# PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

# PCT

## WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

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. | International filing date *(day/month/year)* | Priority date *(day/month/year)* |
|---|---|---|
| PCT/EP2015/060257 | 08.05.2015 | 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 43*bis*.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 notifed the International Bureau under Rule 66.1*bis*(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: | Date of completion of this opinion | Authorized Officer |
|---|---|---|
| European Patent Office<br>P.B. 5818 Patentlaan 2<br>NL-2280 HV Rijswijk - Pays Bas<br>Tel. +31 70 340 - 2040<br>Fax: +31 70 340 - 3016 | see form PCT/ISA/210 | Telephone No. +31 70 340-0 |

**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 43*bis*.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 13*ter*.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 13*ter*.1(a)).

      ☐ on paper or in the form of an image file (Rule 13*ter*.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 43*bis*.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 | 1-12 |
| Inventive step (IS) | Yes: | Claims | |
| | No: | Claims | 1-12 |
| Industrial applicability (IA) | Yes: | Claims | 1-12 |
| | 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)

D2 Prescribing Information: Symbicort Turbohaler 400/12 (XP 055193849)

D3 *Eur. Resp. J.* 2003, **22**(6), 912

D4 EP 2 682 102

D5 US 2005/042175 A1

D6 EP 1 086 697 A2

D7 WO 93/11773 A1

## 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 clams 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 clams 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*'.