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(54) Title: A PHARMACEUTICAL COMPOSITION COMPRISING A COMBINATION OF BETA BLOCKER AND AN ACE  
INHIBITOR

(57) Abstract: A once a day pharmaceutical composition for use in the treatment of cardiovascular disorders includes (a) a first  
active ingredient comprising a beta blocker; (b) a second active ingredient comprising an ACE inhibitor; and (c) optionally one  
or more pharmaceutically acceptable excipients. The beta blocker is present in an extended release form and the ACE inhibitor is  
present in an immediate release form.



WO 2007/010501 A3

# INTERNATIONAL SEARCH REPORT

International application No  
PCT/IB2006/052513

## A. CLASSIFICATION OF SUBJECT MATTER

INV. A61K9/50 A61K9/48 A61K9/20 A61K31/138 A61K31/403

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)

A61K

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

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

EPO-Internal, WPI Data, EMBASE, BIOSIS

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category* | Citation of document, with indication, where appropriate, of the relevant passages                                                                                                     | Relevant to claim No. |
|-----------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------|
| X         | US 2005/032879 A1 (OKARTER TEMPLE [US] ET AL) 10 February 2005 (2005-02-10)<br>cited in the application<br>example<br>paragraph [0032] - paragraph [0052]<br>paragraphs [0001], [0014] | 1-15, 19              |
| Y         | US 4 957 745 A (JONSSON ULF E [SE] ET AL) 18 September 1990 (1990-09-18)<br>examples 1,2,4                                                                                             | 15                    |
| Y         | WO 2004/056336 A (RANBAXY LAB LTD [IN]; JAIN GIRISH KUMAR [IN]; SRITHARAN SEETHARAMAN [I]) 8 July 2004 (2004-07-08)<br>examples 1,2                                                    | 15                    |
|           | -----<br>-/-                                                                                                                                                                           |                       |

☒ 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 document 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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C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

| Category* | Citation of document, with indication, where appropriate, of the relevant passages                                                                                                                                                                                                                                      | Relevant to claim No. |
|-----------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------|
| Y         | <p>BAUER, K. H.; FRÖMMING, K.-H.; FÜHRER, C.:<br/>"Pharmazeutische Technologie"<br/>1997, BAUER, K. H.; G. FISCHER VERLAG;<br/>GOVI VERLAG; , STUTTGART, JENA, LÜBECK,<br/>ULM, FRANKFURT , XP002455496<br/>page 340: fig. 14.41; first paragraph<br/>below title "Abfüllen von<br/>Hartgelatine kapseln"<br/>-----</p> | 15                    |

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/IB2006/052513

## 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:  
  
Although claim 19 is directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
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:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers allsearchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an 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 reportcovers 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.:

1-15, 19

### 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.

## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

## 1. claims: 1-15,19

A once a day pharmaceutical composition according to claims 1-14 for use in the treatment of cardiovascular disorders, the composition comprising:

- a) a first active ingredient comprising a beta blocker
- b) a second active ingredient comprising an ACE inhibitor
- c) optionally one or more pharmaceutically acceptable excipients

wherein the beta blocker is in extended release form and the ACE inhibitor is in immediate release form.

A process according to claim 15 for the preparation of the composition of claim 1 comprising the steps of

- a) coating an inert core with a drug layer comprising a beta blocker
- b) coating the core with an extended release polymer layer
- c) optionally coating the core with a seal coat
- d) preparing a blend of an ACE inhibitor with one or more pharmaceutically acceptable excipients
- e) filling the blend of step d) into capsules
- f) filling the beta blocker beads and the ACE inhibitor capsules into capsules.

Claim 19 which refers back to any of the preceeding claims is assigned in part to each of the four inventions.

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## 2. claim: 16

A process according to claim 16 for the preparation of a pharmaceutical composition of claim 1 comprising the steps of:

- a) extruding a beta blocker with suitable excipients,
- b) breaking the extruded cylinders into an appropriate length and transforming them into spheroids,
- c) coating the spheroids with an extended release polymer coating,
- d) optionally, seal coating the spheroids of step c),
- e) coating the spheroid of step c) or d) with a drug layer comprising an ACE inhibitor, and
- 1) filling the spheroids into capsules or compressing them into tablets.

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## 3. claim: 17

## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

A process according to claim 17 for the preparation of a pharmaceutical composition of claim 1 comprising the steps of:

- a) extruding a beta blocker and an extended release polymer with one or more suitable excipients,
  - b) breaking the extruded cylinders into an appropriate length and transforming them into spheroids,
  - c) optionally, seal coating the spheroids of step c),
  - d) coating the spheroid of step c) or d) with a drug layer comprising an ACE inhibitor, and
  - e) filling the spheroids into capsules or compressing them into tablets.
- 

4. claim: 18

A process according to claim 18 for the preparation of a pharmaceutical composition of claim 1 comprising the steps of:

- i) preparing beta blocker granules in steps comprising
    - a) blending a beta blocker with one or more pharmaceutically inert excipients;
    - b) optionally granulating the blend of step a); and
    - c) lubricating the blend or granules of step a) or step b);
  - ii) preparing ACE inhibitor granules in steps comprising
    - a) blending ACE inhibitor and one or more pharmaceutically inert excipients;
    - b) optionally granulating the blend of step a); and
    - c) lubricating the blend of step a) or granules of step b);
  - and
  - iii) compressing the granules of step i) and step ii) to form a bilayer tablet.
-

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

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