



No. 06-074307- -00003-0000

Fecha: 2008-01-09 15:26:44 Dep. 2020 NUECREACIONE
Tra. 11 PATENTEIYII Eve: 379 FASENACIONALII
Act. 538 PETICION Folios: 2

Señores

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO

DIVISION DE NUEVAS CREACIONES

E. _____ S. _____ D. _____

Ref: Expediente No. 06-074.307

Solicitud de patente de invención titulada:

“COMBINACIÓN DE VORICONAZOL Y UN ANTIFÚNGICO INHIBIDOR DE LA CYP2C19.”.

Solicitante: PFIZER INC.

SOLICITUD DE EXAMEN DE PATENTABILIDAD SEGÚN
EL ARTÍCULO 44 DE LA DECISION 486, GACETA No. 583

CARLOS R. OLARTE, mayor de edad y vecino de Bogotá, D.C., identificado tal como aparece al pie de mi firma, en mi condición de apoderado del solicitante, respetuosamente me permito solicitar que se examine si la invención reúne los requisitos de patentabilidad previstos en la misma, dando cumplimiento a lo establecido en el artículo 44 de la Decisión 486 de la comisión de la Comunidad Andina. Adjunto recibo por el monto de \$210.000 pesos para cubrir la tasa correspondiente, según la Resolución 44372 del año 2007.

Atentamente,

CARLOS R. OLARTE
C.C. 79.782.747 de Bogotá
T.P. 74.295

Anexo: Recibo por \$210.000 pesos

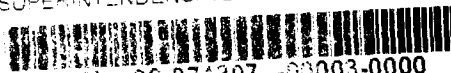
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SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO

NIT : 800176089-2

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO



No. 06-074307-00003-0000

RECIBO OFICIAL DE CAJA : 08 - 2,719
FECHA : ENERO 9 DE 2008

Fecha: 01-09-2008 15:28:44 Dep. 2020 NUECREACIONE
Tib. 11 PATENTEYS Evt. 379 FASENACIONALII
Act. 538 PETICION Folios 2

***** CONSIGNACION *****

DEPOSITANTE	TIPO PAGO	BANCO	CUENTA	No. PAGO	FECHA PGO	Vr. PAGO
ORTE RAISBEK	CONSIGNACION	BANCO DE BOGOTA	062754387	106793	09/01/2008	15,878,000.00

***** CONCEPTO *****

CANT.	RENTISTICO	CONCEPTO	TOTAL CONCEPTO
1	50005-01-01	SOLICITUDES	
		114 PTC CAP-II EXAMEN DE PATENTIBILID	210,000.00
		TOTAL :	\$ 210,000.00

SON: DOSCIENTOS DIEZ MIL PESOS

RESPONSABLE :

RECIBO DE CAJA APLICADO AL EXPEDIENTE No.

DIVISIÓN DE NUEVAS CREACIONES

RADICACIÓN EXPEDIENTE No. 06-74307

EL EXTRACTO DE LA PRESENTE SOLICITUD DE **PATENTE DE INVENCION**

FUE PUBLICADO EN LA GACETA DE PROPIEDAD INDUSTRIAL No **583** DE

FECHA **18 DE DICIEMBRE DE 2007** EL TÉRMINO HÁBIL SEÑALADO POR LA

LEY EXPIRA EL **14 DE MARZO DE 2008**

NOTA: Dentro del plazo de los seis (6) meses siguientes a partir de la fecha de publicación en la gaceta de Propiedad Industrial, deberá solicitar y cancelar el examen de patentabilidad so pena de que la solicitud caiga en abandono, de acuerdo con lo establecido en el Artículo 44 de la Decisión 486/2000.

SE PRESENTARON OPOSICIONES POR PARTE DE TERCEROS.

SI _____

NO X

Introduction: Systemic mycosis due to the non-*Candida* species has emerged as a serious opportunistic complication in transplant recipients.

Methods and results: During 01, 1993, to 01, 2001, in 48 (65.8%) patients a non-*Candida* fungal species was isolated from central venous blood culture specimen. Median age in 36 male and 12 female was 31, $\pm$ s.d 16.6 y. In 35, partially matched (19 had 3 human leukocyte antigen (HLA)-antigen mismatched) marrow graft from a related donor (PMRD), 5 matched, unrelated donor (MUD), 3 matched, sibling donor (MSD), and in 5, autologous transplantation was performed. All patients with PMRD and 4 MUD underwent T-cell depleted transplantation. Acute leukemia was present in 21 (ALL 11; AML 10), chronic leukemia in 12 (CML 11; CLL 1), lymphoma in six (NHL 4; HD 2), MDS in 4, multiple myeloma 2 and 12 had other conditions. And 48.9% had profound neutropenia ($ANC \leq 100$ cells/L). Nine patients were receiving immunosuppressive therapy for acute graft-versus-host disease. The incidence of non-*Candida* fungemia in PMRD was 9.2% (35/379); MUD 14.7% (5/34); MSD 4.9% (3/61), and in recipients of autologous graft was 4.3% (5/115). In 3 individuals, more than one fungal species was isolated during the same hospitalization. Among 55 episodes, 6 *Aspergillus* spp. (1 *A. fumigatus*, 2 *A. niger*, 1 *A. flavus*), 3 Dematiaceous molds (1 *Alternaria*, 1 *Curvularia*), and 2 *Trichosporon beigelii* were treated as systemic fungal infection. Whereas, 20 *Penicillium*, 8 *Cladosporium*, 7 *Geotrichum candidum*, 3 *Chrysosporium*, 2 *Aureobasidium*, and one episode each of *Epicoecum*, *Paecilomyces*, *Sporobolomyces*, and *Saccharomyces cerevisiae* were considered non-pathogenic. In 7 patients (14.6%) death was attributed to fungal infection. A patient with *Aspergillus non-fumigatus* spp. succumbed to hematogenous dissemination 11 days after the initial episode. In the non-pathogen group, 3 patients with *Penicillium*, and a single patient with *G. candidum*, *Chrysosporium*, and *Epicoecum* each (16.2%) died within median $9.5 \pm$ s.d 10 days after the initial positive fungal blood culture.

Conclusions: Systemic infection due to pathogenic non *Candida* species had low-attributable mortality (9%) in this setting. Molds with low intrinsic virulence, and frequent environmental contaminants may occasionally lead to fatal systemic infection in patients at risk.

Endogenous *Aspergillus* endophthalmitis:

Report of three cases and review of the literature

J. Riddell IV, S. A. McNeil, T. M. Johnson, S. F. Bradley, P. H. Kazanjian, and C. A. Kauffman
Division of Infectious Diseases, Department of Internal Medicine, Veterans Affairs Ann Arbor Healthcare System, and University of Michigan Medical School, Ann Arbor, Michigan, USA

We present three cases of *Aspergillus* endogenous endophthalmitis in immunocompromised patients. Case 1 is a 56 year old man with emphysema who developed endogenous *Aspergillus* endophthalmitis after brief treatment with corticosteroids. The eye required enucleation. Case 2 is a 57 year old woman with bronchiolitis obliterans organizing pneumonia (BOOP) treated with corticosteroids who had *Aspergillus* endocarditis and endogenous *Aspergillus* endophthalmitis. She died of a cerebral hemorrhage. Case 3 is a 73 year old man with BOOP on corticosteroids who developed invasive pulmonary aspergillosis with dissemination to the eye. In an effort to define better ways to identify patients at risk for *Aspergillus* endogenous endophthalmitis and to determine optimal diagnostic and treatment strategies, we reviewed 86 cases of endogenous *Aspergillus* endophthalmitis reported since 1949. Predisposing medical conditions were present in 94%. Immunosuppression including organ transplantation, steroids, or malignancy was present in 49%, intravenous drug use was noted in 27%, and underlying lung disease in 17%. Pars plana vitrectomy appears to be the highest-yield procedure for establishing the diagnosis. 90% of vitrectomy specimens yielded *Aspergillus* compared with 54% of vitreous aspirates. *A. fumigatus* caused infection in 51% and *A. flavus* in 26%. Outcomes were generally poor. Only 7 of the 84 patients (8%) with posterior chamber involvement regained useful vision. Treatment with intravenous amphotericin B combined with intravitreal injection of amphotericin B and vitrectomy appears to be the most efficacious therapy. Six of 7 patients reported to have regained useful vision had received such treatment. *Aspergillus* endogenous endophthalmitis is difficult to diagnose and treat effectively. The best strategy appears to include diagnostic vitrectomy in high-risk individuals combined with intravitreal and systemic amphotericin B for patients in whom *Aspergillus* spp. are identified.

In vitro evaluation of voriconazole in combination with antifungals

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¹Center for Medical Mycology/Mycology Reference Laboratory, Department of Dermatology, University Hospitals of Cleveland and Case Western Reserve University, 11100 Euclid Avenue, Cleveland, OH 44106-5028, ²Pfizer Pharmaceuticals Group, NY, NY 10017-5755

Background: The search for safe, effective treatment of invasive fungal infections has yielded novel antifungals, including the triazole voriconazole (Pfizer), liposomal preparations of amphotericin such as Abelcet (Liposome), the echinocandin micafungin (FK) (Fujisawa) and the pneumocandin caspofungin (MK) (Merck). These new antifungals are active against pathogenic

fungi, yet less toxic than amphotericin B. In this study, the effects of combining voriconazole (VOR) with amphotericin B (AM), Abelcet (AB), 5-fluorocytosine (5-FC), fluconazole (FLU), FK463, and MK0991 were investigated.

Methods: The checkerboard combination test method was used to determine the synergistic, additive, indifferent, or antagonistic interactions effect on minimum inhibitory concentration (MIC) values. Two antifungal agents are serially diluted in a desired medium to produce 11 concentrations of the drugs under investigation. The range is chosen to include achievable serum levels of the drugs. The two antifungals are then combined into wells of a microtiter plate so that the concentration of one drug increases as that of the other also increases. Two rows consisting of serial dilutions of each individual drug are included for comparison. Yeast isolates tested include 3 strains each of *Candida albicans*, *Candida glabrata*, *Candida krusei*, *Candida parapsilosis*, *Candida tropicalis*, and *Cryptococcus neoformans*. Both fluconazole-susceptible and resistant strains were included.

Results: All of the isolates tested were susceptible to VOR, AB, and AM. All *Candida* species were susceptible to MK and FK, while all *Cryptococcus* strains were resistant to these two antifungals. Susceptibility to 5-FC and FLU varied. Our data shows that VOR/MK combinations were 33% additive and 67% indifferent. VOR/FK combinations were 11% synergistic, 11% additive, and 78% indifferent. VOR/FLU combinations were 39% additive and 61% indifferent. VOR/AB combinations were 22% additive and 72% indifferent. VOR/AM combinations were 22% additive and 78% indifferent. Finally, VOR/5-FC combinations were 11% additive and 89% indifferent. Importantly, no antagonism was noted.

Conclusion: Overall, 25.9% of all VOR combinations against these yeast isolates were either additive or synergistic, while 74.1% were indifferent, indicating minimal lowering of the individual MIC's. Interactions were strain specific, suggesting that it is necessary to test combinations with each isolate. This study points to the need for expanded combination testing of VOR. Correlation with clinical outcome remains to be determined.

Antifungal activity of voriconazole alone and in two-drug combination with amphotericin B in a guinea pig pulmonary aspergillosis model

P. H. Chandrasekar, J. L. Cutright, L. Ganesan and E. K. Manavathu

Division of Infectious Diseases, Department of Medicine, Wayne State University, Detroit, Michigan, USA

Previous in vitro studies had shown that voriconazole (VCZ) in two-drug combination with conventional and lipid formulations of amphotericin B (AMB) produced

indifferent interaction against *Aspergillus fumigatus*. To confirm our in vitro finding in an animal model, we investigated the susceptibility of *A. fumigatus* 73355 (ATCC 208996), highly susceptible to VCZ (MIC 0.25 µg/mL) and AMB (MIC 0.5 µg/mL), to two-drug combination of AMB with VCZ using a guinea pig pulmonary aspergillosis model. Six-to-eight week old guinea pigs (350±50 gram) were made neutropenic by three successive injections of cyclophosphamide (100 mg/kg) on day -3, -1 and 1 where day 0 was the day of infection. The immunosuppressed animals (14 animals/group) were challenged with 1×10^7 conidia/guinea pig by intratracheal injection. Antifungal treatment was initiated on day 0 (AMB 1 mg/kg/day (i.p.), VCZ 10 mg/kg/b.i.d. (p.o.) and AMB 1 mg/kg/day + VCZ 10 mg/kg/b.i.d.) and continued for 7 days. The effectiveness of the antifungal treatments with VCZ or AMB or in two-drug combination was evaluated by the survival and the fungal burden in the lungs of infected animals. The mean survival of animals infected but not treated (controls) was 3.7 ± 2.5 days whereas those of the AMB, VCZ and AMB+VCZ treated groups were 5.3 ± 1.9 , 5.5 ± 2.1 and 5.6 ± 1.7 days, respectively. The fungal burden in the lungs of infected animals treated with antifungal drugs was significantly lower than that obtained for the untreated (109733 ± 33877 CFU/lungs) group. The fungal burden of the VCZ-treated (985 ± 306 CFU/lung) group was significantly lower than that obtained for the AMB-treated (8191 ± 1800 CFU/lung) group whereas no significant difference in the fungal burden was obtained for the groups treated with VCZ alone (985 ± 306 CFU/lung) and VCZ+AMB (813 ± 298 CFU/lung). We found no antagonism between VCZ and AMB. The results obtained in the guinea pig pulmonary aspergillosis model showed good agreement with our previous in vitro results suggesting indifferent interaction of VCZ in combination with AMB against *A. fumigatus*.

Rhinocerebral zygomycosis – diagnostic dilemma for emergency physician: is reduction in morbidity and mortality possible in this rare but deadly disease?

A. Guleri, S. Samavedam, G. D. Corcoran

Department of Microbiology, Western Infirmary, Glasgow, UK

Rhinocerebral zygomycosis (RCZ) or mucormycosis is a rare, invasive, rapidly progressive opportunistic infection caused by ubiquitous fungi of the order mucorales. It usually occurs in diabetics or immunocompromised patients. Disease is characterized by vascular invasion, thrombosis, and tissue necrosis.

The emergency physician will typically see patients with RCZ in its earliest stages masquerading as a variety of other less serious diseases. The key markers like necrotic patch on hard palate, nasal septum or turbinate, marked facial pain, and cellulites with marked eye and neurological signs may present late in disease.

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(19) World Intellectual Property Organization
International Bureau



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10 May 2002 (10.05.2002)

PCT

(10) International Publication Number
WO 02/36203 A2

- (51) International Patent Classification⁷: A61P 31/10, IL 60657 (US). XUAN, Yongshi [CN/US]; 332 West Cermak Road, Apartment 1B, Chicago, IL 60616 (US).
A61K 45/06
- (21) International Application Number: PCT/US01/46938 (74) Agent: HIGHLANDER, Steven, L.; Fulbright & Jaworski L.L.P., 600 Congress Avenue, Suite 2400, Austin, TX 78701 (US).
- (22) International Filing Date: 2 November 2001 (02.11.2001)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data: 60/245,548 2 November 2000 (02.11.2000) US
- (71) Applicant (for all designated States except US): INFLUX, INC. [US/US]; 2201 West Campbell Park Drive, Suite 116/118, Chicago, IL 60612 (US).
- (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, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.
- (72) Inventors; and
- (75) Inventors/Applicants (for US only): MARKHAM, Penelope, N. [IE/US]; 631 N. Cuyler Avenue, Oak Park, IL 60302 (US). CRICH, David [GB/US]; 800 South Wells, Apartment 1040, Chicago, IL 60607 (US). JABER, Mohamad-Rami [LB/US]; 962 Ontario Drive, Romeoville, IL 60446 (US). JOHNSON, Michael, E. [US/US]; 575 Elm Street, Winnetka, IL 60093-2616 (US). MULHEARN, Debbie, C. [US/US]; 514 Kipling Court, Wheaton, IL 60187 (US). NEYFAKH, Alexander, A. [US/US]; 538 W. Belmont Ave., Apartment 3A, Oak Park, IL 60454 (US).
- (84) Designated States (regional): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).
- Published:**
— without international search report and to be republished upon receipt of that report
- 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 02/36203 A2

(54) Title: ANTIFUNGAL COMPOUNDS AND USES THEREFOR

(57) Abstract: The present invention provides compounds which, when used in combination with antifungal azoles, offer enhanced antifungal therapy. More particularly, these compositions (including carbazoles or triptycenes) can convert fungistatic drugs such as fluconazole into fungicidal drugs.

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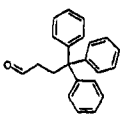
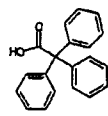
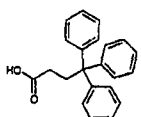
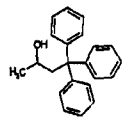
WO 02/36203

PCT/US01/46938

A further series of compounds that the inventors investigated were derived by replacing the triptycene moiety by the triphenylmethyl group. Such compounds were obtained *inter alia* by the action of Grignard reagents on triphenylmethyl chloride (Nesemeyanov and Perevalov, 1954). The scheme below gives the example of addition of alkylmagnesium bromide to triphenylmethyl chloride and illustrates how the ensuing alkene may be converted into any of the desired head groups. Higher and lower homologs are readily accessible by use of the appropriate Grignard reagent. A list of specifically contemplated compounds is shown in Table 3.

Table 3. Examples of Specific Triphenyl Compounds

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ID	Structure	ID	Structure
INF802-1439		78,120-5	
INF802-1440		INF802-1430-1	

V. Additional Antifungal Treatments

In addition, the present invention also provides for new multi-drug therapy regimens. While many fungal infections may be effectively treated by a combination of an azole and a potentiating agent, comprising a carbazole analog or a triptycene, other infections may be treated more effectively using one or more additional agents. Such multi-drug combinations may reduce the amount of drug needed (and hence the side effects ensuing therefrom), may more quickly limit or eliminate the infection, and may more effectively treat, or even prevent, drug resistant fungi.

Traditional antifungal treatments that are suitable for use in combination with the present invention include polyenes, amphotericin B, filipin, nystatin, allylamines (terbinafine and naftifine), echinocandins (caspofungin or MK-0991, V-echinocandin, FK643), sordarins, azosordarins, flucytosine and griseofulvin. One or more of these agents may be combined with the azole + potentiator before, during or after that treatment.

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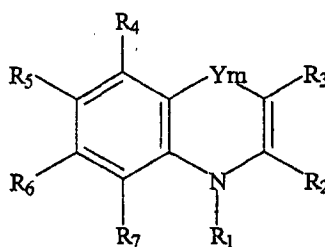
WO 02/36203

PCT/US01/46938

CLAIMS

We claim:

1. A method for enhancing the antifungal action of azoles comprising contacting a fungal cell and an azole with a second agent comprising a triptycene, a triphenyl, a compound having the structure of formula (I'):



or a pharmaceutically acceptable salt or hydrate thereof, wherein:

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Y is S or O;

m is 0 or 1;

R₁ is an $-(CH_2)_nCO_2R_8$, $-(CH_2)_nCHO$, $-(CH_2)_nOH$, $-(CH_2)_nCHOHCH_3$,

$(CH_2)_nCHOHCH_2N(R_8)_2$, $-(CH_2)_nCHOHCH_2OH$, $-(CH_2)_nC(OH)_2CX_3$,

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$-(CH_2)_nCHOHCX_3$, 3-(4-styryl-piperazin-1-yl)propan-2-ol, allyl, benzyl, H, or an alkyl chain up to 4 carbons; wherein

X is a halogen;

R₈ is a H, or an alkyl chain up to 4 carbons;

n is 0, 1, 2, 3, 4, or 5;

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R₂ is a hydrogen, a halogen, acetamido, amino, pyridyl, a halo substituted pyridyl, a pyridyl salt, benzyl, 1- or 2-naphthyl, styryl, phenethyl, furanyl, phenyl, a branched or straight-chained alkyl group up to 4 carbons, an *ortho*, *meta*, or *para* toluoyl, or a halo- or acetamido-substituted phenyl group;

R₃ is a hydrogen, a halogen, acetamido, amino, pyridyl, a halo substituted pyridyl, a pyridyl salt, benzyl, 1- or 2-naphthyl, styryl, phenethyl, furanyl, phenyl, a branched or

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**SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO
DIRECCIÓN DE NUEVAS CREACIONES**

2020
Bogotá, D.C.,

Abogado:
CARLOS REINALDO OLARTE GARCIA

ASUNTO:	Radicación No.	06 07 4307
	Trámite	002
	Evento	379
	Actuación	430
	Oficio	1410
	Folios	

Como resultado del Examen de Fondo, realizado con fundamento en el artículo 45 de la Decisión 486 de la Comisión de la Comunidad Andina, se comunica:

Documentos estudiados:

Descripción:	Folios 49 a 70 como se radicó inicialmente.
Reivindicaciones:	Folios 71 a 72 como se radicó inicialmente.
Prioridad:	UK 0402491.5 (2004-02-04); US 60/545.663 (2004-02-17)

Objeto de la Invención

Título de la invención: "Combinación de voriconazol y un antifúngico inhibidor de la CYP2C19."

Problema Técnico Planteado: "Necesidad de de una terapia de Voriconazol que elimine o reduzca la variabilidad entre sujetos, que además permita una disminución de la dosis administrada de voriconazol, y mediante la cual sea posible una disminución del aclaramiento del fármaco para administrara solamente le fármaco una vez al día."

Solución: "Proveer una combinación terapéutica que comprende voriconazol y un antifúngico inhibidor de CYP2C19 en cantidades o relaciones en peso específicas"

IPC: A61K 31/4196 AC; A61K 31/506 AC; A61P 31/0

Excepciones a la Patentabilidad (Art 20 D 486 literal d)

Las reivindicación 15 se refiere a método de tratamiento, por lo cual deben ser retirada del capítulo reivindicatorio.

Reivindicaciones relativas a un uso o a un segundo uso (Art 14 y 21 D 486)

La reivindicación 14 se refiere al uso de las combinaciones reclamadas, debe ser retirada del capítulo reivindicatorio.

Análisis de la Solicitud de Patente

Reivindicaciones (Art 30 D 486, Art 22 PCT)

Claridad y concisión: La reivindicación 1 reclama la combinación de voriconazol con un antifúngico inhibidor de CYP2C19, el cual no es definido clara ni concisamente y lo cual le concede un alcance demasiado extenso, ya que no está ni siquiera ha sido delimitado por un característica estructural, y de esta forma la combinación podría tener muchas posibilidades que ni siquiera han sido parte del estudio realizado por el solicitante.

Ya que el solicitante exclusivamente presenta sustento acerca de las combinaciones de voriconazol con Fluconazol, la materia a reclamar no podría llegar a incluir otros agentes antifúngicos diferentes.

Análisis de Unidad de Invención (Art 25 D 486)

Las reivindicaciones 10 y 11 se refieren a un kit que comprende varios recipientes separados para depositar voriconazol y un antifúngico. Dado que los componentes del mismo (frasco, composición, empaque, instrucciones) pertenecen a diferentes campos técnicos de manera que no dan cabida al principio de unidad de invención por lo tanto no se considera materia patentable.

Determinación del Estado de la Técnica

El Estado de la Técnica se determinó con base en la fecha de prioridad 2004-02-04 y se encontraron los siguientes documentos que anticipan el objeto de esta solicitud:

Item	Documento	Título	Fecha de Publicación
D1	<i>International journal of infectious diseases. Vol.6</i>	<i>In vitro evaluation of voriconazole in combination with antifungals</i>	2002
D2	WO2002/036203	<i>Antifungal compounds and uses thereof</i>	May 10, 2002

Análisis de Patentabilidad (Art 14 D486)

Nivel Inventivo (Art18 D486)

La reivindicación 1 dice: Una combinación terapéutica que comprende voriconazol y un antifúngico inhibidor de la CYP2C19, en la que el voriconazol está presente en una cantidad de alrededor de 5 a alrededor de 600 mg y el antifúngico inhibidor de la CYP2C19 está presente en una cantidad de alrededor de 5 a alrededor de 500 mg.

D1 revela un estudio de seguridad y efectividad para el tratamiento de infecciones invasivas por hongos, en el cual se determina la actividad sinérgica que existe entre Voriconazo y otros antifúngicos (página 2S50). Se revela específicamente la combinación Voriconazol y Fluconazol(página 2S51) y que esta mezcla es sinérgica.

La solicitud se diferencia de D1 en la proporción que se define para cada uno de los antifúngicos, y en que este no presenta kit o composiciones farmacéuticas para la administración de la combinación.

El Efecto Técnico que logra la diferencia NO es inesperado pues ya se conocía que la combinación de estos dos azoles es sinérgica.

El Problema Técnico Objetivo de esta solicitud es la necesidad de tratamientos mejorados de voriconazol.

D2 revela combinaciones entre agentes antifúngicos que muestran una actividad antifúngica mejorada. En el numeral V (página 31), se revelan un tratamientos adicionales antifúngicos, que se refieren a un régimen multimedicamentoso en el cual un compuesto del tipo azol puede estar en combinación con otro tipo de antifúngicos, lo cual le permite controlar a las infecciones por hongos, y a su vez revela las composiciones farmacéuticas para la administración de las combinaciones.

El experto en la materia habría sido sugerido por D2 para diseñar una formulación que contenga las combinaciones sinérgicas de voriconazol y fluconazol para el tratamiento de enfermedades por hongos presentadas por D1, para llegar al resultado de la presente solicitud.

Se concluye que las reivindicaciones independientes 1 a 13 no poseen nivel inventivo.

Conclusión

Los requisitos de Patentabilidad de la presente Solicitud se encuentran afectados así:

Nº	Documento	Reivindicaciones afectadas	Requisito que afecta
D1	Artículo	1-13	Nivel inventivo
D2	WO2002/036203	1-13	Nivel inventivo

En cumplimiento del artículo 45 de la Decisión 486 de la Comisión de la Comunidad Andina, se le indica que debe dar respuesta dentro del término de 60 días contados a partir de la fecha de notificación de la presente comunicación. En caso de no dar respuesta al presente requerimiento, o si a pesar de la respuesta subsistieran los impedimentos para la concesión, se denegará la patente.

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

ALIX CARMENZA CÉSPEDES DE VERGEL
Directora de Nuevas Creaciones (C)

El anterior requerimiento fue notificado por fijación en lista, de fecha
05.10.2010

CONCEPTO TECNICO NUMERO: 4368	EXAMINADOR TÉCNICO Código:202092
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