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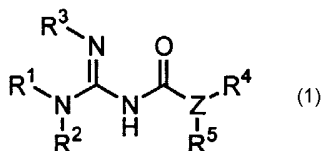
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For two-letter codes and other abbreviations, refer to the "Guid-
ance Notes on Codes and Abbreviations" appearing at the begin-
ning of each regular issue of the PCT Gazette.

(54) Title: AMIDINO-UREA SEROTONIN RECEPTOR LIGANDS AND COMPOSITIONS, THEIR PHARMACEUTICAL
USES, AND METHODS FOR THEIR SYNTHESIS



(57) Abstract: Novel amidino-urea 5-HT₇ receptor ligands, methods of preparing such lig-
ands, intermediate compounds useful in the preparation of the receptor ligands, pharmaceu-
tical compositions comprising the receptor ligands, and methods of treating sleep disorders,
pain, depression, and schizophrenia employing the receptor ligands are disclosed. The re-
ceptor ligands have formula (1): wherein the formula variables are as defined herein, and
pharmaceutically acceptable salts, solvates, active metabolites, or prodrugs thereof.

INTERNATIONAL SEARCH REPORT

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A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07C279/24 A61K31/155 A61P25/24 C07D211/26 C07C279/22
 C07D295/20 C07D211/60 C07D233/61

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 C07C C07D A61K A61P

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, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 98 07420 A (HONG YUFENG ; AGOURON ACQUISITION CORP (US); GREGOR VLAD EDWARD (US) 26 February 1998 (1998-02-26) the whole document ---	1,2,4, 6-15,17, 19
X	WO 99 20599 A (CAMBRIDGE NEUROSCIENCE INC) 29 April 1999 (1999-04-29) the whole document, in particular claim 10 ---	1,2,5,17
X	DD 298 475 A (CHEM & PHARM PATENT HOLD LTD) 27 February 1992 (1992-02-27) claim 1; pages 4-6: tables 1 and 2 ---	1,2,4
X	US 5 827 860 A (MARYANOFF BRUCE E ET AL) 27 October 1998 (1998-10-27) examples, in particular: columns 33,34: compounds 1a-1d; columns 95-96, compounds 54a-54d --- -/--	1,2,6,14



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, 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.
- *G* document member of the same patent family

Date of the actual completion of the international search

3 January 2003

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International Application No

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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.
X	EP 0 671 390 A (LILLY CO ELI) 13 September 1995 (1995-09-13) page 5, formula II; page 6, lines 40-45; page 7, lines 1-9; page 8, lines 25-26 ---	1,2,6
X	WO 99 44987 A (ALANEX CORP) 10 September 1999 (1999-09-10) claims 21,22 ---	14,15
X	US 5 773 646 A (CLARE MICHAEL ET AL) 30 June 1998 (1998-06-30) column 34, lines 20-25 ---	14,15
X	EP 0 902 036 A (ROCHE DIAGNOSTICS GMBH) 17 March 1999 (1999-03-17) the whole document, in particular page 4, formulae (III) and (IV) ---	14,15
X	WO 97 16444 A (PFIZER LTD ; PFIZER (US); PFIZER RES & DEV (IE); BROWN ALAN DANIEL) 9 May 1997 (1997-05-09) page 8, formula (III) ---	14,15
A	WO 00 00472 A (DU PONT PHARM CO) 6 January 2000 (2000-01-06) cited in the application abstract -----	1,10,13, 14,17, 20-24, 26,27

INTERNATIONAL SEARCH REPORT

International application No.
PCT/IB 01/02022

Box I Observations where certain claims were found unsearchable (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:

Although claims 20-23,27 are 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:
see FURTHER INFORMATION sheet PCT/ISA/210
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 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:

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.:

Remark on Protest

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

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

With respect to the compounds and compositions of claims 1,2,4-9,17,19 and the intermediates of claims 14,15 the initial phase of the search revealed a very large number of documents relevant to the issue of novelty. So many documents were retrieved that it is impossible to determine which parts of the claim(s) may be said to define subject-matter for which protection might legitimately be sought (Article 6 PCT). For these reasons, a meaningful search over the whole breadth of the claim(s) is impossible.

Consequently, insofar as claims 1,2,4-9,17,19 are concerned, the search report can only be considered complete for: compounds as defined in claim 3 and claim 24 and compositions containing them.

Insofar as claims 14,15 are concerned, the search report can only be considered complete for: intermediates as defined in claim 16.

Moreover, and in addition to the above, present claims 1,7,8,17-27 relate to compounds defined by reference to a desirable characteristic or property, namely that they are "active metabolites, or prodrugs" of the compounds claimed.

Since no technical features are given which compounds would fulfill these criteria and in-vivo tests would have to be carried out to find out which compounds are actually covered by these parts of the claims, this definition results in a lack of clarity and disclosure (articles 5 and 6 PCT) to such an extent that a meaningful search in this respect is impossible. Consequently, the search has been carried out for those parts of the claims which appear to be clear, supported and disclosed, namely those parts relating to the compounds which are structurally defined in the claims.

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.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/IB 01/02022

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