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Señor

SUPERINTENDENTE DE INDUSTRIA Y COMERCIO
DIVISION DE NUEVAS CREACIONES

E. S. D.

Re P1.-PHARMACIA & UPJOHN COMPANY.-Solicitud de Patente de Invención para "MEZCLA DE LINEZOLID Y OTROS AGENTES ANTIBACTERIANOS".-Clase A.61 -Expediente número 00-083 924.

1 Me refiero a mi solicitud de 3 de Noviembre de 2000 y al auto dictado por ese Despacho notificado por Estado el 30 de Noviembre del mismo año

2 Anexas me permito presentar a usted

(a) Copia auténtica debidamente certificada de la solicitud de patente presentada para el invento arriba nombrado respecto de la cual reclamo prioridad, a saber la solicitud estadinense número 60/163,990 de 8 de Noviembre de 1999, junto con su traducción oficial correspondiente a las legalizaciones y reivindicaciones, y

(b) Copia debidamente autenticada por el Notario Sexto del Circulo de Bogotá de los documentos que acreditan la calidad de traductor oficial de la señora María Mercedes Uncochea, quien elaboró la traducción de la solicitud estadinense numero 60/163,990, respecto de la cual se reivindica prioridad en el presente caso

3 Ruego a usted tomar atenta nota de lo anterior y proceder de conformidad

Señor Superntendente,

JOSE ANTONIO LLOREDA
TP 10 784
Código 231

REPUBLICA DE COLOMBIA
MINISTERIO DE RELACIONES EXTERIORES

CERTIFICACION

Se hace constar que el Señor(a) MARIA MERCEDES URICOECHEA TORRES

se encuentra debidamente registrado(a) ante el Ministerio de Relaciones

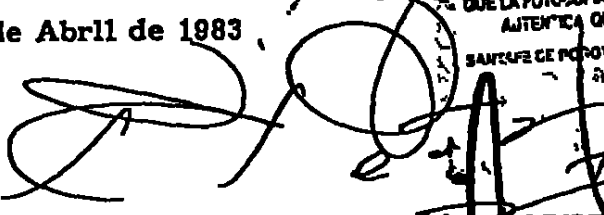
Exteriores, como traductor e interprete oficial para los idiomas _____

Inglés - Español - Inglés según resolución N° 10607

de fecha 31 de Diciembre de 1981 del Ministerio de Justicia

Se expide a los 6 días del mes de Abril de 1983

Atentamente,


RAFAEL HUMBERTO PEÑA FLORES

JEFE DE NEGOCIOS GENERALES

COMO NOTARIO EN CARGO
DE SANTAFE DE BOGOTA
HAGO CONSTAR
QUE LA FOTOCOPIA CONCORDA CON LA FOTOCOPIA
AUTENTICA QUE HE TENIDO A LA VISTA
SANTAFE DE BOGOTA
16 AGO. 1998

COMO NOTARIO EN CARGO
DE SANTAFE DE BOGOTA
HAGO CONSTAR
QUE LA FOTOCOPIA CONCORDA CON LA FOTOCOPIA
AUTENTICA QUE HE TENIDO A LA VISTA
SANTAFE DE BOGOTA
15 ABR. 2000
PABLO MENDEZ BARRAJAS

COMO NOTARIO EN CARGO
DE SANTAFE DE BOGOTA
HAGO CONSTAR
QUE LA FOTOCOPIA CONCORDA CON LA FOTOCOPIA
AUTENTICA QUE HE TENIDO A LA VISTA
SANTAFE DE BOGOTA
29 JUL 1989
JUAN MARCEL BUTERO MEJIA
NOTARIO

16 JUN 1998

COMO NOTARIO EN CARGO
DE SANTAFE DE BOGOTA
HAGO CONSTAR
QUE LA FOTOCOPIA CONCORDA CON LA FOTOCOPIA
AUTENTICA QUE HE TENIDO A LA VISTA
SANTAFE DE BOGOTA
24 NOV 1998

Pharmacia
6293.1
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ESTADOS UNIDOS DE AMÉRICA

A TODOS A QUIENES LLEGUE EL PRESENTE:

DEPARTAMENTO DE COMERCIO DE LOS ESTADOS UNIDOS

Oficina de Marcas y Patentes

10 de octubre de 2000.

LA PRESENTE CERTIFICA QUE LA ADJUNTA ES UNA COPIA TOMADA DE LOS REGISTROS DE LA OFICINA DE MARCAS Y PATENTES DE LOS ESTADOS UNIDOS, DE LOS DOCUMENTOS DE LA SOLICITUD DE PATENTE ABAJO IDENTIFICADA Y LA CUAL CUMPLE CON LOS REQUISITOS PARA QUE LE SEA CONFERIDA UNA FECHA DE RADICACIÓN SEGÚN 35 USC 111.

NUMERO DE SOLICITUD 60/163.990

FECHA DE RADICACIÓN: 08 de noviembre de 1999

Por Autoridad del

COMISIONADO DE MARCAS Y PATENTES

(FIRMA P.R. GRANT

Oficial de Certificaciones

(SELLO DORADO DE OBLEA)

Maria Mercedes Uribech
R.S. No. 11.07
Traductora Juramentada

Urb. Uribech

CERTIFICACION BAJO 37 CFR § 1.10**CERTIFICADO DE CORREO No. EM177639035 US**

Certifico que esta Remisión de Nueva Solicitud y los documentos que en ella se refieren como adjuntos son depositados en el Servicio Postal de lo EE.UU. el 12 de octubre de 1999 en un sobre como "Oficina Postal al Destinatario" bajo el rótulo de correo No. EM177639035 US y dirigido al Comisionado Asistente de Patentes, Washington, D.C. 20231.

(FIRMA) JULIE K. LYONS - Asistente

CUBIERTA SOLICITUD PROVISIONAL

La presente es una solicitud para la radicación de UNA SOLICITUD PROVISIONAL bajo 37 CFR § 1.53 (c). La Solicitud se titula Mezcla de Linezolid y otros Agentes Antibacterianos. Nuestro Caso No. 6293 y consta de:

8 páginas de Especificación

3 páginas de Reivindicaciones

1 página de Resumen

[x] El/los nombre(s) y residencia(s) del(os) inventor(es) se indican en la Hoja de Información del Inventor adjunta.

AUTORIZACION DE CUENTA DE DEPÓSITO. Sírvanse cargar a mi Cuenta de depósito No. 21-0718 el monto total de la comisión de radicación de la Solicitud Provisional para una compañía grande (US\$150.00) o la suma mayor o menor que el Comisionado requiera.

Por la presente, la compañía suscrita solicita que toda la correspondencia y comunicaciones telefónicas relacionadas con esta solicitud sean dirigidas a la

Maria Mercedes Mendez
P.O. Box 1000
Toluca, Mexico

GA.
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persona que firma este documento a la dirección y teléfono que se indican a continuación.

Respetuosamente,

Bruce Stein, Abogado
Registro No. 27,231

fecha: 99-11-08

Pharmacia & Upjohn Company
Global Intellectual Property
301 Henrietta Street
Kalamazoo, Michigan 49001

Tel: (616) 833-1127 o (616) 833-9500
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Documentos adjuntos:

- ☒ Solicitud de patente
- ☒ Hoja de Información del Inventor

Maria Mercedes Urzúa
Ces. No. 10507 A. J. Urzúa
Traductora Jurasada

Maria Mercedes

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MEZCLA DE LINEZOLID Y OTROS AGENTES ANTIBACTERIANOS
REFERENCIA A SOLICITUDES RELACIONADAS

REIVINDICACIONES:

1. Una composición farmacéutica acuosa para administración IV de linezolid y uno o más agentes antibacterianos seleccionados del grupo compuesto por aminoglicosidas, cefalosporinas, aztreonam, quinolonas y penicilinas, y sales farmacéuticamente aceptables de lo mismo donde existan.
2. Una composición farmacéutica acuosa según la reivindicación 1, donde el agente antibacteriano es seleccionado del grupo compuesto por gentamicina, tobramicina, aztreonam, cefazolin, ceftazidina, piperacilina, ciprofloxacina, ofloxacina, levofloxacina.
3. Una composición farmacéutica acuosa según la reivindicación 1, donde el agente antibacteriano es gentamicina.
4. Una composición farmacéutica acuosa según la reivindicación 1, donde el agente antibacteriano es tobramicina.
5. Una composición farmacéutica acuosa según la reivindicación 1, donde el agente antibacteriano es aztreonam.

6. Una composición farmacéutica acuosa según la reivindicación 1, donde el agente antibacteriano es cefazolina.
7. Una composición farmacéutica acuosa según la reivindicación 1, donde el agente antibacteriano es ceftazidima.
8. Una composición farmacéutica acuosa según la reivindicación 1, donde el agente antibacteriano es piperacilina.
9. Una composición farmacéutica acuosa según la reivindicación 1, donde el agente antibacteriano es ciprofloxacina.
10. Una composición farmacéutica acuosa según la reivindicación 1, donde el agente antibacteriano es ofloxacina.
11. Una composición farmacéutica acuosa según la reivindicación 1, donde el agente antibacteriano es levofloxacina.
12. Una composición farmacéutica acuosa según la reivindicación 1, donde la composición acuosa es una solución.
13. Una composición farmacéutica acuosa según la reivindicación 1, donde la solución es estéril.
14. Una composición farmacéutica acuosa según la reivindicación 1, donde la mezcla linezolid-agente antibacteriano se hace combinando una solución acuosa de linezolid y una solución acuosa del agente antibacteriano.

15. Una composición farmacéutica acuosa según la reivindicación 1, donde la mezcla linezolid-agente antibacteriano se hace combinando una solución acuosa de linezolid y un agente antibacteriano sólido.
16. Una composición farmacéutica acuosa según la reivindicación 1, donde la mezcla linezolid-agente antibacteriano se hace combinando una solución acuosa del agente antibacteriano y linezolid sólido.
17. Una composición farmacéutica acuosa según la reivindicación 1, donde la mezcla linezolid-agente antibacteriano se hace combinando una solución acuosa de linezolid y un concentrado del agente antibacteriano.
18. Una composición farmacéutica acuosa según la reivindicación 1, donde la mezcla linezolid-agente antibacteriano se hace combinando una solución acuosa del agente antibacteriano y un concentrado de linezolid.
19. Un método para tratar a un ser humano con una infección bacteriana que consiste en administrar IV al humano infectado una composición farmacéutica acuosa de linezolid y uno o más agentes antibacterianos del grupo compuesto por aminoglicósidos, cefalosporinas, aztreonam, quinolonas y penicilinas, y sales farmacéuticamente aceptables de lo mismo, donde existan.

20. Un método para tratar a un ser humano que tenga una Infección bacteriana según la reivindicación 19, donde el agente antibacteriano es seleccionado del grupo compuesto por gentamicina, tobramicina, aztreonam, cefazolina, ceftazidima, piperacilina, ciprofloxacina, ofloxacina, levofloxacina.
21. Un método para tratar a un ser humano que tenga una Infección bacteriana según la reivindicación 19, donde la composición acuosa es una solución.
22. Un método para tratar a un ser humano que tenga una Infección bacteriana según la reivindicación 21, donde la solución es estéril.

Pharmacia
PUC 62431
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PA 309266

THE UNITED STATES OF AMERICA**TO ALL TO WHOM THESE PRESENTS SHALL COME:****UNITED STATES DEPARTMENT OF COMMERCE****United States Patent and Trademark Office****October 10, 2000**

THIS IS TO CERTIFY THAT ANNEXED HERETO IS A TRUE COPY FROM THE RECORDS OF THE UNITED STATES PATENT AND TRADEMARK OFFICE OF THOSE PAPERS OF THE BELOW IDENTIFIED PATENT APPLICATION THAT MET THE REQUIREMENTS TO BE GRANTED A FILING DATE UNDER 35 USC 111.

APPLICATION NUMBER: 60/163,990**FILING DATE: November 08, 1999**

**By Authority of the
COMMISSIONER OF PATENTS AND TRADEMARKS**


P. R. GRANT
Certifying Officer

PROVISIONAL APPLICATION COVER SHEET

A/PROV
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CERTIFICATE OF MAILING (37 CFR 1.10)

"Express Mail" No: EM177639035 USDate of Deposit: November 8, 1999

I hereby certify that this transmittal together with the patent application referred to below is being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 CFR 1.10 on the date indicated above and is addressed to the Commissioner of Patents and Trademarks, Washington, DC 20231.

Julie K. Lyons, Legal Assistant

Name of Person Mailing Paper

Signature

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Commissioner of Patents and Trademarks
Washington, DC 20231

TRANSMITTAL OF A PROVISIONAL APPLICATION
UNDER 37 CFR 1.53(c)

Sir:

This is a request for filing a provisional application under 37 CFR 1.53(c). The application is entitled Admixture of Linezolid and other Antibacterial Agents, our Docket No. 6293, and consists of:

- [8] page(s) of Specification
- [3] page(s) of Claims
- [0] page(s) of Drawings
- [0] page(s) of Sequence Listings
- [1] page(s) of Abstract

- ☐ A disk containing nucleotide and/or amino acid sequences in a computer readable format is attached. The contents of the sequence listing in the application is the same as the document on the disk. (37 CFR 1.821(f) and MPEP 2422.06)
- ☒ The name(s) and residence address(es) of the inventor(s) are set forth on the attached Inventor Information Sheet.
- ☐ As provided in 37 CFR 1.41(a)(3), instead of providing the names of the inventors at this time, the applicant identifier is: PNU.

This application is being sent by Express Mail under 37 CFR 1.10 and the required certificate appears above.

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SPECIFIC DEPOSIT ACCOUNT AUTHORIZATION. Please charge my Deposit Account No. 21-0718 in the amount of the total Provisional Application filing fee for a large entity (\$150.00 or such greater or lesser amount as the Commissioner may require). Triplicate copies of this sheet are enclosed for this purpose.

The undersigned hereby requests that all correspondence and telephone communications in connection with this application be directed to the undersigned person at the mailing address and telephone number shown below.

Respectfully submitted,

Bruce Stein
Bruce Stein, Attorney
Registration No. 27,231

Date: 99-11-8

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Enclosures:

- ☒ Patent Application
- ☐ Disk containing Nucleotide and/or Amino Acid Sequence Listing
- ☒ Inventor Information Sheet

668011-066E9T09

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INVENTOR INFORMATION SHEET

Full name of sole or first inventor:
Address:

Donald H. Batts
4303 Old Colony
Kalamazoo, MI 49008

Citizenship:

USA

68011-06 E9T09

ADMIXTURE OF LINEZOLID AND OTHER ANTIBACTERIAL AGENTS
CROSS-REFERENCE TO RELATED APPLICATIONS

None.

BACKGROUND OF THE INVENTION

1. Field of the Invention

The present invention is a mixture of sterile solutions of linezolid and particular antibacterial agents.

2. Description of the Related Art

US Patent 5,688,792 (EXAMPLE 5) discloses the antibacterial agent,
 linezolid.

The 53rd edition of the Physicians Desk Reference (PDR), Medical Economics Company, Montvale, NJ, 1999 discloses the other antibacterial agents of the invention. See for gentamicin (p. 964), tobramycin (599, 1562), aztreonam (p.820), cefazolin (p. 3023), ceftazidime (p.1100), piperacillin (p. 1531), ciprofloxacin (p. 647), ofloxacin (p. 2180), and levofloxacin (2192).

It is known to those skilled in the art that mixing solutions of pharmaceutical agents can result in physical and/or chemical instability rendering the mixture unfit for pharmaceutical use.

SUMMARY OF INVENTION

Disclosed is an aqueous pharmaceutical composition for IV administration of linezolid and one or more antibacterial agents selected from the group consisting of an aminoglycosides, cephalosporins, aztreonam, quinolones and penicillins and pharmaceutically acceptable salts thereof where such exist.

Also disclosed is a method of treating a human with a bacterial infection which comprises IV administration to the infected human an aqueous pharmaceutical composition of linezolid and one or more antibacterial agents selected from the group consisting of an aminoglycosides, cephalosporins, aztreonam, quinolones and penicillins and pharmaceutically acceptable salts thereof where such exist.

DETAILED DESCRIPTION OF THE INVENTION

Linezolid, (S)-N-[[3-[3-fluoro-4-(4-morpholinyl)phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide, is a known antibacterial agent, see US Patent 5,688,792 (EXAMPLE 5). Linezolid can be used as an oral tablet, capsule or oral suspension or given by IV as a sterile solution.

Gentamicin is a known antibacterial agent, see page 964 of the 53rd Edition of the PDR (1999) and can be given by IV as a sterile solution.

Tobramycin is a known antibacterial agent, see page 599 and 1562 of the 53rd Edition of the PDR (1999) and can be given by IV as a sterile solution.

5 Aztreonam is a known antibacterial agent, see page 820 of the 53rd Edition of the PDR (1999) and can be given by IV as a sterile solution.

Cefazolin is a known antibacterial agent, see page 3023 of the 53rd Edition of the PDR (1999) and can be given by IV as a sterile solution.

10 Ceftazidime is a known antibacterial agent, see page 1100 of the 53rd Edition of the PDR (1999) and can be given by IV as a sterile solution.

 Piperacillin is a known antibacterial agent, see page 1531 of the 53rd Edition of the PDR (1999) and can be given by IV as a sterile solution.

Ciprofloxacin is a known antibacterial agent, see page 647 of the 53rd Edition of the PDR (1999) and can be given by IV as a sterile solution.

15 Ofloxacin is a known antibacterial agent, see page 2180 of the 53rd Edition of the PDR (1999) and can be given by IV as a sterile solution.

Levofloxacin is a known antibacterial agent, see page 2192 of the 53rd Edition of the PDR (1999) and can be given by IV as a sterile solution.

20 Linezolid is a member of a new class of antibacterial agent known as an oxazolidinone and is useful in treating infections caused by gram positive bacteria including gram positive infections that are resistant to other gram positive antibacterial agents.

Often in medical treatment a physician does not know for sure whether or not a bacterial infection is caused by gram positive bacteria or gram negative bacteria or both. Therefore, often a physician desires to use an agent(s) which are effective against both gram positive and gram negative bacteria. Hence, often a physician will combine two agents, one useful against gram positive bacteria and the other useful against gram negative bacteria. The following agents are known to be useful against gram negative bacteria, gentamicin, tobramycin, aztreonam. The following

30 antibacterial agents are known as "broad spectrum antibacterials" because they are active against both gram positive and gram negative bacteria, cefazolin, ceftazidime, piperacillin, ciprofloxacin, ofloxacin and levofloxacin.

If one combines sterile solutions of two different agents it is quite possible that there will not be chemical or physical compatibility between the two different sterile solutions and/or agents. In fact, for this very reason, the corporation conducting the clinical trials on linezolid specifically warned physicians against combining the sterile solution of linezolid and other antibacterial agents.

It now has been found that there is both chemical and physical stability between linezolid sterile solution and sterile solutions of the following antibacterial agents; aminoglycosides, cephalosporins, aztreonam, quinolones and penicillins and pharmaceutically acceptable salts thereof where such exist. It is preferred that the antibacterial agent be selected from the group consisting of gentamicin, tobramycin, aztreonam, cefazolin, ceftazidime, piperacillin, ciprofloxacin, ofloxacin and levofloxacin.

When combining an aqueous composition of linezolid with an aqueous composition of the other antibacterial agents the concentration of both linezolid and the other antibacterial agents will be affected by a dilution factor as is well known to those skilled in the art. The actual final concentration of linezolid and/or the other antibacterial agents is not very important. The concentration can vary considerably. What is critical is that the patient receive an antibacterial effective amount of linezolid and an antibacterial effective amount of the other antibacterial agent. The effective amounts for each of these agents, for adults, is as follows: linezolid (about 200 mg to about 600 mg/dose), gentamicin (about 1 mg/kg to about 7.5 mg/kg/dose), tobramycin (about 1 mg/kg to about 7.5 mg/kg/dose), aztreonam (about 500 mg to about 2 g/dose), ciprofloxacin (about 200 mg to about 400 mg/dose), ofloxacin (about 200 mg to about 400 mg/dose), levofloxacin (about 250 mg to about 500 mg/dose), piperacillin sodium (about 2 g to about 4 g/dose), piperacillin/tazobactam (about 2 g to about 4 g/dose based on piperacillin), ceftazidime (about 250 mg to about 2 g/dose) and cefazolin (about 500 mg to about 1 g/dose). One skilled in the art would be able to calculate an effective amount for children (of various ages and weights) as well as the elderly.

It is preferred that the aqueous pharmaceutical composition of the present invention be an aqueous solution. It is further preferred that the aqueous solution be a sterile solution.

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There are different ways that one skilled in the art could make an aqueous pharmaceutical composition of linezolid and an antibacterial agent selected from the group consisting of gentamicin, tobramycin, aztreonam, cefazolin, ceftazidime, piperacillin, ciprofloxacin, ofloxacin and levofloxacin.

- 5 First, one can combine an aqueous pharmaceutical composition of linezolid and an aqueous pharmaceutical composition of one of the following agents; gentamicin, tobramycin, aztreonam, cefazolin, ceftazidime, piperacillin, ciprofloxacin, ofloxacin and levofloxacin. If this is done it must be realized that the concentration of each antibacterial agent is being diluted by the other as explained above.
- 10 Alternatively, so as not to dilute the linezolid aqueous pharmaceutical composition, it is preferred to add solid antibacterial agent selected from the group consisting of gentamicin, tobramycin, aztreonam, cefazolin, ceftazidime, piperacillin, ciprofloxacin, ofloxacin and levofloxacin to the linezolid aqueous pharmaceutical composition. Also so as not to dilute an aqueous pharmaceutical composition of one of the
- 15 following antibacterial agents, gentamicin, tobramycin, aztreonam, cefazolin, ceftazidime, piperacillin, ciprofloxacin, ofloxacin and levofloxacin, solid linezolid powder can be added to the aqueous pharmaceutical composition of one of the other antibacterial agents. In addition, should more than one of the non-linezolid antibacterial agents be desired for use with linezolid, it can be added in the same way.
- 20 Besides adding solid antibacterial agent to a solution, to keep the dilution factor low, the solid antibacterial agent or linezolid can be suspended or dissolved in an appropriate solvent such as water, ethanol, polyethylene glycol, propylene glycol, DMSO, DMAC, DMI, glycerine and M-pyrol and mixtures thereof. The concentrate can then be added to the aqueous pharmaceutical composition.
- 25 The advantage of admixing is to lower the total volume administered and/or to use the same infusion line. The lowering of the total volume to be given to the patient is accomplished in a number of ways by using the admixing of the present invention. For example, an number of antibacterial agents come as concentrates to be diluted with acceptable diluents. With these concentrates the diluent used is the linezolid
- 30 sterile solution there by saving the volume of diluent normally used to dilute the other antibacterial agent. Alternatively, other antibacterial agents are marketed as sterile powders which are then compounded into concentrates for dilution. With these sterile powders the first step is performed in making the concentrate. But rather than using a

diluent that has no active ingredient, the concentrate is added to linezolid sterile solution (as described above). This reduces the overall volume of aqueous composition administered to the patient. In situations where the antibacterial agent is marketed as a ready to use large volume parenteral sterile solution, there is no way to reduce the volume unless it is combined with linezolid in a concentrated form. If it is combined with sterile aqueous linezolid solution the advantage is that the same infusion line can be used for administering both the linezolid and the other antibacterial agent.

The exact dosage and frequency of administration of the aqueous pharmaceutical composition depends on the particular combination of linezolid and antibacterial agent used, the particular condition being treated, the severity of the condition being treated, the age, weight, general physical condition of the particular patient, other medication the individual may be taking as is well known to those skilled in the art and can be more accurately determined by measuring the blood level or concentration of the antibacterial agents in the patient's blood and/or the patient's response to the particular condition being treated.

DEFINITIONS AND CONVENTIONS

The definitions and explanations below are for the terms as used throughout this entire document including both the specification and the claims.

DEFINITIONS

All temperatures are in degrees Centigrade.

Linezolid refers to (S)-N-[[3-[3-Fluoro-4-(4-morpholinyl)phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide and pharmaceutically acceptable salts thereof.

Physiological saline refers to an aqueous 0.9% sodium chloride solution.

Pharmaceutically acceptable refers to those properties and/or substances which are acceptable to the patient from a pharmacological/toxicological point of view and to the manufacturing pharmaceutical chemist from a physical/chemical point of view regarding composition, formulation, stability, patient acceptance and bioavailability.

When solvent pairs are used, the ratios of solvents used are volume/volume (v/v).

When the solubility of a solid in a solvent is used the ratio of the solid to the solvent is weight/volume (wt/v).

qsad refers to addition of a sufficient quantity of that material to bring the final composition to the specified volume.

DMSO refers to dimethylsulfoxide [$\text{CH}_3\text{-SO-CH}_3$].

DMAC refers to dimethylacetamide [$\text{CH}_3\text{-CO-N(CH}_3)_2$].

5 DMI refers to dimethyl isosorbide.

M-PYROL refers to N-methyl-2-pyrrolidone.

EXAMPLES

Without further elaboration, it is believed that one skilled in the art can, using the preceding description, practice the present invention to its fullest extent. The following detailed examples describe how to prepare the various compounds and/or perform the various processes of the invention and are to be construed as merely illustrative, and not limitations of the preceding disclosure in any way whatsoever. Those skilled in the art will promptly recognize appropriate variations from the procedures both as to reactants and as to reaction conditions and techniques.

15 PREPARATION 1 Linezolid sterile solution:

Linezolid sterile solution:

	<u>Item</u>	<u>mg/ml</u>
	Linezolid	2.0
	Dextrose	50.24
20	Citric acid	0.85
	Sodium citrate	1.64
	Water for injection, USP	qsad

EXAMPLE 1 Linezolid and Gentamicin Sulfate

Linezolid sterile solution (PREPARATION 1) is admixed with commercial gentamicin concentrate. One admixture is stored at 4° and another at 23°. The admixtures were sampled at one, three, five days and seven days. The samples were tested for both chemical and physical stability. The results of the samples for both temperatures show there is good chemical and physical stability over 7 days at 4° and 5 days at 23°. It is concluded that the admixture of linezolid and commercial gentamicin concentrate is acceptable for human use.

EXAMPLE 2 Linezolid and Tobramycin Sulfate

Following the general procedure of EXAMPLE 1 and making non-critical variations, Linezolid sterile solution (PREPARATION 1) is admixed with commercial

tobramycin concentrate. The results of the samples for both temperatures show there is good chemical and physical stability over 7 days at 4° and 1 day at 23°. It is concluded that the admixture of linezolid and commercial tobramycin concentrate is acceptable for human use.

5 **EXAMPLE 3 Linezolid and Aztreonam**

Following the general procedure of EXAMPLE 1 and making non-critical variations, Linezolid sterile solution (PREPARATION 1) is admixed with commercial reconstituted aztreonam. The results of the samples for both temperatures show there is good chemical and physical stability over 7 days at 4° and 7 days at 23°.

10 It is concluded that the admixture of linezolid and commercial reconstituted aztreonam is acceptable for human use.

EXAMPLE 4 Linezolid and Cefazolin Sodium

Following the general procedure of EXAMPLE 1 and making non-critical variations, Linezolid sterile solution (PREPARATION 1) is admixed with commercial reconstituted cefazolin. The results of the samples for both temperatures show there is good chemical and physical stability over 7 days at 4° and 3 day at 23°. It is concluded that the admixture of linezolid and commercial cefazolin concentrate is acceptable for human use.

20 **EXAMPLE 5 Linezolid and Ceftazidime**

Following the general procedure of EXAMPLE 1 and making non-critical variations, Linezolid sterile solution (PREPARATION 1) is admixed with commercial reconstituted ceftazidime. The results of the samples for both temperatures show there is good chemical and physical stability over 7 days at 4° and 1 day at 23°. It is concluded that the admixture of linezolid and commercial ceftazidime concentrate is acceptable for human use.

EXAMPLE 6 Linezolid and Piperacillin Sodium

Following the general procedure of EXAMPLE 1 and making non-critical variations, Linezolid sterile solution (PREPARATION 1) is admixed with commercial reconstituted piperacillin. The results of the samples for both temperatures show there is good chemical and physical stability over 7 days at 4° and 3 days at 23°. It is concluded that the admixture of linezolid and commercial piperacillin concentrate is acceptable for human use.

EXAMPLE 7 Linezolid and Ciprofloxacin

Following the general procedure of **EXAMPLE 1** and making non-critical variations, Linezolid sterile solution (PREPARATION 1) is admixed with commercial ciprofloxacin concentrate. The results of the samples show there is good chemical and physical stability over 7 days at 23°. It is concluded that the admixture of linezolid and commercial ciprofloxacin concentrate is acceptable for human use.

EXAMPLE 8 Linezolid and Ofloxacin

Following the general procedure of **EXAMPLE 1** and making non-critical variations, Linezolid sterile solution (PREPARATION 1) is admixed with commercial ofloxacin concentrate. The results of the samples for both temperatures show there is good chemical and physical stability over 7 days at 4° and 7 days at 23°. It is concluded that the admixture of linezolid and commercial ofloxacin concentrate is acceptable for human use.

EXAMPLE 9 Linezolid and Levofloxacin

Following the general procedure of **EXAMPLE 1** and making non-critical variations, Linezolid sterile solution (PREPARATION 1) is admixed with commercial levofloxacin concentrate. The results of the samples for both temperatures show there is good chemical and physical stability over 7 days at 4° and 7 days at 23°. It is concluded that the admixture of linezolid and commercial levofloxacin concentrate is acceptable for human use.

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45CLAIMS

1. An aqueous pharmaceutical composition for IV administration of linezolid and one or more antibacterial agents selected from the group consisting of an aminoglycosides, cephalosporins, aztreonam, quinolones and penicillins and pharmaceutically acceptable salts thereof where such exist.
2. An aqueous pharmaceutical composition according to claim 1 where the antibacterial agent is selected from the group consisting of gentamicin, tobramycin, aztreonam, cefazolin, ceftazidime, piperacillin, ciprofloxacin, ofloxacin, levofloxacin.
3. An aqueous pharmaceutical composition according to claim 1 where the antibacterial agent is gentamicin.
4. An aqueous pharmaceutical composition according to claim 1 where the antibacterial agent is tobramycin.
5. An aqueous pharmaceutical composition according to claim 1 where the antibacterial agent is aztreonam.
6. An aqueous pharmaceutical composition according to claim 1 where the antibacterial agent is cefazolin.
7. An aqueous pharmaceutical composition according to claim 1 where the antibacterial agent is ceftazidime.
8. An aqueous pharmaceutical composition according to claim 1 where the antibacterial agent is piperacillin.
9. An aqueous pharmaceutical composition according to claim 1 where the antibacterial agent is ciprofloxacin.
10. An aqueous pharmaceutical composition according to claim 1 where the antibacterial agent is ofloxacin.

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11. An aqueous pharmaceutical composition according to claim 1 where the antibacterial agent is levofloxacin.

5 12. An aqueous pharmaceutical composition according to claim 1 where the aqueous composition is a solution.

13. An aqueous pharmaceutical composition according to claim 12 where the solution is sterile.

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14. An aqueous pharmaceutical composition according to claim 1 where the linezolid-antibacterial agent mixture is made by combining an aqueous solution of linezolid and an aqueous solution of the antibacterial agent.

15 15. An aqueous pharmaceutical composition according to claim 1 where the linezolid-antibacterial agent mixture is made by combining an aqueous solution of linezolid and solid antibacterial agent.

16. An aqueous pharmaceutical composition according to claim 1 where the
20 linezolid-antibacterial agent mixture is made by combining an aqueous solution of the antibacterial agent and solid linezolid.

17. An aqueous pharmaceutical composition according to claim 1 where the
25 linezolid-antibacterial agent mixture is made by combining an aqueous solution of linezolid and a concentrate of the antibacterial agent.

18. An aqueous pharmaceutical composition according to claim 1 where the
linezolid-antibacterial agent mixture is made by combining an aqueous solution of the
antibacterial agent and a concentrate of linezolid.

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19. A method of treating a human with a bacterial infection which comprises
IV administration to the infected human an aqueous pharmaceutical composition of
linezolid and one or more antibacterial agents selected from the group consisting of an

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aminoglycosides, cephalosporins, aztreonam, quinolones and penicillins and
pharmaceutically acceptable salts thereof where such exist.

20. A method of treating a human with a bacterial infection according to claim 19
5 where the antibacterial agent is selected from the group consisting of gentamicin,
tobramycin, aztreonam, cefazolin, ceftazidime, piperacillin, ciprofloxacin, ofloxacin,
levofloxacin.

21. A method of treating a human with a bacterial infection according to claim 19
10 where the aqueous composition is a solution.

22. A method of treating a human with a bacterial infection according to claim 21
where the solution is sterile.

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ADMIXTURE OF LINEZOLID AND OTHER ANTIBACTERIAL AGENTSABSTRACT

The present invention is a aqueous admixture of linezolid and an antibacterial agent selected from the group consisting of gentamicin, tobramycin, aztreonam, cefazolin, ceftazidime, piperacillin, ciprofloxacin, ofloxacin, levofloxacin for IV administration.

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2do. EXAMEN DE FORMA PATENTE DE INVENCION

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Folio ~~53~~

Radicación No 00-83824

**Concepto Técnico No 1329 Clasificación Internacional de Patentes A61K31/5375/31/42
/31/16/35/66**

Practicado el examen de acuerdo a lo establecido en el Art. 38 de la Decisión 486 se determinó que esta solicitud de Patente de Invención:

- SI ☒ NO ☐ Contiene un resumen de la invención (Art.26-e).
- SI ☒ NO ☐ Contiene el título o nombre de la invención (Art.27-d).
- SI ☒ NO ☐ Contiene la descripción de la invención (Art.26-b).
- SI ☐ NO ☐ NO ES APLICABLE ☒ Contiene los dibujos necesarios para comprender la invención (Art.26-d)
- SI ☒ NO ☐ Contiene una o más reivindicaciones. (Art.26-c).
- SI ☐ NO ☐ NO ES APLICABLE ☒ Han sido desarrollados los productos y/o procedimientos a partir de recursos genéticos o de sus productos derivados de los que cualquiera de los Países Miembros es país de origen. (Art. 26- h).
- SI ☐ NO ☐ NO ES APLICABLE ☒ Los productos y/o procedimientos han sido obtenidos o desarrollados a partir de los conocimientos tradicionales de las comunidades indígenas, afroamericanas, o locales de los países miembros, de acuerdo a lo establecido en la Decisión 391 y sus modificaciones y reglamentaciones Vigentes.(Art.26-i).
- SI ☐ NO ☒ La invención se refiere a un producto relativo a un material biológico. (Art.26-J).
- SI ☒ NO ☐ La prioridad coincide con la materia reivindicada.
- SI ☒ NO ☐ **CUMPLE LOS REQUISITOS TÉCNICOS**

OBSERVACIONES Y OTROS:

1. Anexa copia y traducción del capítulo reivindicatorio de la patente estadounidense No.60/193,990 del 08 / 11 /99 a partir del folio No. 32.

EXAMINADOR TÉCNICO
202047

Bogotá D. C., Septiembre 10/ 2002 .

Carrera 13 No. 27-00 Piso 5 y 10
Conmutador: 334 12 21-2-3-4
Fax: 281 31 25 e-mail: info@sic.gov.co
Santa Fe de Bogotá D.C. - Colombia

50

Folio 54

2020
Bogotá DC

Doctor
JOSE ANTONIO LLOREDA
Apoderado

REFERENCIA:	Radicación No.	00-83924
	Trámite	002
	Evento	001
	Actuación	416
	Oficio No.	1838
	Folios	001

Teniendo en cuenta que la solicitud de privilegio de patente que se tramita bajo el expediente indicado en la referencia, reúne los requisitos de forma establecidos en los artículos 26 y 27 de la Decisión 486 de la Comisión de la Comunidad Andina, y en las demás disposiciones vigentes sobre la materia, se envía el extracto de la solicitud a la Oficina de Comunicaciones para efecto de su publicación en la Gaceta de Propiedad Industrial, conforme lo establece el artículo 40 de la misma Decisión.

Cúmplase

Dado en Bogotá DC, a los

18 de Noviembre, 2002

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

202047

Nº 525

DIVISION DE NUEVAS CREACIONES

RADICACIÓN EXPEDIENTE No. 00-83924

**EL EXTRACTO DE LA PRESENTE SOLICITUD DE PATENTE DE INVENCION FUE
PUBLICADO EN LA GACETA DE PROPIEDAD INDUSTRIAL No 525, DE FECHA 28 DE
FEBRERO DE 2003, EL TERMINO HABIL SEÑALADO POR LA LEY EXPIRA EL 29 DE MAYO
DE 2003.**

**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 _____

Bogotá D.C., Septiembre 19 de 2003

**Carrera 13 No. 27-00 Piso 5 y 10
Conmutador: 334 12 21-2-3-4
Fax: 281 31 25 e-mail: info@sk.gov.co
Santa Fe de Bogotá D.C. - Colombia**

SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO

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RADICACIÓN: 0-83824

EDICTO No. 15737

LA SECRETARÍA GENERAL AD-HOC HACE SABER:

Que esta Superintendencia profirió Resolución No. 28923 de 26-SEP-2003. Que el contenido de la parte resolutive es como sigue: El Superintendente de Industria y Comercio.

RESUELVE

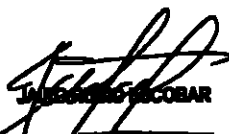
ARTICULO PRIMERO: Declarar abandonada la solicitud de privilegio de patente de invención contenida en el expediente de la referencia.

ARTICULO SEGUNDO: Notificar personalmente el contenido de la presente resolución al doctor José Antonio Llereda, o a quien haga sus veces, quien actúa como apoderado de Pharmacia & Upjohn Company, entregándole copia de la misma, advirtiéndole que contra ella procede el recurso de reposición interpuesto ante el Superintendente de Industria y Comercio, al momento de la notificación o dentro de los 5 días hábiles siguientes a ella.

NOTIFÍQUESE Y CUMPLASE

Dada en Bogotá, D.C., a los 26 SET. 2003

EL SUPERINTENDENTE DE INDUSTRIA Y COMERCIO,


JAIME ESCOBAR

Para notificar a los interesados, se fija el presente EDICTO en lugar visible al público en la SUPERINTENDENCIA DE INDUSTRIA Y COMERCIO, por el término de (10) diez días hábiles contados a partir de las 8:30 a.m. de hoy.

Secretaría General Ad-Hoc 07-OCT-2003
Secretaría General Ad-Hoc
EDICTO No. 15737

Este edicto se desfiña hoy 21-OCT-2003 a las cinco (5:00 p.m.)