STATE INTELLECTUAL PROPERTY OFFICE OF THE P. R. CHINA

EXAMINATION REPORT

Under Memorandum of Understanding between GCC and SIPO

SIPO's Reference No.: GCC/CN2010/000221
Filing date (day/month/year) 12 Feb. 2005 (12.02.2005)

FOR FURTHER ACTION Please refer to the Memorandum of Understanding.

Application No.: GCC/P/2005/4293
Time validity of Priority Yes No, See also Box No. II

International Patent Classification (IPC) or national classification and IPC
See Supplemental Box

Applicant Les Laboratoires Servier

1. This report is the FIRST examination report, established by the SIPO (hereinafter referred to as “the Authority”) and transmitted to the GCCPO under the Memorandum of Understanding between the GCC and the SIPO.

2. This REPORT consists of a total of 6 sheets, including this cover sheet.
☐ It is also accompanied by a copy of each prior art document cited in this report (See Form GCC/SIPO/611).

3. This report is also accompanied by ANNEXES, comprising:
   a. ☐ a total of sheets, as follows:
      ☐ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority.
      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
   b. ☐ a total of (indicate type and number of electronic carrier(s)) sheets containing a sequence listing and/or tables related thereto, in electronic form only, as indicated in the Supplemental Box Relating to Sequence Listing.

4. This report contains indications relating to the following items:
☐ 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 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 application
☐ Box No. VIII Certain observations on the application

Date of receipt of the demand 05 Aug. 2010 (05.08.2010)
Date of completion of this report 03 Dec. 2010 (03.12.2010)

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Form GCC/SIPO/637 (cover sheet)
1. With regard to the search report(s) used, this examination report is based on:

- [ ] the search report(s) prepared by the [blank], as selected by the GCCPO.
- [x] the search report prepared by the SIPO completed on 22 Nov. 2010 (22.11.2010).

2. With regard to the elements of the application, this report is based on:

- [x] the application as originally filed/furnished
  - Description: pages * as originally filed/furnished, pages * received by this Authority on .
  - Claims: pages * as originally filed/furnished, pages * received by this Authority on .
  - Drawings: pages * as originally filed/furnished, pages * received by this Authority on .
  - A sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing.

3. [ ] The amendments have resulted in the cancellation of:

- [ ] the description, pages .
- [ ] the claims, Nos. .
- [ ] the drawings, sheets/figs .
- [ ] the sequence listing (specify): .
- [ ] any table(s) related to sequence listing (specify): .

4. [x] This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box .

- [ ] the description, pages .
- [ ] the claims, Nos. .
- [ ] the drawings, sheets/figs .
- [ ] the sequence listing (specify): .
- [ ] any table(s) related to sequence listing (specify): .

* If item 4 applies, some or all of those sheets may be marked “superseded.”
1. ☐ This report has been established as if no priority had been claimed due to the failure to furnish within the prescribed time limit the requested copy/translation of the earlier application whose priority has been claimed.

2. ☐ This report has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid. Thus for the purposes of this report, the filing date indicated above is considered to be the relevant date.

3. Additional observations, if necessary:
The priority is valid after verification.
1. This Authority considers that the requirement of unity of invention is not complied with for the following reasons:

   There are multiple inventions in this application, as follows:

   I. Claims 1-16 relate to a process for the industrial synthesis of compound (I).

   II. Claim 17 relates to crystalline II form of agomelatine. Claim 18 relates to a pharmaceutical composition comprising crystalline II form of agomelatine. Claims 19-20 relate to the use of a pharmaceutical composition according to claim 18.

   Because compound (I) or agomelatine is known in the prior art. Therefore, the two groups of inventions do not contain any same or corresponding special technical feature, and are not so linked as to form a single general inventive concept. The application, hence does not meet the requirement of unity of invention as required by Article 5/1/3 of the GCC Patent Regulation.

2. Consequently, this report has been established in respect of the FIRST mentioned invention as required by the Memorandum, namely: Claims No. 1-16
1. Statement:

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<th>Novelty (N)</th>
<th>Claims</th>
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<th>Inventive step (IS)</th>
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<table>
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<th>Industrial applicability (IA)</th>
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<td></td>
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</table>

2. Citations and explanations

I. cited documents


D2: US3931188A (BRISTOL-MYERS COMPANY) 06 Jan. 1976 (06.01.1976)


II. Novelty

D1 discloses the method of preparing compound 7 (agomelatine). But D1 does not disclose the intermediate (VI) of the present claim 1. Therefore, claim 1 is novel in the sense of Article 2/2 of the GCC Patent Regulation. For the same reason, claims 2-14 are novel in the sense of Article 2/2 of the GCC Patent Regulation.

Claim 15 relates to a process for the synthesis of agomelatine starting from the compound of formula (VII). The difference between claim 15 and D1 is that acetic anhydride is used as coupling reagent in claim 15 in stead of acetyl chloride in D1. Therefore, claim 15 is novel in the sense of Article 2/2 of the GCC Patent Regulation. Similarly, claim 16 is novel in the sense of Article 2/2 of the GCC Patent Regulation.

D2 (see example 1) discloses the condensation of acetonitrile with tetralone leading to a cyano intermediate which is directly engaged in the subsequent reaction.

D3 (see example 1) discloses the condensation of cyanomethyl phosphonate with 6-fluoro-1-tetralone.

None of D2-D3 discloses agomelatine and the intermediate (VI) of the present application. Therefore, claims 1-16 are novel in the sense of Article 2/2 of the GCC Patent Regulation in view of D2 or D3.

III. Inventive step

D1 is regarded as the closest prior art. D1 does not disclose the process of aromatizing the intermediate (VI) to obtain compound (VII). The problem underlying the present application may therefore be seen as the provision of an improved process for the production of compound (VII). The solution, including the intermediate (VI) and the preparation thereof, is not considered as obvious since there exists no incentive in the prior art, including D2-D3, for the skilled person to adapt the prior art in such a way as to arrive at the present application. Therefore, the subject-matter of claim 1 appears to involve an inventive step in the sense of Article 2/3 of the GCC Patent Regulation. For the same reason, claims 2-14 involve an inventive step in the sense of Article 2/3 of the GCC Patent Regulation.

Claim 15 relates to a process for the synthesis of agomelatine starting from the compound of formula (VII). D1 (see Scheme 1 in page 3232 and left column in page 3236) discloses reduction compound 4 to compound 5A, and then coupling with acetyl chloride to obtain compound 7. Although the method of preparing formula (VII) is different, the method has no effect on the structure of formula (VII). Therefore, the difference between claim 15 and D1 is that acetic anhydride is used as coupling reagent in claim 15 in stead of acetyl chloride in D1. But it is obvious to replace acetyl chloride with acetic anhydride in the acetylation process. Therefore, claim 15 does not involve an inventive step in the sense of Article 2/3 of the GCC Patent Regulation. Similarly, claim 16 does not involve an inventive step in the sense of Article 2/3 of the GCC Patent Regulation.

IV. Industrial applicability

The industrial applicability can be acknowledged for claims 1-16 because the subject-matter claimed can be made in pharmaceutical industry in the sense of Article 2/4 of the GCC Patent Regulation.
In case the space in any of the preceding boxes is not sufficient.

Continuation of: International Patent Classification (IPC) or national classification and IPC

C07C233/18 (2006.01)i
C07C253/30 (2006.01)i