

From the INTERNATIONAL BUREAU

PCTNOTIFICATION CONCERNING
TRANSMITTAL OF COPY OF INTERNATIONAL
PRELIMINARY REPORT ON PATENTABILITY
(CHAPTER I OF THE PATENT COOPERATION
TREATY)

(PCT Rule 44bis.1(c))

To:

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Date of mailing (<i>day/month/year</i>) 23 July 2020 (23.07.2020)		
Applicant's or agent's file reference 143989.04402		IMPORTANT NOTICE
International application No. PCT/IB2019/000017	International filing date (<i>day/month/year</i>) 09 January 2019 (09.01.2019)	Priority date (<i>day/month/year</i>) 09 January 2018 (09.01.2018)
Applicant DERMAVANT SCIENCES GMBH		

The International Bureau transmits herewith a copy of the international preliminary report on patentability (Chapter I of the Patent Cooperation Treaty)

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No. +41 22 338 82 70	Authorized officer Cécile Chatel e-mail: ro.ib@wipo.int
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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 143989.04402	FOR FURTHER ACTION	See item 4 below
International application No. PCT/IB2019/000017	International filing date (<i>day/month/year</i>) 09 January 2019 (09.01.2019)	Priority date (<i>day/month/year</i>) 09 January 2018 (09.01.2018)
International Patent Classification (8th edition unless older edition indicated) See relevant information in Form PCT/ISA/237		
Applicant DERMAVANT SCIENCES GMBH		

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).																								
2.	This REPORT consists of a total of 13 sheets, including this cover sheet. 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.																								
3.	This report contains indications relating to the following items: <table style="width: 100%; border: none;"> <tr> <td style="width: 10%; text-align: center;">☒</td> <td style="width: 30%;">Box No. I</td> <td style="width: 80%;">Basis of the report</td> </tr> <tr> <td style="text-align: center;">☐</td> <td>Box No. II</td> <td>Priority</td> </tr> <tr> <td style="text-align: center;">☐</td> <td>Box No. III</td> <td>Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</td> </tr> <tr> <td style="text-align: center;">☒</td> <td>Box No. IV</td> <td>Lack of unity of invention</td> </tr> <tr> <td style="text-align: center;">☒</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 style="text-align: center;">☒</td> <td>Box No. VI</td> <td>Certain documents cited</td> </tr> <tr> <td style="text-align: center;">☒</td> <td>Box No. VII</td> <td>Certain defects in the international application</td> </tr> <tr> <td style="text-align: center;">☒</td> <td>Box No. VIII</td> <td>Certain observations on the international application</td> </tr> </table>	☒	Box No. I	Basis of the report	☐	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 Article 35(2) with regard to novelty, inventive step or 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
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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).																								

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No. +41 22 338 82 70	<table style="width: 100%; border: none;"> <tr> <td style="width: 50%;">Date of issuance of this report 14 July 2020 (14.07.2020)</td> <td style="width: 50%;">Authorized officer Cécile Chatel</td> </tr> <tr> <td colspan="2">e-mail: ro.ib@wipo.int</td> </tr> </table>	Date of issuance of this report 14 July 2020 (14.07.2020)	Authorized officer Cécile Chatel	e-mail: ro.ib@wipo.int	
Date of issuance of this report 14 July 2020 (14.07.2020)	Authorized officer Cécile Chatel				
e-mail: ro.ib@wipo.int					

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.
PCT/IB2019/000017

International filing date (day/month/year)
09.01.2019

Priority date (day/month/year)
09.01.2018

International Patent Classification (IPC) or both national classification and IPC
INV. A61K9/00 A61K47/08 A61K47/10 A61K9/06 A61K47/38 A61K31/506

Applicant
DERMAVANT SCIENCES GMBH

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 notified 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:



European Patent Office
P.B. 5818 Patentlaan 2
NL-2280 HV Rijswijk - Pays Bas
Tel. +31 70 340 - 2040
Fax: +31 70 340 - 3016

Date of completion of
this opinion

see form
PCT/ISA/210

Authorized Officer

Konter, Jörg

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. IV Lack of unity of invention

1. ☒ In response to the invitation (Form PCT/ISA/206) to pay additional fees, the applicant has, within the applicable time limit:
- ☒ paid additional fees
 - ☐ paid additional fees under protest and, where applicable, the protest fee
 - ☐ paid additional fees under protest but the applicable protest fee was not paid
 - ☐ not paid additional fees
2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose not to invite the applicant to pay additional fees.
3. This Authority considers that the requirement of unity of invention in accordance with Rule 13.1, 13.2 and 13.3 is
- ☐ complied with
 - ☒ not complied with for the following reasons:
see separate sheet
4. Consequently, this report has been established in respect of the following parts of the international application:
- ☒ all parts.
 - ☐ the parts relating to claims Nos.

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>1-45, 50-53</u>
	No: Claims	<u>46-49, 54-61</u>
Inventive step (IS)	Yes: Claims	
	No: Claims	<u>1-61</u>
Industrial applicability (IA)	Yes: Claims	<u>1-61</u>
	No: Claims	

2. Citations and explanations

see separate sheet

Box No. VI Certain documents cited

1. Certain published documents (Rules 43*bis*.1 and 70.10)

and / or

2. Non-written disclosures (Rules 43*bis*.1 and 70.9)

see form 210

Box No. VII Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

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

Re Item IV

Lack of unity of invention

This Authority considers that the application does not meet the requirements of unity of invention and that there are 2 inventions covered by the claims indicated as follows:

The reasons for which the inventions are not so linked as to form a single general inventive concept, as required by Rule 13.1 PCT, are as follows:

Claims 1-45 disclose pharmaceutical compositions suitable for topical use comprising cerdulatinib, polyalkylene glycol and propylene glycol.

Claims 46-61 disclose methods of treating a dermatological disorder comprising topically administering a therapeutically effective amount of cerdulatinib.

The common matter linking together the independent claims 1,28,42-45 and claims 46-47 is the following: Cerdulatinib suitable for topical administration.

This common matter does not comprise a single general inventive concept, based on same or corresponding special technical features within the meaning of Rule 13.2 PCT, because document D1 (WO 2017/096303) discloses cerdulatinib suitable for topical administration (claim 1; page 17, lines 15-27).

Accordingly, the single general concept applying to all the claims is already known and therefore does not represent a single general inventive concept.

Furthermore, the claims are also not linked by the same or corresponding technical feature. Claims 1,28,42-45 disclose polyalkylene glycol and propylene glycol as special technical feature, claims 46-47 disclose treating a dermatological disorder as special technical feature. These technical features are obviously not the same and also do not correspond by providing the same effect.

Hence, the following separate inventions or groups of inventions are not so linked as to form a single general inventive concept:

Invention I (Claims 1-45): Pharmaceutical compositions suitable for topical use comprising cerdulatinib, polyalkylene glycol and propylene glycol.

Invention II (Claims 46-61): Methods of treating a dermatological disorder comprising topically administering a therapeutically effective amount of cerdulatinib.

The applicant has paid the additional fees and requested the search to be carried out for all the claims with the letter dated 03.06.2019.

I. Invention I (Claims 1-45): Pharmaceutical compositions suitable for topical use comprising cerdulatinib, polyalkylene glycol and propylene glycol.

Re Item V

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

1. Reference

Reference is made to the following documents:

- D1 WO 2017/096303 A2 (PORTOLA PHARM INC [US]) 8 June 2017
 (2017-06-08)
- D2 WO 2017/027829 A1 (PORTOLA PHARM INC [US]) 16 February 2017
 (2017-02-16)

2. Novelty

The subject-matter of claims 1-45 is new in the sense of Article 33(2) PCT.

3. Inventive Step

The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claims 1-45 does not involve an inventive step in the sense of Article 33(3) PCT.

3.1 Document D1 (WO 2017/096303) discloses cerdulatinib suitable for topical administration (claim 1; page 17, lines 15-27).

3.2 Present claim 1 differs over D1 in that: i) the carrier is polyalkylene glycol having an average molecular weight of from 100 Da to 10000 Da and ii) that propylene glycol is present.

3.3 There is no effect as a result of this difference.

Examples 1, 2,5-8 of the application relate to pharmacodynamic effects and efficacy not related to the differences of claim 1 over the prior art.

Example 3 is a skin permeation study which discloses multiple formulations, also comparative samples not disclosing e.g. propylene glycol (see table 2, "NA79"). There are no conclusions which can be drawn from this comparison.

Example 4 discloses that all formulations are stable, which also does not show any unexpected effect from the differences over the prior art.

3.4 The problem to be solved by claim 1 is thus to provide an alternative pharmaceutical composition suitable for topical use comprising cerdulatinib.

3.5 The solution to this problem offered by present claim 1 is obvious for the following reasons. Polyalkylene glycol according to claim 1, such as e.g. PEG 400, and propylene glycol are well known excipients in topical formulations (see e.g. Handbook of Pharmaceutical Excipients; not cited in the search report). Using these to provide alternative topical formulations is obvious to the skilled person using only common general knowledge.

Additionally, document D2 (WO2017/027829) discloses that propylene glycol is suitable to modify the ionic strength of cerdulatinib (page 16, line 22) and that its solubility can also be enhanced using PEGs or propylene glycol (page 16, lines 25-29).

3.6 The same arguments apply to the lacking inventiveness of the remaining claims.

The examples of the application do not disclose any unexpected effect related to PEG molecular weight modification, addition of Transcutol HP or antioxidants, variations in the dose of active, glycerol or hydroxypropyl cellulose addition. The claims are thus at best further obvious alternatives. Several features of these claims are also directly known from the prior art, such as the addition of preservatives, BHT, variation in active concentration, etc., rendering the subject-matter of claims 2-45 obvious alternatives.

3.7 Should the Applicant recognize an improved effect over the prior art, the nature of the comparison with the closest state of the art must be such that said effect is convincingly shown to have its origin in the distinguishing feature. The discussion concerning this effect is to be based with reference to the present application, citing the appropriate passages.

Any reasoning for the presence of an inventive step should be given using the problem-solution approach.

All alternatives of a claim should solve the technical problem underlying the claimed invention.

4. Industrial Applicability

The subject-matter of claims 1-45 meets the criteria for industrial applicability according to Article 33(4) PCT.

Re Item VII

Certain defects in the international application

1. Contrary to the requirements of Rule 5.1(a)(ii) PCT, the relevant background art disclosed in the documents cited herein is not mentioned in the description, nor are these documents identified therein.

2. The attention to the applicant is drawn to the following:

The use of the expression "... incorporated by reference..." is not allowed in some designated Contracting States. When entering the Regional/National phase these expressions should be deleted from the application.

Re Item VIII

Certain observations on the international application

1. Although claims 1,28,42,43,44,45 have been drafted as separate independent claims, they appear to relate effectively to the same subject-matter and to differ from each other only with regard to the definition of the subject-matter for which protection is sought and/or in respect of the terminology used for the features of that subject-matter. The aforementioned claims therefore lack conciseness and as such do not meet the requirements of Article 6 PCT.

2. The term "Transcutol HP" employed in the claims is a registered trade mark and has no precise meaning as it is not internationally accepted as a standard descriptive term, thereby rendering the definition of the subject-matter of this claim unclear, Article 6 PCT.

II. Invention II (Claims 46-61): Methods of treating a dermatological disorder comprising topically administering a therapeutically effective amount of cerdulatinib.

Re Item V

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

1. Reference

Reference is made to the following documents:

- D3 WO 2016/179605 A1 (UNIV COLUMBIA [US]) 10 November 2016 (2016-11-10)
- D4 DAMSKY WILLIAM ET AL: "JAK inhibitors in dermatology: The promise of a new drug class", JOURNAL OF THE AMERICAN ACADEMY OF DERMATOLOGY, MOSBY, INC, US, vol. 76, no. 4, 28 January 2017 (2017-01-28), pages 736-744, XP029945995, ISSN: 0190-9622, DOI: 10.1016/J.JAAD.2016.12.005
- D5 WO 2018/200786 A1 (UNIV YALE [US]; UNIV MASSACHUSETTS [US]) 1 November 2018 (2018-11-01)
- D6 VARIOUS: "Abstracts", EXPERIMENTAL DERMATOLOGY, vol. 27, no. S2, 1 December 2018 (2018-12-01), pages 3-58, XP55582555, COPENHAGEN; DK ISSN: 0906-6705, DOI: 10.1111/exd.13795

2. Novelty

The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claims 46-49,54-61 is not new in the sense of Article 33(2) PCT.

2.1 Document D3 (WO 2016/179605) discloses a method of inducing hair growth in a mammal. Treatment of alopecia areata and atopic dermatitis (claims 1-7).

Note that the selection of cerdulatinib in claim 7 of D3 is from a single list.

Note that present claims 60 and 61 of the application are results to be achieved rather than technical or functional features. Since the subject-matter is otherwise identical to the disclosure of D3, it can only be concluded that the results are achieved in the prior art as well.

The subject-matter of claims 46-49,54-61 is not new in the sense of Article 33(2) PCT.

3. Inventive Step

The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claims 46-61 does not involve an inventive step in the sense of Article 33(3) PCT.

3.1 Lacking novelty, claims 46-49,54-61 are not inventive.

3.2 Present claim 50 differs over D1 in that the dermatological disorder is chronic urticaria.

3.3 There is no effect as a result of this difference. It is noted that none of the examples in the application disclose an effect in view of the treatment of chronic urticaria.

3.4 The problem to be solved is thus to provide an alternative method for treating a dermatological disorder.

3.5 A method of treating chronic urticaria with cerdulatinib is obvious in view of common general knowledge.

Document D4 (Damsky et al) is a review article and therefore is considered to qualify as common general knowledge. It discloses JAK inhibitors and their use in dermatological disorders such as atopic dermatitis, alopecia areata, psoriasis, vitiligo and others (abstract). Since cerdulatinib is known to be a JAK inhibitor, the skilled person has reasonable expectation of success when using cerdulatinib in a method of the mentioned diseases.

Present claim 50 is thus not inventive.

3.6 The same arguments apply to the lacking inventiveness of claims 51-53.

3.7 Should the Applicant recognize an improved effect over the prior art, the nature of the comparison with the closest state of the art must be such that said effect is convincingly shown to have its origin in the distinguishing feature. The discussion concerning this effect is to be based with reference to the present application, citing the appropriate passages.

Any reasoning for the presence of an inventive step should be given using the problem-solution approach.

All alternatives of a claim should solve the technical problem underlying the claimed invention.

4. Industrial Applicability

The subject-matter of claims 46-61 meets the criteria for industrial applicability according to Article 33(4) PCT.

5. Remaining Objections / Remarks

The subject-matter of claims 46-61 refers to the use of compositions for the treatment of the human or animal body by surgery, therapy or diagnostic methods practiced on the human or animal body. The 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.

Re Item VI

Certain documents cited

Documents D5 (WO 2018/200786) and D6 (Piscitelli et al and Azzolino et al) may become relevant in the national/regional phase.

D5 discloses treating vitiligo with cerdulatinib (claims 1 and 2).

D6 discloses cerdulatinib as agent in the treatment of atopic dermatitis (Abstract 103 on page 44) and cerdulatinib as agent in the treatment of vitiligo (Abstract 104 on page 45)

It is noted that a priority document is not on file at the date of this search report. To fully assess the relevance of the documents cited herein, the validity of the priority must be checked.

Re Item VII

Certain defects in the international application

1. Contrary to the requirements of Rule 5.1(a)(ii) PCT, the relevant background art disclosed in the documents cited herein is not mentioned in the description, nor are these documents identified therein.

2. The attention to the applicant is drawn to the following:

The use of the expression "... incorporated by reference..." is not allowed in some designated Contracting States. When entering the Regional/National phase these expressions should be deleted from the application.

Re Item VIII

Certain observations on the international application

1. Although claims 46,47 have been drafted as separate independent claims, they appear to relate effectively to the same subject-matter and to differ from each other only with regard to the definition of the subject-matter for which protection is sought and/or in respect of the terminology used for the features of that subject-matter. The aforementioned claims therefore lack conciseness and as such do not meet the requirements of Article 6 PCT.