

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44bis)

Applicant's or agent's file reference HAR056-PCT	FOR FURTHER ACTION		See item 4 below
International application No. PCT/EP2015/060257	International filing date (<i>day/month/year</i>) 08 May 2015 (08.05.2015)	Priority date (<i>day/month/year</i>) 12 May 2014 (12.05.2014)	
International Patent Classification (8th edition unless older edition indicated) See relevant information in Form PCT/ISA/237			
Applicant TEVA PHARMACEUTICALS EUROPE B.V.			

<p>1. This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 bis.1(a).</p> <p>2. This REPORT consists of a total of 7 sheets, including this cover sheet.</p> <p>In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead.</p>																								
<p>3. This report contains indications relating to the following items:</p> <table> <tr> <td><input checked="" type="checkbox"/></td> <td>Box No. I</td> <td>Basis of the report</td> </tr> <tr> <td><input type="checkbox"/></td> <td>Box No. II</td> <td>Priority</td> </tr> <tr> <td><input type="checkbox"/></td> <td>Box No. III</td> <td>Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</td> </tr> <tr> <td><input type="checkbox"/></td> <td>Box No. IV</td> <td>Lack of unity of invention</td> </tr> <tr> <td><input checked="" type="checkbox"/></td> <td>Box No. V</td> <td>Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</td> </tr> <tr> <td><input type="checkbox"/></td> <td>Box No. VI</td> <td>Certain documents cited</td> </tr> <tr> <td><input type="checkbox"/></td> <td>Box No. VII</td> <td>Certain defects in the international application</td> </tr> <tr> <td><input checked="" type="checkbox"/></td> <td>Box No. VIII</td> <td>Certain observations on the international application</td> </tr> </table> <p>4. The International Bureau will communicate this report to designated Offices in accordance with Rules 44bis.3(c) and 93bis.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44bis .2).</p>	<input checked="" type="checkbox"/>	Box No. I	Basis of the report	<input type="checkbox"/>	Box No. II	Priority	<input type="checkbox"/>	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability	<input type="checkbox"/>	Box No. IV	Lack of unity of invention	<input checked="" type="checkbox"/>	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement	<input type="checkbox"/>	Box No. VI	Certain documents cited	<input type="checkbox"/>	Box No. VII	Certain defects in the international application	<input checked="" type="checkbox"/>	Box No. VIII	Certain observations on the international application
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	Date of issuance of this report 15 November 2016 (15.11.2016)
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PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

PCT

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY
(PCT Rule 43bis.1)**

To:

see form PCT/ISA/220

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.
PCT/EP2015/060257

International filing date (day/month/year)
08.05.2015

Priority date (day/month/year)
12.05.2014

International Patent Classification (IPC) or both national classification and IPC
INV. A61K31/167 A61K31/58 A61K9/00 A61P11/00 A61P11/08 A61P43/00

Applicant
TEVA PHARMACEUTICALS EUROPE B.V.

1. This opinion contains indications relating to the following items:

- Box No. I Basis of the opinion
- Box No. II Priority
- Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- Box No. IV Lack of unity of invention
- Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step and industrial applicability; citations and explanations supporting such statement
- Box No. VI Certain documents cited
- Box No. VII Certain defects in the international application
- Box No. VIII Certain observations on the international application


2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

Name and mailing address of the ISA:




European Patent Office
P.B. 5818 Patentlaan 2
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Date of completion of this opinion

see form
PCT/ISA/210

Authorized Officer

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Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of:
 - the international application in the language in which it was filed.
 - a translation of the international application into , which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1 (b)).
2. This opinion has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43bis.1(a))
3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, this opinion has been established on the basis of a sequence listing:
 - a. forming part of the international application as filed:
 - in the form of an Annex C/ST.25 text file.
 - on paper or in the form of an image file.
 - b. furnished together with the international application under PCT Rule 13ter.1(a) for the purposes of international search only in the form of an Annex C/ST.25 text file.
 - c. furnished subsequent to the international filing date for the purposes of international search only:
 - in the form of an Annex C/ST.25 text file (Rule 13ter.1(a)).
 - on paper or in the form of an image file (Rule 13ter.1(b) and Administrative Instructions, Section 713).
4. In addition, in the case that more than one version or copy of a sequence listing has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that forming part of the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
5. Additional comments:

Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	
	No: Claims	<u>1-12</u>
Inventive step (IS)	Yes: Claims	
	No: Claims	<u>1-12</u>
Industrial applicability (IA)	Yes: Claims	<u>1-12</u>
	No: Claims	

2. Citations and explanations

see separate sheet

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

Cited Prior Art

- D1 Prescribing Information: Symbicort Turbohaler 200/6 (XP 055193843) D5 US 2005/042175 A1
- D2 Prescribing Information: Symbicort Turbohaler 400/12 (XP 055193849) D6 EP 1 086 697 A2
- D3 *Eur. Resp. J.* 2003, **22**(6), 912 D7 WO 93/11773 A1
- D4 EP 2 682 102

Section V

- 1 Claims 1-12 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 39.1(iv) / 67.1(iv) PCT. Patentability can be dependent upon the formulation of the claims. The EPO, for example, does not recognise as patentable claims to the use of a compound in medical treatment, but may allow claims to a product, in particular substances or compositions for use in a first or further medical treatment.

Patentability of claims 1-12, in particular novelty and inventive step, has been assessed on the basis of a purpose-limited product claim taking into account the alleged effects of the compound/composition.

- 2 Claims 1-12 do not meet the requirements of Art. 33(2) PCT.

D1 discloses fixed-dose compositions of formoterol fumarate dihydrate and budesonide, as dry powder inhalations having a lactose carrier. The delivered dose of budesonide is 160 mcg/inhalation whilst that of formoterol fumarate dihydrate is 4.5 mcg/inhalation (see Section 2). The compositions are for use in the treatment of chronic obstructive pulmonary disease (COPD), both long-term (maintenance dose) and of repeated exacerbations (*pro re nata* or *p.r.n.*). For adults, the recommended daily dose is *b.i.d.* and not more than six doses should be taken on any single occasion. See Section 4.

D2 discloses the same as D1, but having a delivered dose of budesonide is 320 mcg/inhalation whilst that of formoterol fumarate dihydrate is 9 mcg/inhalation.

D3 discloses maintenance therapy of COPD using Symbicort® inhalers according to D2 as a single inhaler.

D4, which is relevant to claims 1-6, discloses inhalation compositions comprising budesonide and formoterol fumarate dihydrate for once/twice daily administration in the treatment of COPD.

D5, which is relevant to claims 1 and 4-12, discloses dry powder inhalation compositions comprising budesonide and formoterol fumarate dihydrate for once/twice daily administration in the treatment of COPD.

See the passages cited in the International Search Report.

- 3 The application does not meet the requirements of Art. 33(3) PCT, when taken alone or in combination with Art. 5 and 6 PCT.
- 3.1 Not being novel, the subject-matter of claims 1-12 cannot be seen as being inventive.
- 3.2 Compositions of budesonide and formoterol fumarate in the amounts claimed in the present application are known for the treatment of COPD. Variations of dose and administration frequency, including maximum doses, and their determination, would be obvious within the normal work of the skilled person and hence cannot be seen as involving an inventive step. Moreover, the use of a different inhaler device (*cf.* Example 1) would not appear to render inventive the subject-matter of the application.
- 3.3 The application as filed does not appear to demonstrate any novel or inventive technical effect. Indeed, the therapeutic example presented in the description (Example 2) would appear to be merely speculative in nature (*cf.* Rule 67.1(i) PCT) and does not provide evidence of the solution to a technical problem, nor indeed does it even state a technical problem to be solved. Thus, this Example describes *on-going* clinical studies, '*...investigating whether symptom-driven maintenance and reliever/rescue therapy with budesonide/formoterol is more effective as a single device dual treatment regimen that manages and also concomitantly reduces the number of exacerbations of COPD compared to a multiple device fixed maintenance dose of fluticasone/salmeterol and salbutamol as a rescue medication*'. However, it should be noted that in order to establish an inventive step, comparisons must be made with the closest prior art available. In the present case, this would not be '*a multiple device fixed maintenance dose of fluticasone/salmeterol and salbutamol*', but rather the combinations of any one of D1 - D3.

The Applicant should also be aware that in some Regional/National procedures, a technical problem and its solution cannot be used to demonstrate inventive step if this problem/solution is not immediately and unambiguously derivable from the application documents as originally filed.

Section VIII

- 4 Claim 1 does not meet the requirements of Art. 6 PCT because the following expressions are vague and indefinite, and do not appear to have well-defined and accepted meanings within the art:

'long-term treatment';

'acute exacerbations of COPD';

'a maintenance dose'.