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(54) Title: SOLID ORAL DOSAGE FORMS OF GATIFLOXACIN

(57) Abstract: The present invention relates to solid oral dosage forms of gatifloxacin having reproducible release characteristics and processes for their preparation. The solid oral dosage form includes an intragranular phase and an extragranular phase. The intragranular phase includes gatifloxacin and one or more of a filler, a binder, a wicking agent, and a disintegration aid. The extragranular phase is free of any disintegration aid.

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SOLID ORAL DOSAGE FORMS OF GATIFLOXACIN

Technical Field of the Invention

The present invention relates to solid oral dosage forms of gatifloxacin having reproducible release characteristics and processes for their preparation.

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Background of the Invention

Tablet dosage forms are the most widely used of the various dosage forms. From the patient's perspective the tablet dosage forms provides a unit dose of the active substance accurately in a form that is easy to consume and is convenient for storage and transport. From the manufacturer's perspective, the tablet dosage forms are more economical to manufacture than any other dosage form. Tablets are available in various types, such as mouth-dissolving tablets, water-soluble tablets, dispersible tablets, effervescent tablets, buccal tablets, etc. In short, tablets are versatile and can be designed with considerations to the specific requirements of the patient.

It is imperative that a tablet should provide uniform therapeutic levels of the drug with each dose to the patient for maximum efficacy. The drug should be in solution form in the gastrointestinal fluid for absorption. For most tablets, the first important step towards going into the solution form is breaking down of the tablet into smaller particles or granules, a process known as disintegration. Thus, the disintegration time of the tablet may give an indication about the extent of the availability of the drug for absorption into the systemic circulation. Designing a manufacturing process to achieve a constant disintegration time, or at least with acceptable levels of variation, serves to minimize the batch-to-batch variability during the manufacturing process. An ideal tablet should have a reproducible disintegration time or an ultimately reproducible dissolution time to attain a predictable therapeutic effect of the intended dose.

U.S. Patent No. 6,291,462 discloses solid dosage forms of gatifloxacin which are characterized as having reproducible disintegration times. The dosage forms have a granular phase and an extragranular phase. The granules contain gatifloxacin, fillers, binders, and disintegration aids. The extragranular phase contains at least one disintegration aid and a lubricant. The use of an extragranular disintegration aid has been considered to be critical for the reproducible disintegration time of gatifloxacin tablets.

Summary of the Invention

In one general aspect there is provided a solid oral dosage form that includes an intragranular phase and an extragranular phase. The intragranular phase includes gatifloxacin and one or more of a filler, a binder, a wicking agent, and a disintegration aid.

5 The extragranular phase is free of any disintegration aid.

Embodiments of the oral dosage form may include one or more of the following features. For example, the filler may be selected from starch, dicalcium phosphate, calcium carbonate, lactose, mannitol, dextrose, sorbitol, sucrose, sodium chloride and combinations thereof. The binder may be selected from polyvinylpyrrolidone,
10 hydroxypropylmethylcellulose, hydroxypropylcellulose, starch mucilage, carbopols, gums, and combinations thereof.

The wicking agent may be selected from water soluble excipients, hydrophilic polymers, silicon dioxide, colloidal silicon dioxide, microcrystalline cellulose and combinations thereof. In particular, the wicking agent may be a water soluble excipient
15 and the water-soluble excipient may be one or more of sodium chloride, sugar, and sugar alcohols. The sugar or sugar alcohol may be selected from dextrose, mannitol, sorbitol, lactose, sucrose, and combinations thereof. The hydrophilic polymer may be selected from croscarmellose sodium, crosslinked polyvinylpyrrolidone, starches, gums, hydroxymethylcellulose, hydroxypropylcellulose, hydroxypropylmethylcellulose,
20 carbopol, and combinations thereof.

The disintegration aid may be selected from ion exchange resins, hydroxypropylcellulose, crospovidone, croscarmellose sodium, starches, pectins, alginates, surfactants, microcrystalline cellulose, sodium starch glycolate, and combinations thereof. In particular, the disintegration may be croscarmellose sodium.
25 The disintegration aid may be an ion exchange resin and, in particular, may be polacrillin potassium.

The extragranular phase may further include one or more lubricants. The lubricant may be selected from talc, polyethylene glycol, sodium chloride, stearic acid, calcium stearate, zinc stearate, magnesium stearate, sodium stearyl fumarate, and combinations
30 thereof. The lubricant may be a water soluble lubricant selected from one or more of sodium stearyl fumarate, polyethylene glycol, sodium chloride, and combinations thereof. In particular, the lubricant may be sodium stearyl fumarate.

The extragranular phase may further include a water soluble filler. The water soluble filler may be selected from lactose, mannitol, dextrose, sorbitol, sucrose and sodium chloride.

The solid dosage form may be in the form of a tablet and the tablet may be coated.

5 In another general aspect there is provided a process for the preparation of a solid oral dosage form. The process includes blending gatifloxacin and one or more of fillers, binders, wicking agent and disintegration aids; granulating the blend to form granules; mixing the granules with an extragranular phase to form a mixture of the granules and the extragranular phase, the extragranular phase being free of any disintegration aid; and
10 compressing the mixture into a solid dosage form.

Embodiments of the process may include one or more of the following features. For example, the granulation may be wet granulation and the wet granulation may include a granulating liquid selected from water, ethanol, isopropyl alcohol, acetone, dichloromethane, and a binder solution. The granulation may be dry granulation and the
15 dry granulation may be compaction or slugging. In particular, the dry granulation may be compaction.

The filler may be selected from starch, dicalcium phosphate, calcium carbonate, lactose, mannitol, dextrose, sorbitol, sucrose, sodium chloride and combinations thereof. The binder may be selected from polyvinylpyrrolidone, hydroxypropylmethylcellulose, hydroxypropylcellulose, starch mucilage, carbopols and gums. The wicking agent may be
20 selected from water soluble excipient, hydrophilic polymers, silicon dioxide, colloidal silicon dioxide, microcrystalline cellulose, and combinations thereof. In particular, the wicking agent may be a water-soluble excipient and the water-soluble excipient may be selected from sodium chloride, sugar, sugar alcohols, and combinations thereof. The
25 disintegration aid may be selected from ion exchange resins, hydroxypropylcellulose, crospovidone, croscarmellose sodium, starches, pectins, alginates, surfactants, microcrystalline cellulose, sodium starch glycolate, and combinations thereof.

The process may further include adding one or more of a lubricant and water soluble filler to the extragranular phase. The solid dosage form may be in the form of a
30 tablet and the tablet may be coated.

In another general aspect there is provided a method of treating infections and conditions for which gatifloxacin is indicated. The method includes administering a solid

dosage form that includes an intragranular phase and an extragranular phase. The intragranular phase includes gatifloxacin and one or more of a filler, a binder, a wicking agent, and a disintegration aid. The extragranular phase is free of any disintegration aid.

5 The details of one or more embodiments of the inventions are set forth in the description below. Other features, objects and advantages of the inventions will be apparent from the description and claims.

Detailed Description of the Invention

10 We have now discovered that tablets of gatifloxacin with a reproducible disintegration time or dissolution rate can be prepared without using any extragranular disintegration aid.

The term "solid dosage form" as used herein includes tablets or coated tablets, pellets and capsules filled with tablets, or pellets prepared as per the embodiments described herein. A particularly suitable solid dosage form is that of tablets. The solid dosage form can include gatifloxacin and pharmaceutically acceptable excipients, including one or more of fillers, binders, wicking agents, disintegration aids, and lubricants.

20 The term "gatifloxacin" as used herein includes gatifloxacin or a pharmaceutically acceptable salt or hydrate thereof, such as, but not limited to, gatifloxacin anhydrous, gatifloxacin hydrochloride, gatifloxacin hemihydrate or sesquihydrate, and any other pharmaceutically acceptable form known to the skilled in the art. Generally, the amount of gatifloxacin can be from about 20%w/w to about 80% w/w, particularly from about 40%w/w to about 80%w/w of the solid dosage form. Gatifloxacin is currently approved by FDA in various forms and strengths, including 200 mg and 400 mg tablets as a broad spectrum antibacterial agent for the treatment of infections due to susceptible strains of particular microorganisms, as approved by the FDA.

The fillers can be any substance which can provide bulk to the tablet and include, without limitation, starch, dicalcium phosphate, calcium carbonate, lactose, mannitol dextrose, sorbitol, sucrose, sodium chloride and combinations thereof. The filler may be up to about 40% by weight of the solid dosage form.

30 The binders can be selected from the group that includes polyvinylpyrrolidone, hydroxypropyl methylcellulose, hydroxypropylcellulose, starch mucilage, carbopols and

gums. The binder may be present at an amount from about 0.1% to about 10% by weight of the solid dosage form.

Wicking agents are substances that are capable of drawing water into the dosage form and assist in the breaking of the tablets into granules. Any excipient that can serve to transport moisture as discussed above can be considered to be a wicking agent. These agents help in maintaining a reproducible disintegration time or drug release rate of the tablets even on aging of the tablet (e.g., storage). The wicking agent is present in the intragranular phase and includes, for example, water soluble excipients such as sodium chloride; sugars or sugar alcohols such as dextrose, mannitol, sorbitol, lactose and sucrose; hydrophilic polymers such as croscarmellose sodium, cross linked polyvinylpyrrolidone, starches, gums, hydroxymethylcellulose, hydroxypropylcellulose, hydroxypropylmethylcellulose and carbopol; silicon dioxide, colloidal silicon dioxide and microcrystalline cellulose. Particularly suitable wicking agents are silicon dioxide, colloidal silicon dioxide, microcrystalline cellulose and sugars or sugar alcohols. The wicking agent may make up from about 1% w/w to about 50% w/w, particularly from about 1% w/w to about 40% w/w, of the solid dosage form.

The disintegration aid is present intragranularly and can be selected from the group that includes ion exchange resins such as polacrillin potassium (Amberlite® IRP88), hydroxypropylcellulose, crospovidone, croscarmellose sodium, starches, pectins, alginates, surfactants, microcrystalline cellulose, sodium starch glycolate and the like. Particularly suitable disintegration aids are croscarmellose sodium, sodium starch glycolate, and polacrillin potassium. The disintegration aid can be present in a concentration of up to about 30%w/w of the solid dosage form.

Lubricants can be talc, polyethylene glycol, sodium chloride, stearic acid, calcium stearate, zinc stearate, magnesium stearate and sodium stearyl fumarate. Use of a water-soluble lubricant is particularly advantageous. The lubricant may be present in a concentration of about 0.1%w/w to about 5%w/w of the solid dosage form.

The granulating liquid can be, but is not limited to, water, ethanol, isopropyl alcohol, acetone, dichloromethane and the like. Alternatively, the binder can be dissolved in the granulating liquid and used as a solution/dispersion.

In one embodiment gatifloxacin tablets may be prepared by blending gatifloxacin with intragranular excipients such as filler, binder, wicking agent, and disintegrant;

granulating the above blend with a granulating liquid; drying and sizing the granules; and blending the granules with a lubricant and, optionally, other excipients such as fillers, and compressing to form a tablet.

5 In another embodiment, gatifloxacin tablets may be prepared by blending gatifloxacin and intragranular excipients such as filler, binder, wicking agent, and disintegrant; compacting or slugging the above blend; sizing the compacts or slugs to get granules; and blending the granules with a lubricant and optionally other excipients such as fillers and compressing to form a tablet.

10 In yet another embodiment, gatifloxacin tablets may be prepared by blending gatifloxacin and a wicking agent, such as silicon dioxide, colloidal silicon dioxide and sodium chloride, along with binders, fillers and disintegration aids, granulating the blend with a granulating liquid, drying and mixing the granules with lubricant and, optionally, fillers, and then compressing into tablets.

15 In still another embodiment, gatifloxacin tablets may be prepared by blending gatifloxacin, fillers, binders, wicking agents, and disintegrants, granulating the blend with a granulating liquid, drying and mixing the granules with sodium stearyl fumarate, and compressing into tablets.

20 In still another embodiment, gatifloxacin tablets may be prepared by blending gatifloxacin, fillers, binders, wicking agents and disintegration aids, granulating the blend with a granulating liquid, drying and mixing the granules with an extragranular water-soluble filler such as lactose, mannitol, dextrose, sorbitol or sucrose and a lubricant, and compressing into tablets.

25 In still another embodiment, the gatifloxacin solid oral dosage form may be prepared by blending gatifloxacin and ion exchange resin, binder, filler and wicking agent; granulating the blend with a granulating liquid; drying and mixing the granules with a lubricant; and compressing into tablets.

The tablets thus formed can additionally be coated with coating compositions such as Opadry® or Lustreclear® (sold by Colorcon) to impart aesthetic appeal. Such a coating may comprise up to about 3% w/w by weight of the tablet.

30 The invention described herein is further illustrated by the following examples, which should not be construed as limiting the scope of the invention.

Example 1

Ingredients	Quantity (mg)
Intragranular	
Gatifloxacin	400
Microcrystalline cellulose	135
Croscarmellose sodium	70
Povidone	14
Colloidal silicon dioxide	20
Mannitol	47
Purified Water	Q.S.
Extragranular	
Sodium Stearyl Fumarate	14
Total	700

- Procedure:** Gatifloxacin was blended with microcrystalline cellulose, croscarmellose sodium, povidone, colloidal silicon dioxide and mannitol. The above blend was
- 5 granulated with purified water. The granules were dried, sized, mixed with sodium stearyl fumarate, and compressed using appropriate tooling.

Example 2

Ingredients	Quantity (mg)
Intragranular	
Gatifloxacin	400
Microcrystalline cellulose	98
Croscarmellose sodium	70
Povidone	14
Colloidal silicon dioxide	40
Mannitol	40
Polacrillin potassium	14
Purified Water	Q.S.
Extragranular	
Sodium Stearyl Fumarate	24
Total	700

- Procedure:** Gatifloxacin was blended with microcrystalline cellulose, croscarmellose sodium, povidone, colloidal silicon dioxide, mannitol and polacrillin potassium. The
- 10 above blend was granulated with purified water. The granules were dried, sized, mixed with sodium stearyl fumarate, and compressed using appropriate tooling.

Example 3

Ingredients	Quantity (mg)
Intragranular	
Gatifloxacin	400
Microcrystalline cellulose	105
Croscarmellose sodium	70
Povidone	7
Colloidal silicon dioxide	40
Mannitol	40
Polacrillin potassium	14
Purified Water	Q.S.
Extragranular	
Lactose	20
Sodium Stearyl Fumarate	24
Total	720

- Procedure:** Gatifloxacin was blended with microcrystalline cellulose, croscarmellose sodium, povidone, colloidal silicon dioxide, mannitol and polacrillin potassium. The
- 5 above blend was granulated with purified water. The granules were dried, sized, mixed with lactose and sodium stearyl fumarate, and compressed using appropriate tooling.

Example 4

Ingredients	Quantity (mg)
Intragranular	
Gatifloxacin	400
Microcrystalline cellulose	98
Croscarmellose sodium	70
Povidone	7
Colloidal silicon dioxide	40
Mannitol	33
Polacrillin potassium	28
Purified Water	Q.S.
Extragranular	
Mannitol	20
Sodium Stearyl Fumarate	24
Total	720

- Procedure:** Gatifloxacin was blended with microcrystalline cellulose, croscarmellose
- 10 sodium, povidone, colloidal silicon dioxide, mannitol and polacrillin potassium. The above blend was granulated with purified water. The granules were dried, sized, mixed with mannitol and sodium stearyl fumarate, and compressed using appropriate tooling.

The tablets of Examples 1 – 4 were subjected to dissolution in a USP type II dissolution apparatus, at 50 rpm in 1000 ml of 0.1 N hydrochloric acid. The resulting dissolution profiles are given in Table 1.

5 Table 1: Dissolution profiles of the tablets of Examples 1 - 4 measured in a USP type II dissolution apparatus, at 50 rpm in 1000 ml of 0.1 N hydrochloric acid

Time (min)	% Drug Release			
	Example 1	Example 2	Example 3	Example 4
10	93	98	98	101
20	94	100	99	100
30	94	101	100	100
45	93	101	99	102
60	93	100	102	101

10 As illustrated in Table 1, between about 93% and about 100% of the gatifloxacin in the tablets of Examples 1 – 4 is released within 10 minutes. This indicates the effective dissolution of a gatifloxacin tablet formulated without using any disintegration aid in the extragranular phase.

15 While several particular forms of the inventions have been described, it will be apparent that various modifications and combinations of the inventions detailed in the text can be made without departing from the spirit and scope of the inventions. Accordingly, it is not intended that the inventions be limited, except as by the appended claims.

We Claim:

1. A solid oral dosage form comprising:
an intragranular phase comprising gatifloxacin and one or more of a filler, a binder, a wicking agent, and a disintegration aid, and
an extragranular phase, wherein the extragranular phase is free of any disintegration aid.
2. The oral dosage form according to claim 1 wherein the filler is selected from starch, dicalcium phosphate, calcium carbonate, lactose, mannitol, dextrose, sorbitol, sucrose, sodium chloride and combinations thereof.
3. The oral dosage form according to claim 1 wherein the binder is selected from polyvinylpyrrolidone, hydroxypropylmethylcellulose, hydroxypropylcellulose, starch mucilage, carbopols, gums, and combinations thereof.
4. The oral dosage form according to claim 1 wherein the wicking agent is selected from water soluble excipients, hydrophilic polymers, silicon dioxide, colloidal silicon dioxide, microcrystalline cellulose and combinations thereof.
5. The oral dosage form according to claim 4 wherein the wicking agent comprises a water soluble excipient.
6. The oral dosage form according to claim 5 wherein the water-soluble excipient comprises one or more of sodium chloride, sugar, and sugar alcohols.
7. The oral dosage form according to claim 6 wherein the sugar or sugar alcohol is selected from dextrose, mannitol, sorbitol, lactose, sucrose, and combinations thereof.
8. The oral dosage form according to claim 4 wherein the hydrophilic polymer is selected from croscarmellose sodium, crosslinked polyvinylpyrrolidone, starches, gums, hydroxymethylcellulose, hydroxypropylcellulose, hydroxypropylmethylcellulose, carbopol, and combinations thereof.
9. The oral dosage form according to claim 1 wherein the disintegration aid is selected from ion exchange resins, hydroxypropylcellulose, crospovidone, croscarmellose sodium, starches, pectins, alginates, surfactants, microcrystalline cellulose, sodium starch glycolate, and combinations thereof.
10. The oral dosage form according to claim 9 wherein the disintegration aid comprises croscarmellose sodium.
11. The oral dosage form according to claim 9 wherein the disintegration aid comprises an ion exchange resin.

12. The oral dosage form according to claim 11 wherein the ion exchange resin comprises polacrillin potassium.
13. The oral dosage form according to claim 1 wherein the extragranular phase further comprises one or more lubricants.
14. The oral dosage form according to claim 13 wherein the lubricant is selected from talc, polyethylene glycol, sodium chloride, stearic acid, calcium stearate, zinc stearate, magnesium stearate, sodium stearyl fumarate, and combinations thereof.
15. The solid dosage form according to 13 wherein the lubricant comprises a water soluble lubricant selected from one or more of sodium stearyl fumarate, polyethylene glycol, sodium chloride, and combinations thereof.
16. The solid dosage form according to claim 15 wherein the lubricant comprises sodium stearyl fumarate.
17. The oral dosage form according to claim 1 wherein the extragranular phase further comprises one or more water soluble fillers.
18. The oral dosage form according to claim 17 wherein the water soluble filler is selected from lactose, mannitol, dextrose, sorbitol, sucrose and sodium chloride.
19. The oral dosage form according to claim 1 wherein the oral dosage form comprises a tablet and the tablet includes an outer coating.
20. A process for the preparation of a solid oral dosage form, the process comprising:
 - blending gatifloxacin and one or more of fillers, binders, wicking agent and disintegration aids;
 - granulating the blend to form granules;
 - mixing the granules with an extragranular phase to form a mixture of the granules and the extragranular phase, the extragranular phase being free of any disintegration aid;
 - and
 - compressing the mixture into a solid dosage form.
21. The process according to claim 20 wherein the granulation comprises wet granulation.
22. The process according to claim 21 wherein the wet granulation comprises a granulating liquid selected from water, ethanol, isopropyl alcohol, acetone, dichloromethane, and a binder solution.
23. The process according to claim 20 wherein the granulation comprises dry granulation.

24. The process according to claim 23 wherein the dry granulation comprises compaction or slugging.
25. The process according to claim 24 wherein the dry granulation comprises compaction.
26. The process according to claim 20 wherein the filler is selected from starch, dicalcium phosphate, calcium carbonate, lactose, mannitol, dextrose, sorbitol, sucrose, sodium chloride and combinations thereof.
27. The process according to claim 20 wherein the binder is selected from polyvinylpyrrolidone, hydroxypropylmethylcellulose, hydroxypropylcellulose, starch mucilage, carbopols and gums.
28. The process according to claim 20 wherein the wicking agent is selected from water soluble excipient, hydrophilic polymers, silicon dioxide, colloidal silicon dioxide, microcrystalline cellulose, and combinations thereof.
29. The process according to claim 28 wherein the wicking agent comprises a water-soluble excipient.
30. The process according to claim 29 wherein the water-soluble excipient is selected from sodium chloride, sugar, sugar alcohols, and combinations thereof.
31. The process according to claim 20 wherein the disintegration aid is selected from ion exchange resins, hydroxypropylcellulose, crospovidone, croscarmellose sodium, starches, pectins, alginates, surfactants, microcrystalline cellulose, sodium starch glycolate, and combinations thereof.
32. The process according to claim 20 further comprising adding one or more of a lubricant and water soluble filler to the extragranular phase.
33. The process according to claim 20 further comprising coating the solid dosage form.
34. A method of treating infections and conditions for which gatifloxacin is indicated, the method comprising administering a solid dosage form comprising:
 - an intragranular phase comprising gatifloxacin and one or more of a filler, a binder, a wicking agent, and a disintegration aid; and
 - an extragranular phase, wherein the extragranular phase is free of any disintegration aid.

INTERNATIONAL SEARCH REPORT

International Application No

PCT/IB2004/002802

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61K31/496 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, WPI Data, PAJ, MEDLINE, EMBASE, BIOSIS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 6 291 462 B1 (BETZING JUERGEN ET AL) 18 September 2001 (2001-09-18) cited in the application examples 1-6 table 1	1-34
A	WO 01/12162 A (EGYT GYOGYSZERVEGYESZETI GYAR ; FELLNER GYOERGYNE (HU); GORA LASZLONE) 22 February 2001 (2001-02-22) page 7, last paragraph - page 9, paragraph 1; table III page 11, last paragraph - page 12, paragraph 2	1-34
A	EP 0 805 156 A (KYORIN SEIYAKU KK) 5 November 1997 (1997-11-05) page 3, lines 1-4	1-34
	-/--	

☒ 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.

Z document member of the same patent family

Date of the actual completion of the international search

18 January 2005

Date of mailing of the international search report

28/01/2005

Name and mailing address of the ISA

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Vermeulen, S

INTERNATIONAL SEARCH REPORT

International Application No
PCT/IB2004/002802

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>US 2002/052379 A1 (DAVIDOVICH MARTHA ET AL) 2 May 2002 (2002-05-02) paragraph '0004! paragraph '0034! example 4</p> <p>-----</p>	1-34

INTERNATIONAL SEARCH REPORT

International application No.
PCT/IB2004/002802

Box II Observations where certain claims were found unsearchable (Continuation of item 2 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:

Although claim 34 is directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

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

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

Remark on Protest

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

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/IB2004/002802

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
US 6291462	B1	18-09-2001	DE 19820801 A1	25-11-1999
			AT 235242 T	15-04-2003
			AU 753482 B2	17-10-2002
			AU 4035299 A	29-11-1999
			BR 9910350 A	25-09-2001
			CA 2325636 A1	18-11-1999
			CN 1300216 T	20-06-2001
			DE 59904737 D1	30-04-2003
			DK 1077703 T3	23-06-2003
			WO 9958129 A1	18-11-1999
			EP 1077703 A1	28-02-2001
			ES 2195573 T3	01-12-2003
			HK 1033281 A1	15-08-2003
			HU 0101597 A2	28-11-2001
			JP 2002514600 T	21-05-2002
			NO 20005385 A	26-10-2000
			NZ 507968 A	20-12-2002
			PL 343936 A1	10-09-2001
			PT 1077703 T	29-08-2003
			RU 2226394 C2	10-04-2004
			SI 1077703 T1	31-10-2003
			SK 16772000 A3	10-05-2001
			ZA 200006440 A	08-02-2002
WO 0112162	A	22-02-2001	HU 9902725 A2	28-12-2001
			AT 241967 T	15-06-2003
			AU 6716100 A	13-03-2001
			BG 106404 A	30-09-2002
			CZ 20020505 A3	12-06-2002
			DE 60003196 D1	10-07-2003
			DE 60003196 T2	29-04-2004
			EP 1207857 A1	29-05-2002
			HK 1046234 A1	19-03-2004
			HR 20020153 A2	31-12-2003
			WO 0112162 A1	22-02-2001
			PL 352331 A1	11-08-2003
			SK 2132002 A3	06-08-2002
EP 0805156	A	05-11-1997	JP 3449658 B2	22-09-2003
			JP 8176143 A	09-07-1996
			AT 216381 T	15-05-2002
			AU 694946 B2	06-08-1998
			AU 3994695 A	10-07-1996
			DE 69526453 D1	23-05-2002
			DE 69526453 T2	12-12-2002
			DK 805156 T3	06-05-2002
			EP 0805156 A1	05-11-1997
			US 5880283 A	09-03-1999
			CA 2208704 A1	27-06-1996
			CN 1171108 A ,C	21-01-1998
			ES 2173982 T3	01-11-2002
			HU 77945 A2	28-12-1998
			WO 9619472 A1	27-06-1996
			PT 805156 T	30-09-2002
			TW 393479 B	11-06-2000
US 2002052379	A1	02-05-2002	AU 8659201 A	26-03-2002
			BR 0113866 A	06-07-2004

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/IB2004/002802

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 2002052379 A1		CA 2422616 A1	21-03-2002
		EP 1326612 A1	16-07-2003
		HU 0300972 A2	29-09-2003
		JP 2004508403 T	18-03-2004
		WO 0222126 A1	21-03-2002
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