(54) Title: USE OF COMPOUND IN THE MANUFACTURE OF A PHARMACEUTICAL FOR INHIBITING STEROID SULPHATASE AND STEROID DEHYDROGENASE ACTIVITY

(57) Abstract: There is provided use of a compound in the manufacture of a pharmaceutical for inhibiting steroid sulphatase (STS) activity and steroid dehydrogenase (DH) activity wherein the compound has Formula (I) wherein X is a ring having at least 4 atoms in the ring; K is a hydrocarbyl group; R1 is any one of a sulphonate group, a phosphonate group, a thio phosphonate group, a sulphonate group or a sulphonamide group.
**INTERNATIONAL SEARCH REPORT**

**A. CLASSIFICATION OF SUBJECT MATTER**

| IPC 7 | A61K31/565 | A61K31/566 | A61P35/00 | C07J1/00 |

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)

| IPC 7 | A61K | A61P | C07J |

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, PAJ, BIOSIS, MEDLINE, CHEM ABS Data

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

<table>
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<tr>
<th>Category *</th>
<th>Citation of document, with indication, where appropriate, of the relevant passages</th>
<th>Relevant to claim No.</th>
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<tr>
<td>P,X</td>
<td>WO 01 51055 A (PROSKE HENRICH THOMAS ;SCHERING AG (DE); ELGER WALTER (DE); RODDER) 19 July 2001 (2001-07-19) page 46; claims 1,20</td>
<td>1-9, 23-25, 39,47-50</td>
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<td>X</td>
<td>GB 2 331 987 A (UNIV BATH ;IMPERIAL COLLEGE (GB)) 9 June 1999 (1999-06-09) page 4; claims 1-8; examples 1-3</td>
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<td>X</td>
<td>DE 44 29 398 A (JENAPHARM GMBH) 15 February 1996 (1996-02-15) claims 1,3,5</td>
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Further documents are listed in the continuation of box C. Patent family members are listed in 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, used, 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 in conflict with the application but cited to understand the principle or theory underlining 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.
  * "W" document member of the same patent family

Date of the actual completion of the international search: 20 February 2002

Date of mailing of the international search report:

Name and mailing address of the ISA

European Patent Office, P.B. 5816 Patentlaan 2
NL-2280 HV Rijswijk
Tel. (+31-70) 940-2040, Tx. 51 651 epc nl,
Fax: (+31-70) 940-3016

Authorized officer

Winger, R
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| X        | WO 98 24802 A (POTTER BARRY VICTOR LLOYD ; REED MICHAEL JOHN (GB) ; IMPERIAL COLLEGE)  
page 4; figures 5-10; examples 1,2 | 1-13,17,  
18,  
23-25,  
39,47-50 |
| X        | US 5 880 115 A (SELCER KYLE W ET AL)  
9 March 1999 (1999-03-09)  
column 5; claim 1; examples 3,4 | 1-9,  
23-26,  
39,47-50 |
| X        | US 6 046 186 A (CHAO WAN-RU ET AL)  
4 April 2000 (2000-04-04)  
column 8 -column 13  
column 14; claim 11; example 33 | 1-9,  
23-25,  
27,39,  
47-50 |
| X        | LI P-K ET AL: "Development of potent non-estrogenic estrone sulfatase inhibitors"  
STEROIDS: STRUCTURE, FUNCTION, AND REGULATION, ELSEVIER SCIENCE PUBLISHERS, NEW YORK, NY, US,  
vol. 63, no. 7-8,  
8 July 1998 (1998-07-08), pages 425-432,  
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abstract; figure 1 | 1-9,  
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J. MED. CHEM.,  
vol. 42, 1999, pages 2280-2286,  
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abstract; figure 2; table 1 | 1-9,  
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| A        | TREMBLAY M R ET AL: "OVERVIEW OF A RATIONAL APPROACH TO DESIGN TYPE I 17BETA-HYDROXYSTEROID DEHYDROGENASE INHIBITORS WITHOUT ESTROGENIC ACTIVITY: CHEMICAL SYNTHESIS AND BIOLOGICAL EVALUATION"  
JOURNAL OF STEROID BIOCHEMISTRY, PERGAMON PRESS PLC, GB,  
vol. 66, no. 4, 1998, pages 179-191,  
XP001055919  
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cited in the application | 1-9,  
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<td>A</td>
<td>US 5 891 620 A (PUROHIT ATUL ET AL) 6 April 1999 (1999-04-06)</td>
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Box I  Observations where certain claims were found unsearchovable (Continuation of item 1 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.: 1-22 (in part) 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:
   see FURTHER INFORMATION sheet PCT/ISA/210

3.☐ Claims Nos.: because they are dependant claims and are not drafted in accordance with the second and third sentences of Rule 6.4(e).

Box II  Observations where unity of invention is lacking (Continuation of item 2 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 all searchable claims.

2.☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

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.:
   1-31 (partially) and 39-50 (partially)

Remark on Protest
☐ The additional search fees were accompanied by the applicant's protest.
☐ No protest accompanied the payment of additional search fees.

Form PCT/ISA/210 (continuation of first sheet (1)) (July 1996)
Continuation of Box I.2

Claims Nos.: 1-22 (in part)

Present claims 1-22 relate to an extremely large number of possible compounds, because even for the formulae, where the basic ring structures are defined, there is no information about the character of the rings or the substituents.

Support within the meaning of Article 6 PCT is to be found, however, for only a very small proportion of the compounds. In the present case, the claims so lack support, that a meaningful search over the whole of the claimed scope is impossible. Consequently, the search has been carried out for those parts of the claims which appear to be supported and disclosed, namely those parts relating to the compounds of formula II.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.
This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1-31 (partially) and 39-50 (partially)

   Use of a compound in the manufacture of a pharmaceutical for inhibiting steroid sulphatase activity and steroid dehydrogenase activity, wherein the compound of formula I in claim 1 has formula II and R1 is a sulphamate group, the corresponding compounds and assays using said compounds

2. Claims: 1-31 (partially)

   Use of a compound in the manufacture of a pharmaceutical for inhibiting steroid sulphatase activity and steroid dehydrogenase activity defined by formula II and R1 being a phosphonate group and the corresponding compounds

3. Claims: 1-31 (partially)

   Use of a compound in the manufacture of a pharmaceutical for inhibiting steroid sulphatase activity and steroid dehydrogenase activity defined by formula II and R1 being a thiophosphonate group and the corresponding compounds

4. Claims: 1-31 (partially)

   Use of a compound in the manufacture of a pharmaceutical for inhibiting steroid sulphatase activity and steroid dehydrogenase activity defined by formula II and R1 being a sulphonate group and the corresponding compounds

5. Claims: 1-31 (partially)

   Use of a compound in the manufacture of a pharmaceutical for inhibiting steroid sulphatase activity and steroid dehydrogenase activity defined by formula II and R1 being a sulphonamide group and the corresponding compounds

6. Claims: 23-31 (partially)

   Compound according to the formula of claim 23, ring D being a 6-ring as defined in claim 25

7. Claims: 23-38 (partially)

   Compound according to the formula of claim 23, ring D being a N-containing-ring as defined in claim 25
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