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14 December 2017 (14.12.2017)

(54) Title: A PROCESS FOR THE PREPARATION OF A SALT OF SACUBITRIL AND VALSARTAN

(57) Abstract: The present invention provides a process for the preparation of a salt of sacubitril and valsartan. Specifically, the present invention provides a process for the preparation of a sodium salt of sacubitril and valsartan.



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INTERNATIONAL SEARCH REPORT

International application No.

PCT/IB17/52672

A. CLASSIFICATION OF SUBJECT MATTER

IPC - A61K 9/14, 31/216, 31/41 (2017.01)

CPC - A61K 9/14, 31/216, 31/41

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)

See Search History document

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

See Search History document

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

See Search History document

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2007/056546 A1 (NOVARTIS AG) 18 May 2007; page 2, paragraph [4]; page 3, paragraphs [1], [3]; page 8, paragraph [1]; page 9, paragraphs [2], [4]-[5]; page 13, paragraphs [4]-[5]; page 15, paragraph [3]; page 18, paragraph [1]; page 19, paragraph [2]; page 21, paragraph [4]; page 38, paragraph [3]; page 43, paragraphs [3]-[7]	1, 3-4, 13-16 ----- 2
Y	US 2013/0109729 A1 (NOVARTIS AG) 02 May 2013; claims 11-13	2
A	FENG, L et al. 'LCZ696: a dual-acting sodium supramolecular complex'; 18 January 2012, Tetrahedron Letters; Volume 53, Issue 33, pages 275-276; entire document	1-4, 13-16
P, X	WO 2017/042700 A1 (SUN PHARMACEUTICAL INDUSTRIES LIMITED) 16 March 2017; entire document	1-4, 13-16

☐ Further documents are listed in the continuation of Box C.☐ See patent family 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 application or patent 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

"&" document member of the same patent family

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INTERNATIONAL SEARCH REPORT

International application No.

PCT/IB17/52672

Box No. 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:

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 No. 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:

---Please See Within the Next Supplemental Box---

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 additional fees, this Authority did not invite payment of additional fees.
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.:
1-16 (in-part)

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
- ☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/IB17/52672

-Continued from Box No. III Observations where unity of invention is lacking-

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Groups I+, Claims 1-16 (in-part); a process for the preparation of a sodium salt of sacubitril and valsartan, wherein the process comprises treating sacubitril and valsartan with a sodium salt of an organic acid in a solvent, wherein the solvent is water.

The compound, compositions and methods will be searched to the extent the compound encompasses a process for the preparation of a sodium salt of sacubitril and valsartan, wherein the process comprises treating sacubitril and valsartan with a sodium salt of an organic acid in a solvent selected from water (first exemplary solvent). Applicant is invited to elect additional solvent(s), with fully specified solvent (e.g. no optional or variable solvents) for each, to be searched. Additional solvent(s) will be searched upon the payment of additional fees. It is believed that claims 1 (in-part), 2 (in-part), 3 (in-part), 4 (in-part), 13 (in-part), 14 (in-part), 15 (in-part), and 16 (in-part) encompass this first named invention and thus these claims will be searched without fee to the extent that they encompass a process for the preparation of a sodium salt of sacubitril and valsartan, wherein the process comprises treating sacubitril and valsartan with a sodium salt of an organic acid in a solvent, wherein the solvent is water (first exemplary solvent). Applicants must specify the claims that encompass any additionally elected solvent(s). Applicants must further indicate, if applicable, the claims which encompass the first named invention, if different than what was indicated above for this group. Failure to clearly identify how any paid additional invention fees are to be applied to the "+" group(s) will result in only the first claimed invention to be searched/examined. An exemplary election would be a process for the preparation of a sodium salt of sacubitril and valsartan, wherein the process comprises treating sacubitril and valsartan with a sodium salt of an organic acid in a solvent, wherein the solvent is an aromatic hydrocarbon (first exemplary elected solvent).

Groups I+ share the technical features including: a process for the preparation of a sodium salt of sacubitril and valsartan, wherein the process comprises treating sacubitril and valsartan with a sodium salt of an organic acid in a solvent, wherein the solvent is water.

However, these shared technical features are previously disclosed by WO 2007/056546 A1 (NOVARTIS AG) (hereinafter 'Novartis').

Novartis discloses a process for the preparation of a sodium salt of sacubitril and valsartan (process of producing a supramolecular complex comprising an angiotensin receptor antagonist, such as Valsartan, and a neutral endopeptidase inhibitor, such as formula II (sacubitril), both formulated as sodium salts; page 2, paragraph [4]; page 3, paragraphs [1], [3]; page 13, paragraph [5]; page 15, paragraph [3]; page 18, paragraph [1]; page 19, paragraph [2]), wherein the process comprises treating sacubitril and valsartan with a sodium salt of an organic acid in a solvent (process comprises dissolving angiotensin receptor antagonist, such as Valsartan, and a neutral endopeptidase inhibitor, such as formula II (sacubitril), in a solvent with a basic compound of (Cat)HCO₃, wherein Cat is Na (sodium salt of organic acid); page 8, paragraph [1]; page 13, paragraph [4]; page 18, paragraph [1]), wherein the solvent is water (solvent is water; page 9, paragraph [5]; page 21, paragraph [4]).

Since none of the special technical features of the Groups I+ inventions is found in more than one of the inventions, and since all of the shared technical features are previously disclosed by the Novartis reference, unity of invention is lacking.