEARCH REPORT

Information on patent family members

International Application No
PCT/EP 02/14674

Patent document cited in search report		Publication date	Patent family member(s)		Publication date
WO 0057857	A	05-10-2000	AU	3574500 A	16-10-2000
			WO	0057857 A1	05-10-2000
			KR	2001006835 A	26-01-2001
			US	2002071864 A1	13-06-2002
WO 0010526	A	02-03-2000	AU	5623299 A	14-03-2000
			BG	105257 A	30-11-2001
			BR	9913135 A	08-05-2001
			CA	2338794 A1	02-03-2000
			CN	1323200 T	21-11-2001
			EE	200100104 A	17-06-2002
			WO	0010526 A2	02-03-2000
			EP	1104289 A2	06-06-2001
			FR	2799123 A1	06-04-2001
			FR	2782454 A1	25-02-2000
			FR	2784899 A1	28-04-2000
			HR	20010123 A1	28-02-2002
			HU	0103431 A2	28-01-2002
			IT	MI991826 A1	19-02-2001
			JP	2002523351 T	30-07-2002
			NO	20010863 A	26-03-2001
			PL	346764 A1	25-02-2002
			SK	2432001 A3	11-09-2001
			TR	200100361 T2	21-06-2001
			TR	200102259 T2	21-06-2002
			ZA	200101095 A	08-05-2002

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

CHAPTER II

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 4-32293A
International application No. PCT/EP 02/14674	International filing date *(day/month/year)* 20 December 2002 (20.12.02)	(Earliest) Priority date *(day/month/year)* 21 December 2001 (21 12.01)

Title of invention

5-HT$_4$ PARTIAL AGONIST PHARMACEUTICAL COMPOSITIONS

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.)*	Telephone No. +4161 324 11 11
Novartis AG Lichtstrasse 35 4056 Basel CH	Facsimile No. +4161 322 75 32
	Teleprinter No.
	Applicant's registration No. with the Office

State *(that is, country)* of nationality CH	State *(that is, country)* of residence: CH

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.)*

Novartis Pharma GmbH
Brunner Strasse 59
1230 Vienna
AT

State *(that is, country)* of nationality AT	State *(that is, country)* of residence: AT

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.)*

AUBERT Jérome
4 rue de la Féculerie
45150 Jargeau
FR

State *(that is, country)* of nationality FR	State *(that is, country)* of residence: FR

☒ Further applicants are indicated on a continuation sheet.

Sheet No. 2

International application No.
PCT/EP 02/14674

Continuation of Box No. II APPLICANT(S)

If none of the following sub-boxes is used, this sheet should not be included in the demand.

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.)*

VITZLING, Christian
39, rue de Pommard
75012 Paris
FR

State *(that is, country)* of nationality:	State *(that is, country)* of residence:
FR	FR

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.)*

State *(that is, country)* of nationality:	State *(that is, country)* of residence:

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.)*

State *(that is, country)* of nationality:	State *(that is, country)* of residence:

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.)*

State *(that is, country)* of nationality:	State *(that is, country)* of residence:

☐ Further applicants are indicated on another continuation sheet.

Sheet No. 3

International application No.
PCT/EP 02/14874

Box No. III AGENT OR COMMON REPRESENTATIVE; OR ADDRESS FOR CORRESPONDENCE

The following person is ☒ agent ☐ common representative

and ☐ 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.)*

GRUBB, Philip
Novartis AG
Corporate Intellectual Property
4002 Basel
CH

Telephone No.
+4161 324 11 11

Facsimile No.
+4161 322 75 32

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 filed

the description
☐ as originally filed
☐ as amended under Article 34

the claims
☐ as originally filed
☐ as amended under Article 19 (together with any accompanying statement)
☐ as amended under Article 34

the drawings
☐ as originally filed
☐ as amended under Article 34

2. ☐ 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:

Sheet No. 4.

International application No.
PCT/EP 02/14674

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:

			For International Preliminary Examining Authority use only: received	not received
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	☐	☐

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

1 ☒ fee calculation sheet
2. ☐ original separate power of attorney
3 ☐ original general power of attorney
4. ☐ copy of general power of attorney; reference number if any:
5. ☐ statement explaining lack of signature
6. ☐ sequence listings in computer readable form
7 ☐ tables in computer readable form related to sequence listings
8 ☒ other *(specify)*: Letter dated June 2, 2003 (Request for a detailed preliminary examination)

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).

In the name of the applicants
The representative

PW Grubb

05 06.2003

GRUBB Philip AV 36671 + 46171

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:

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PCT

CHAPTER II

FEE CALCULATION SHEET

Annex to the Demand

International application No. PCT/EP 02/14674	For International Preliminary Examining Authority use only
Applicant's or agent's file reference 4-32293A	Date stamp of the IPEA

Applicant
Novartis AG et al.

CALCULATION OF PRESCRIBED FEES

1	Preliminary examination fee	EUR 1530 – P	
2	Handling fee *(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.)*	EUR 159 – H	
3	Total of prescribed fees Add the amounts entered at P and H and enter total in the TOTAL box	EUR 1689 – TOTAL	

MODE OF PAYMENT

- [X] 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
(This mode of payment may not be available at all IPEAs)

IPEA/ EP

- [X] Authorization to charge the total fees indicated above.
- [X] *(This check-box may be marked only if the conditions for deposit accounts of the IPEA so permit)* Authorization to charge any deficiency or credit any overpayment in the total fees indicated above.

Deposit Account No.. 2811 0031

Date: 05 06 2003

Name: Novartis AG

Signature: E. Rubchmann

Adrian Spillmann
Patent Specialist

Novartis AG
Corporate Intellectual Property
CH-4002 Basel
Switzerland
Tel: +41 61 324 53 91
Fax: +41 61 322 75 32

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NOVARTIS

Europäisches Patentamt
D-80298 München

TELEFAX + Mail
From. +41 61 322 75 32
To 004989 2399 4465

Total pages. 1

June 2, 2003

Your Ref.

Our Ref.
4-32293A

International Application PCT/EP02/14674
(Request for a detailed preliminary examination)

Ladies and Gentlemen

Based on the Notice of the President of the EPO dated Nov 2, 2001, concerning rationalisation of the international preliminary examination procedure at the EPO, we herewith request under Rule 66.3 PCT a detailed preliminary examination (second written opinion) of the above-identified application according to Section II, point 7 of the Notice of the President.

Yours very truly
In the name of Novartis AG

Patrick Crawley
European Patent Attorney,
Professional Representative for the Applicant
GA No. 36671

PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To

Grubb Philip
NOVARTIS AG
Corporate Intellectual Property
Patent & Trademark Department
CH-4002 Basel
SUISSE

PCT

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Rule 71 1)

Date of mailing *(day/month/year)*	19 02 2004
Applicant's or agent's file reference 4 32293A	**IMPORTANT NOTIFICATION**

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/EP 02/14874	20 12 2002	21 12 2001

Applicant
NOVARTIS AG et al

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	Authorized Officer
European Patent Office P.B 5818 Patentlaan 2 NL-2280 HV Rijswijk Pays Bas Tel +31 70 340 2040 Tx. 31 651 epo nl Fax: +31 70 340 3016	Rossi C Tel +31 70 340-3322

Form PCT/IPEA/416 (January 2004)

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PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT
(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 4-32293A	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No PCT/EP 02/14674	International filing date (day/month/year) 20 12 2002	Priority date (day/month/year) 21 12.2001
International Patent Classification (IPC) or both national classification and IPC A61K31/404 A61K31/404		
Applicant NOVARTIS AG et al		

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	Date of completion of this report
07 06 2003	19 02.2004
Name and mailing address of the international preliminary examining authority: European Patent Office P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk Pays Bas Tel. +31 70 340 2040 Tx: 31 651 epo nl Fax: +31 70 340 3016	Authorized Officer von Eggelkraut-Gotta Telephone No. +31 70 340-4732

Form PCT/IPEA/409 (Cover Sheet) (January 2004)

INTERNATI NAL PRELIMINARY EXAMINATION REP RT

International application No PCT/EP 02/14674

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 11 as originally filed

Claims Numbers

1 22 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/EP 02/14674

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

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

☐ the entire international application

☒ claims Nos 1 3-5 7 16 18 20 (partially)

because:

☐ the said international application or the said claims Nos relate to the following subject matter which does not require an international preliminary examination (specify)

☒ the description claims or drawings *(indicate particular elements below)* or said claims Nos 1 3-5 7 16 18,20 (partially) are so unclear that no meaningful opinion could be formed *(specify)*:

see separate sheet

☐ 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	2 6 12,17 22
	No	Claims	1,3-5 7 11 13-16
Inventive step (IS)	Yes	Claims	17 19,21,22
	No	Claims	1 16,20
Industrial applicability (IA)	Yes	Claims	1-22
	No	Claims	

2 Citations and explanations

see separate sheet

III Re Item III

Non-establishment of Opinion

1 A search has only been performed in as far as the claims 1,3-5,7-16,18,20 are clear supported and disclosed (see ISA 210) Consequently only searched subject-matter is subject of an international preliminary examination (Rule 66 1(e) PCT)

V Re Item V

Reasoned statement under Rule 66 2(a)(ii) with regard to novelty, inventive step or industrial applicability, citations and explanations supporting such statement

2 Reference is made to the following documents

D1 WO 00 57857 A (YUHAN CORP) 5 October 2000 (2000-10-05)
D2 WO 00 10526 A (NOVARTIS ERFIND VERWALT GMBH NOVARTIS AG (CH), ZUEGER OTHMAR (CH)) 2 March 2000 (2000-03-02)

3 **NOVELTY** (Art 33(2) PCT)

3 1 Document D1 discloses a tablet for oral administration comprising 5 % (w/w) of the 5 HT4 agonist cisapride 77 % mannitol, 5% crospovidone as well as colloidal silicium dioxide, magnesium trisilicate and magnesium stearate (D1, p 6 l 5-9, p 6-7 ex 6, claims 1-3)

3 2 The present application does not meet the requirements of Article 33(2) PCT because the subject-matter of claims 1, 3-5, 7-11, 13-16 is not new

4 **INVENTIVE STEP** (Art 33(3) PCT)

4 1 The subject-matter of claims 1, 3-5, 7-11, 13-16 is not new and therefore not inventive

4 2 Document D2 is considered to represent the most relevant state of the art and discloses a solid pharmaceutical composition for oral administration comprising 3 %

(w/w) tegaserod 40 % crospovidone and 33 % lactose (D2, p 18-20, ex 2) The subject matter of claim 2 differs in that the diluent is present in an amount of 70 % to 90 % It further differs in that the amount of disintegrant is less than 15 % by weight (D2, claims 1, 2 6-11)

4 3 The problem to be solved by the present invention may therefore be regarded as providing an alternative solid pharmaceutical composition for tegaserod The proposed solution is the composition presented in claim 2

4 4 This solution cannot however be considered as involving an inventive step for the following reasons

4 4 1 The alleged commercial advantage (description page 1 3 paragraph) cannot support the case for inventive step since it has not been demonstrated that such commercial advantage is directly derivable from the technical features of the invention claimed in claims 2, 6, 12 and 20

4 4 2 The composition is merely one of several straightforward possibilities from which the skilled person would select, in accordance with circumstances without the exercise of inventive skill, in order to solve the problem posed

4 5 Claims 6 12 and 20 do not appear to contain any additional features which, in combination with the features of any claim to which they refer, involve an inventive step

4 6 In view of the above, the present application seems not meet the requirements of Article 33(3) PCT because the subject matter of claims 1-16 20 seems not to involve an inventive step

5 Certain defects

5 1 The present application provides support for only one compound, namely tegaserod, while the term "5-HT4 partial agonist" being an essential feature of the invention encompasses potentially a great number of compounds that cannot be identified without undue burden Furthermore, the present application does not provide instructions which are clear for an expert to determine what a "5-HT4 partial agonist" should be without undue burden and inventive skill There is no test or data provided

allowing to differentiate an antagonist from an agonist or a partial agonist of 5-HT4 receptors

Consequently, claims 1, 3 5 7 16, 18, 20 lack clarity and support according to Art 6 PCT

17 01 2004
4-32293A
Adrian Spillmann

OFFACT
PCT
EP02/14674

EATY

Corporate Intellectual Property
20. Okt. 2003
APPL | M/D | F/L | PS | Copy

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

PCT

To

Grubb Philip
NOVARTIS AG
Corporate Intellectual Property
Patent & Trademark Department
CH-4002 Basel
SUISSE

WRITTEN OPINION
(PCT Rule 66)

Date of mailing (day/month/year)	17.10.2003
Applicant's or agent's file reference: 4-32293A	REPLY DUE: within 3 month(s) from the above date of mailing

International application No	International filing date (day/month/year)	Priority date (day/month/year)
PCT/EP02/14674	20.12.2002	21.12.2001

International Patent Classification (IPC) or both national classification and IPC
A61K31/404

Applicant
NOVARTIS AG et al

1 This written opinion is the first drawn up by this International Preliminary Examining Authority

2. This opinion 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

3. The applicant is hereby invited to reply to this opinion.

When? See the time limit indicated above The applicant may before the expiration of that time limit, request this Authority to grant an extension see Rule 66.2(d)

How? By submitting a written reply accompanied where appropriate, by amendments, according to Rule 66.3
For the form and the language of the amendments, see Rules 66.8 and 66.9

Also For an additional opportunity to submit amendments, see Rule 66.4.
For the examiner's obligation to consider amendments and/or arguments, see Rule 66.4 bis.
For an informal communication with the examiner see Rule 66.6.

If no reply is filed the international preliminary examination report will be established on the basis of this opinion.

4 The final date by which the international preliminary examination report must be established according to Rule 69.2 is 21.04.2004

Name and mailing address of the international preliminary examining authority:
European Patent Office P.B. 5818 Patentlaan 2
NL-2280 HV Rijswijk Pays Bas
Tel. +31 70 340 2040 Tx: 31 651 epo nl
Fax: +31 70 340 3016

Authorized Officer
von Eggelkraut-Gotta

Formalities officer (incl. extension of time limits)
Janzing M
Telephone No. +31 70 340-4140

WRITTEN OPINION International application No PCT/EP02/14674

I Basis of the opinion

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 opinion as "originally filed")*

Description, Pages

1 11 as originally filed

Claims, Numbers

1-22 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)

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- ☐ furnished subsequently to this Authority in written form
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- ☐ the description pages
- ☐ the claims Nos
- ☐ the drawings sheets

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

6 Additional observations if necessary

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

WRITTEN PINION International application No. PCT/EP02/14674

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 and will not be examined in respect of

☐ the entire international application

☒ claims Nos 1 3-5 7 16 18 20 (partially)

because

☐ the said international application or the said claims Nos relate to the following subject matter which does not require an international preliminary examination (specify)

☒ the description claims or drawings *(indicate particular elements below)* or said claims Nos 1,3-5 7 16 18 20 (partially) are so unclear that no meaningful opinion could be formed *(specify)*

see separate sheet

☐ 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 written opinion cannot be drawn 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 Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability citations and explanations supporting such statement

1 Statement

Novelty (N)	Claims	1,3-5 7 11 13-16
Inventive step (IS)	Claims	1 16,20
Industrial applicability (IA)	Claims	

2. Citations and explanations

see separate sheet

III Re Item III

Non-establishment of Opinion

1 A search has only been performed in as far as the claims 1,3-5,7-16,18,20 are clear, supported and disclosed (see ISA 210) Consequently only searched subject-matter is subject of an international preliminary examination (Rule 66 1(e) PCT)

V Re Item V

Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

2 Reference is made to the following documents

D1 WO 00 57857 A (YUHAN CORP) 5 October 2000 (2000-10-05)
D2 WO 00 10526 A (NOVARTIS ERFIND VERWALT GMBH ,NOVARTIS AG (CH), ZUEGER OTHMAR (CH)) 2 March 2000 (2000-03-02)

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3 1 Document D1 discloses a tablet for oral administration comprising 5 % (w/w) of the 5-HT4 agonist cisapride, 77 % mannitol, 5% crospovidone, as well as colloidal silicium dioxide, magnesium trisilicate and magnesium stearate (D1, p 6, l 5-9, p 6-7, ex 6, claims 1-3)

3 2 The present application does not meet the requirements of Article 33(2) PCT because the subject-matter of claims 1, 3-5, 7-11, 13-16 is not new

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4 1 The subject-matter of claims 1, 3-5, 7-11, 13-16 is not new and therefore not inventive

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4 3 The problem to be solved by the present invention may therefore be regarded as providing an alternative solid pharmaceutical composition for tegaserod The proposed solution is the composition presented in claim 2

4 4 This solution cannot however be considered as involving an inventive step for the following reasons

4 4 1 The alleged commercial advantage (description, page 1, 3 paragraph) cannot support the case for inventive step, since it has not been demonstrated that such commercial advantage is directly derivable from the technical features of the invention claimed in claims 2, 6, 12 and 20

4 4 2 The composition is merely one of several straightforward possibilities from which the skilled person would select, in accordance with circumstances without the exercise of inventive skill, in order to solve the problem posed

4 5 Claims 6, 12 and 20 do not appear to contain any additional features which, in combination with the features of any claim to which they refer, involve an inventive step

4 6 In view of the above, the present application seems not meet the requirements of Article 33(3) PCT because the subject-matter of claims 1-16 20 seems not to involve an inventive step

5 **Certain defects**

5 1 The present application provides support for only one compound, namely tegaserod, while the term "5-HT4 partial agonist" being an essential feature of the invention encompasses potentially a great number of compounds that cannot be identified without undue burden Furthermore, the present application does not provide instructions which are clear for an expert to determine what a "5-HT4 partial agonist" should be without undue burden and inventive skill There is no test or data provided allowing to differentiate an antagonist from an agonist or a partial agonist of 5-HT4 receptors
Consequently, claims 1 3-5 7-16, 18, 20 lack clarity and support according to Art 6 PCT

5 2 If amendments are filed, it should be by way of replacement pages in the manner stipulated by Rule 66 8(a) PCT In particular, fair copies of the amendments should be filed preferably in triplicate Moreover, the applicant's attention is drawn to the fact that as a consequence of Rule 66 8(a) PCT the examiner is not permitted to carry out any amendments under the PCT procedure, however minor these may be

5 3 In order to facilitate the examination of the conformity of the amended application with the requirements of Article 34(2)(b) PCT, the applicant is requested to clearly identify the amendments carried out, no matter whether they concern amendments by addition, replacement or deletion, and to indicate the passages of the application as filed on which these amendments are based (see also Rule 66 8(a) PCT)

Corporate Intellectual Property
4 Feb 2003

PATENT COOPERATION TREATY

PCT/EP 02/14674

65

ASP

PCT

From the RECEIVING OFFICE

To:
Gros, Florent
NOVARTIS AG
Corporate Intellectual Property
Patent & Trademark Department
CH-4002 Basel
SUISSE

NOTIFICATION OF THE INTERNATIONAL APPLICATION NUMBER AND OF THE INTERNATIONAL FILING DATE

(PCT Rule 20.5(c))

Date of mailing *(day/month/year)*	11 02 2003
Applicant's or agent's file reference: 4-32293A	IMPORTANT NOTIFICATION

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/EP 02/ 14674 ✓	20/12/2002 ✓	21/12/2001 ✓

Applicant: NOVARTIS AG ✓

Title of the invention:

1 The applicant is hereby notified that the international application has been accorded the international application number and the international filing date indicated above

2. The applicant is further notified that the record copy of the international application was transmitted to the International Bureau on the above date of mailing

3 ☐ Other* _____

* The International Bureau monitors the transmittal of the record copy by the receiving Office and will notify the applicant (with Form PCT/IB/301) of its receipt. Should the record copy not have been received by the expiration of 14 months from the priority date the International Bureau will notify the applicant (Rule 22.1(c)).

Name and mailing address of the Receiving Office	Authorized officer
European Patent Office P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk Tel. (+31 70) 340-2040 Fax. (+31 70) 340-3016	F.J Hoorn SIS 07 PCT

Form PCT/RO/105 (July 1992)

6C

RAD 04-67463

MANTENIMIENTO DE PROTOCOLOS

|Numero 17398
|Fecha 16/04/1997
|Confendo NOVARTIS AG (NOVARTIS SA) (NOVARTIS INC)
|
|Pais CH SUIZA
|Ciudad 3 BASILEA
|Represent. S Sustituir S Desistir S
|No Radicacion 97 19953 Clase 0 Seev 0 Seac 0
|---

scncia	Codigo Ctr	Nombre
1	5376	ESCOBAR URIBE JIMENA
2	267	ESCOBAR URIBE IGNACIO

|
| Encontrados (1/1) registro(s)
+---

67

SUPERINDUSTRIA Y COMERCIO
Radicacion 04067463 0000000 Folios: 65
Fecha (AMD): 2004-07-15 16 10:08
Tramite 011 PCT-PATENT 379 FASE NACI 411 PRESENTAR
Dependencia 2020 DIVISION DE NUEVAS CREACIONES

REQUISITOS NECESARIOS PARA PRESENTACION Y AGILIZACION DEL TRAMITE

		Usuario	Radicador
PATENTE DE INVENCIÓN ✓	MODELO DE UTILIDAD	( )	( )
Indicacion de que se solicita la concesion 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		( )	( )
Representacion grafica o fotografica 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

Fecha

Industria y Comercio
SUPERINTENDENCIA

68

2020
Bogotá D C

Doctor
JIMENA ESCOBAR URIBE
Apoderado
NOVARTIS A G

Oficio N° 07401

ASUNTO		
	Radicación N°	04-67463
	Solicitud internacional	PCT/EP2002/14674
	Fecha inicio fase nacional	21/07/2004
	Trámite	011
	Evento	379
	Actuación	430
	Folios	001

Como resultado del examen de forma realizado con fundamento el 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 Unica de la Superintendencia de Industria y Comercio se le comunica que

☐ La solicitud no contiene la copia del documento en que consta la cesión del derecho a la 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 Unica N° 10 de 2001

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

El anterior requerimiento fue notificado por fijación en lista de fecha 06 AGO 2004

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