

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

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PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.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.
PCT/EP2022/055521

International filing date (day/month/year)
04.03.2022

Priority date (day/month/year)
09.03.2021

International Patent Classification (IPC) or both national classification and IPC
INV. A61P7/02 C07D401/10 A61K31/4439

Applicant
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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.

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this opinion

see form
PCT/ISA/210

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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:

see separate sheet

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	<u>4-6, 8-10, 12</u>
	No: Claims	<u>1-3, 7, 11</u>
Inventive step (IS)	Yes: Claims	<u>4-6, 8-10, 12</u>
	No: Claims	<u>1-3, 7, 11</u>
Industrial applicability (IA)	Yes: Claims	<u>1-12</u>
	No: Claims	

2. Citations and explanations

see separate sheet

Re Item I

Basis of the report

- A crystalline form of a compound of formula (I) according to independent claim 1.
- Process for preparing the crystalline modification I of the compound of formula (I) using a seed of the crystalline modification A of the compound of formula (II), according to claim 8.
- Process for preparing the crystalline modification II of the compound of formula (I) by drying in an oven, according to claim 11.
- A compound of formula (II), according to claim independent claim 12.

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Reference is made to the following documents:

- D1 WO 2019/175043 A1 (BAYER AG [DE]; BAYER PHARMA AG [DE]) 19 September 2019 (2019-09-19) cited in the application
- D2 WO 2017/005725 A1 (BAYER PHARMA AG [DE]) 12 January 2017 (2017-01-12) cited in the application
- D3 WO 2020/126682 A1 (BAYER AG [DE]) 25 June 2020 (2020-06-25)

V.1 Novelty

1.1 The crystalline modification form I or form II of a compound of formula (I) is validly characterized only by the specific X-ray powder diffraction values according to claim 2 or 3. The term "form I or II" used in claim 1 is just considered as a label and not as a valid technical feature.

Furthermore claims 4 and 5 characterize the respective form via the Raman spectroscopy values.

1.2 Unfortunately, document D1, page 30, third column anticipates the values given in claims 2 and 3 considering the $\pm 0.2^\circ$ deviation margin.

Claims 1 to 3 are therefore anticipated by the relevant disclosure of D1. In this regard, it is worth noting that the presence of residual solvent is not excluded in main claim 1 as well as dependent claims 2 to 3 anticipated by D1 solvated form (IIc).

D2 and D3 do not sufficiently characterize the solid state of the compounds provided, among which also compound of claimed formula (I).

1.3 As a matter of fact, no compound of formula (II) according to current claim 12, i.e. the compound that is employed in the process of current claims 8 to 10, could be retrieved from the available prior art.

1.4 Dependent claims 4 to 7, 8 to 10 and compound claim 12 are new over the disclosures of documents d1 to D3.

Thus, the subject-matter of at least claims 1 to 3 and claim 11 appears not to be novel in the sense of Article 33(2) PCT.

V.2 Inventive Step

2.1 Prior art document D1, which can be regarded as the closest prior art to the present application, discloses the preparation of the compounds (IIa) to (IIc). As previously mentioned, the present application, claims 1 to 3, does not differ from D1 formula (IIc). The relevant document further describes the drying of the solvates provided (see claim 5 of D1).

2.1.1 The problem to be solved by the present application could be regarded as the provision of further crystalline forms via, in part, an alternative process for the preparation of compound (I), crystalline modification (I) using the seed of a compound as defined in claim 8.

2.2 Novelty is not recognized and, consequently, no definitive opinion on inventive step can be offered.

The working examples seem to indicate that the processes of current claims 8-11 actually solve the technical problem of providing the further crystalline forms.

However, the whole disclosure in the prior art D1 would have prompted the skilled person to arrive at compounds which are not solvated, D1 suggests at least how to arrive at the essential step of current claim 11.

The preparation process of current claim 8 appears to meet the requirements of Article 33(3) PCT and so does the synthetic seeding intermediate of current claim 12 that is useful in said specific process.