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

(54) Title: POLYMORPHS OF ZALEPLON AND METHODS FOR THE PREPARATION THEREOF

(57) Abstract: This invention relates to novel crystalline polymorphic forms of zaleplon (N-[3-(3-cyanopyrazolo[1,5a]pyrimidin-7-yl)phenyl]-N-ethylacetamide), methods for the preparation thereof, and their uses as anxiolytic, antiepileptic, and sedative-hypnotic agents and skeletal muscle relaxants.



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INTERNATIONAL SEARCH REPORT

In* ational Application No
PCT/US 01/24510

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07D487/04 A61K31/519 A61P25/08 A61P25/22 A61P21/02
A61P25/20 //(C07D487/04,239:00,231:00)

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 C07D

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, CHEM ABS Data, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 4 626 538 A (DUSZA JOHN P ET AL) 2 December 1986 (1986-12-02) cited in the application examples 13,14	1,17,32
A	column 1, line 16 - line 24	45,48, 53-56
X	examples 13,14	57
X,Y	EP 0 776 898 A (AMERICAN CYANAMID CO) 4 June 1997 (1997-06-04) examples & US 5 714 607 A 3 February 1998 (1998-02-03) cited in the application	1,17,32



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 April 2002

Date of mailing of the international search report

15/04/2002

Name and mailing address of the ISA

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Hass, C

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, 45 (as far as Form I is concerned), 46, 47, 53-56 (partly), 57-59

Crystalline polymorph Form I of zaleplon, pharmaceutical composition containing it, its pharmaceutical use, and processes for preparation of Form I of zaleplon.

2. Claims: 2-5

Crystalline polymorph of zaleplon, characterized by X-ray powder diffraction pattern.

3. Claims: 6-13

Crystalline polymorph of zaleplon, characterized by chemical shift data of solid state ¹³C NMR.

4. Claims: 14, 15

Crystalline polymorph of zaleplon, characterized by delta values in a ¹³C solid state NMR spectrum.

5. Claim : 16

Crystalline polymorph of zaleplon, characterized by single crystal X-ray crystallographic analysis data at 295 K.

6. Claims: 17, 48 (as far as Form II is concerned), 49, 50, 53-56 (partly), 60

Crystalline polymorph Form II of zaleplon, pharmaceutical composition containing it, its pharmaceutical use, and process for preparation of Form II of zaleplon.

7. Claims: 18-30, 33-44

Variable-water hydrate crystalline polymorph of zaleplon, optionally characterized by X-ray and ¹³C solid state NMR data.

8. Claim : 31

Crystalline polymorph of zaleplon, characterized by single

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

crystal X-ray crystallographic analysis data at 150 K.

9. Claims: 32, 48 (as far as Form III is concerned), 51, 52,
53-56 (partly), 61

Crystalline polymorph form III of zaleplon, pharmaceutical
composition containing it, its pharmaceutical use, and
process for preparation of form III of zaleplon.

10. Claim : 45 (partly)

Pharmaceutical composition comprising any anhydrous
crystalline polymorph of zaleplon.

11. Claim : 48 (part)

Pharmaceutical composition comprising any hydrate
crystalline polymorph of zaleplon.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Remark: In claims 1, 17, 32, 46, 47, 49-56, the terms "Form I of zaleplon", "Form II of zaleplon" and "Form III of zaleplon" are not further defined; these claims are therefore unclear in the sense of Article 6 PCT. Since a meaningful search with regard to these terms was not possible, for the purpose of search, these claims were thus considered as to comprise any crystalline form of zaleplon.

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/US 01/24510

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
US 4626538	A	02-12-1986	AT 97414 T	15-12-1993
			AU 587617 B2	24-08-1989
			AU 5736086 A	20-11-1986
			CA 1270825 A1	26-06-1990
			DE 3689294 D1	23-12-1993
			DE 3689294 T2	09-06-1994
			DK 218286 A	14-11-1986
			EP 0208846 A1	21-01-1987
			ES 554887 D0	01-03-1989
			ES 8900165 A1	01-05-1989
			FI 861973 A ,B,	14-11-1986
			HK 127795 A	18-08-1995
			IE 61755 B	30-11-1994
			IL 78700 A	30-06-1989
			JP 2050408 C	10-05-1996
			JP 7084468 B	13-09-1995
			JP 61260083 A	18-11-1986
			KR 9001887 B1	26-03-1990
			MX 9202927 A1	30-06-1992
			NZ 216052 A	26-04-1989
			PH 24037 A	09-02-1990
			SG 9590509 A2	18-08-1995
			ZA 8603499 A	12-11-1987
			AT 53391 T	15-06-1990
			AU 568656 B2	07-01-1988
			AU 2977084 A	03-01-1985
			CA 1233174 A1	23-02-1988
			DD 228257 A5	09-10-1985
			DE 3422844 A1	17-01-1985
			DE 3482419 D1	12-07-1990
			DK 307184 A	24-12-1984
			EP 0129847 A2	02-01-1985
			ES 533654 D0	01-07-1985
			ES 8505958 A1	16-10-1985
			HK 91592 A	27-11-1992
			HU 37620 A2	23-01-1986
			IE 58012 B1	16-06-1993
			IL 72208 A	30-11-1987
			JP 1822784 C	10-02-1994
			JP 5031551 B	12-05-1993
			JP 60019788 A	31-01-1985
			KR 9001886 B1	26-03-1990
			MX 9202928 A1	30-06-1992
			NZ 208554 A	30-06-1987
			PH 21523 A	16-11-1987
			US 4521422 A	04-06-1985
			US 4654347 A	31-03-1987
			ZA 8404776 A	27-02-1985
EP 0776898	A	04-06-1997	AU 718310 B2	13-04-2000
			AU 7409196 A	05-06-1997
			BR 9605760 A	25-08-1998
			CA 2191647 A1	02-06-1997
			CN 1163893 A ,B	05-11-1997
			CZ 9603505 A3	17-09-1997
			EP 0776898 A1	04-06-1997
			HU 9603275 A2	28-08-1997
			IL 119710 A	30-11-1999

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 01/24510

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP 0776898	A	JP 9216885 A	19-08-1997
		NO 965084 A	02-06-1997
		NZ 299848 A	24-09-1998
		SK 153696 A3	05-11-1997
		TW 382629 B	21-02-2000
		US 5714607 A	03-02-1998
		ZA 9610008 A	28-08-1998
