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- Published:**
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(54) Title: METHODS AND COMPOSITIONS EMPLOYING OPTICALLY PURE S(+) VIGABATRIN

(57) Abstract: Methods and compositions for the prevention, treatment, and/or management of the symptoms of peripheral neuropathy and related disorders, drug or alcohol addiction or the symptoms thereof, or symptoms associated with drug or alcohol withdrawal, using substantially optically pure S(+) vigabatrin, or a pharmaceutically acceptable salt thereof.

INTERNATIONAL SEARCH REPORT

International Application No

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A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61K31/195 A61K31/00 A61K31/55 A61K31/495 A61K31/445
A61K31/15 A61P25/30 A61P25/02

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

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)

EMBASE, SCISEARCH, MEDLINE, CANCERLIT, AIDSLINE, CHEM ABS Data, BIOSIS, WPI Data, EPO-Internal, PAJ

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 4 595 697 A (SEILER NIKOLAUS ET AL) 17 June 1986 (1986-06-17)	43-51, 53-56, 61-69, 71-74, 79,82-84
A	column 2, line 6 - line 22 column 2, line 53 - line 64 column 3, line 19 - line 24 column 3, line 61 - column 4, line 9 column 4, line 21 - line 42 column 4, line 55 - line 66 claims 1,5,6,10 --- -/--	1-42



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.
- "&" document member of the same patent family

Date of the actual completion of the international search

5 September 2000

Date of mailing of the international search report

13. 09. 2000

Name and mailing address of the ISA

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INTERNATIONAL SEARCH REPORT

Inte ional Application No
PCT/US 99/19346

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	ALVES N D: "Behavioral-pharmacological study of a possible analgesic effect of vigabatrin (gamma-vinil-GABA) in experimental chronic neuropathic pain" ARQUIVOS DE NEURO-PSIQUIATRIA, (MAR 1998) VOL. 56, NO. 1, PP. 150-150. PUBLISHER: ASSOC ARQUIVOS DE NEURO- PSIQUIATRIA, C/O DR OSWALDO LANGE, CAIXA POSTAL 8877, 01065-970 SAO PAULO SP, BRAZIL. ISSN: 0004-282X., vol. 56, no. 1, March 1998 (1998-03), page 150 XP000905078 UNIV FED CEARA, TESE MESTRADO, FORTALEZA, CEARA, BRAZIL the whole document ---	1,15
Y	GRAM L. ET AL: "Experimental studies of the influence of vigabatrin on the GABA system." BRITISH JOURNAL OF CLINICAL PHARMACOLOGY, (1989) 27/SUPPL. 1 (13S-17S)., XP000905099 cited in the application page 13S, column 2, paragraph 2 page 16S, column 1, paragraph 1 ---	1,15, 43-56, 61-74
A	BENNETT GJ, XIE JK: "A peripheral mononeuropathy in rats produces disorders of pain sensation like those seen in man" PAIN, vol. 33, 1988, pages 87-107, XP000905585 abstract page 87, column 1, paragraph 1 -page 88, column 1, paragraph 1 page 106, column 2, paragraph 2 ---	
Y	US 4 621 145 A (FRIEBEN WOLFGANG ET AL) 4 November 1986 (1986-11-04) column 1, line 6 - line 19 column 6, line 18 - line 24 ---	43-56, 61-74
Y	EP 0 509 180 A (MERRELL DOW PHARMA) 21 October 1992 (1992-10-21) abstract page 2, line 23 - line 38 page 2, line 57 -page 3, line 4 page 5, line 46 - line 58 page 6, line 4 - line 21 claims --- -/--	43-56, 61-74

INTERNATIONAL SEARCH REPORT

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.
Y	BUCKETT W R: "THE INFLUENCE OF A GABA TRANSAMINASE INHIBITOR, GAMMA-VINYL GABA, ON VOLUNTARY MORPHINE CONSUMPTION IN THE RAT" PSYCHOPHARMACOLOGY, DE, SPRINGER VERLAG, BERLIN, vol. 75, no. 2, 1981, pages 214-216, XP000856589 ISSN: 0033-3158 the whole document ---	43,44, 49-51, 61,62, 67-69
Y	WEGELIUS K ET AL: "GAMMA-VINYL GABA DECREASES VOLUNTARY ALCOHOL CONSUMPTION IN ALCOHOL-PREFERRING AA RATS" PHARMACOLOGY AND TOXICOLOGY, DK, MUNKSGAARD INTERNATIONAL PUBLISHERS, COPENHAGEN,, vol. 73, no. 3, September 1993 (1993-09), pages 150-152, XP000856621 ISSN: 0901-9928 the whole document ---	43,44, 49-51, 61,62, 67-69
Y	MORGAN ET AL: "Effects of pharmacologic increases in brain GABA levels on cocaine-induced changes in extracellular dopamine" SYNAPSE, GB, WILEY AND SONS, CHICHESTER, vol. 18, no. 1, January 1998 (1998-01), pages 60-65, XP002127041 ISSN: 0887-4476 abstract page 61, column 2, paragraph 2 page 63, column 2, paragraph 3 ---	43,44, 49-51, 61,62, 67-69
Y	STUPPAECK C H ET AL: "THE IRREVERSIBLE GAMMA-AMINOBUTYRATE TRANSAMINASE INHIBITOR VIGABATRIN IN THE TREATMENT OF THE ALCOHOL WITHDRAWAL SYNDROME" ALCOHOL AND ALCOHOLISM. SUPPLEMENT, GB, PERGAMON, OXFORD, vol. 31, no. 1, January 1996 (1996-01), pages 109-111, XP000856593 ISSN: 1358-6173 page 109, column 1, paragraph 1 page 109, column 2, paragraph 1 -page 110, column 1, paragraph 1 page 110, column 2, paragraph 2 -page 111, column 1, paragraph 3 --- -/--	43,44, 46-51, 56,61, 62, 64-69,74

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 99/19346

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	SHERIF FATHI M; TAWATI AHMED M; AHMED SALEEM S; SHARIF SULEIMAN I : "Basic aspects of GABA-transmission in alcoholism, with particular reference to GABA-transaminase. " EUROPEAN NEUROPSYCHOPHARMACOLOGY , vol. 7, no. 1, 1997, pages 1-7, XP000911797 abstract page 3, column 1, paragraph 2 page 4, column 2, paragraph 2 page 5, column 2, paragraph 2 page 6, column 1, paragraph 2 - paragraph 3 ---	43,44, 49,50, 61,62, 67,68
A	SASTRE-GARAU P; THOMAS P; BEAUSSART M; GOUDEMAND M : "Manic attack induced by a vigabatrin-clomipramine association. " ENCEPHALE , vol. 19, no. 4, 1993, pages 351-352, XP000911788 page 351, column 1, paragraphs 1,4,5 ---	57-59, 75,77
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E	WO 00 07583 A (BRODIE JONATHAN D ;DEWEY STEPHEN L (US); ASHBY CHARLES R JR (US);) 17 February 2000 (2000-02-17) abstract page 2, line 12 - line 21 page 7, line 11 - line 17 page 8, line 17 -page 9, line 2 page 11, line 21 -page 12, line 9 page 16, line 15 - line 23 page 17, line 4 - line 13 page 18, line 1 - line 3 page 19, line 15 - line 17 page 21, line 9 - line 14 page 61, line 22 - line 27 claims -----	43-56, 61-74

INTERNATIONAL SEARCH REPORT

International application No.
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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 1-78 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:
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:

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.:

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

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

1. Claims: 1-42, 79-87

A method of treating or preventing peripheral neuropathy in a mammal which comprises administering to a mammal in need of such a treatment a therapeutically effective amount of S(+)-vigabatrin, or a pharmaceutically acceptable salt thereof, substantially free of its R(-) stereoisomer; and a pharmaceutical composition comprising S(+)-vigabatrin.

2. Claims: 43-78

A method of treating or preventing drug or alcohol addiction and/or withdrawal in a mammal which comprises administering to a mammal in need of such a treatment a therapeutically effective amount of S(+)-vigabatrin, or a pharmaceutically acceptable salt thereof, substantially free of its R(-) stereoisomer; and a pharmaceutical composition comprising S(+)-vigabatrin.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 99/19346

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