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(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

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(54) Title: AEROSOL AND INJECTABLE FORMULATIONS OF NANOPARTICULATE BENZODIAZEPINE

(57) Abstract: Described are nanoparticulate formulations of a benzodiazepine, such as lorazepam, that does not require the presence of polyethylene glycol and propylene glycol as stabilizers, and methods of making and using such formulations. The formulations are particularly useful in aerosol and injectable dosage forms, and comprise nanoparticulate benzodiazepine, such as lorazepam, and at least one surface stabilizer. The formulations are useful in the treatment of status epilepticus, treatment of irritable bowel syndrome, sleep induction, acute psychosis, and as a pre-anesthesia medication.



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INTERNATIONAL SEARCH REPORT

International application No

PCT/US2006/005224

A. CLASSIFICATION OF SUBJECT MATTER

INV. A61K9/72 A61K9/10 A61K9/14

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, PAJ, EMBASE, MEDLINE, 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 6 207 178 B1 (WESTESEN KIRSTEN ET AL) 27 March 2001 (2001-03-27)	1-4, 9, 12-16, 21, 24
Y	examples 26, 27 abstract	5-8, 17-20
X	----- LEVY M Y ET AL: "DESIGN AND CHARACTERIZATION OF A SUBMICRONIZED O/W EMULSION OF DIAZEPAM FOR PARENTERAL USE" INTERNATIONAL JOURNAL OF PHARMACEUTICS, AMSTERDAM, NL, vol. 54, no. 2, 1 September 1989 (1989-09-01), pages 103-112, XP000566536 ISSN: 0378-5173 abstract page 105, column 1 - column 2 ----- -/--	1-4, 9, 12-16, 21, 24

☒ 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

Date of the actual completion of the international search

16 August 2006

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12/09/2006

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INTERNATIONAL SEARCH REPORT

International application No

PCT/US2006/005224

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	SCHWARZ J S ET AL: "ENHANCED TRANSDERMAL DELIVERY OF DIAZEPAM BY SUBMICRON EMULSION (SME) CREAMS" PHARMACEUTICAL RESEARCH, NEW YORK, NY, US, vol. 12, no. 5, May 1995 (1995-05), pages 687-692, XP008003571 ISSN: 0724-8741 abstract table 3	1-4, 13-16
Y	US 2004/185003 A1 (RABINOWITZ JOSHUA D ET AL) 23 September 2004 (2004-09-23) claims 1-4 examples 1-8	5-8, 17-20
Y	WO 03/041693 A (ALEXZA MOLECULAR DELIVERY CORPORATION) 22 May 2003 (2003-05-22) claims 1-7 examples 1-4	5-8, 17-20
A	EP 0 685 233 A (ELI LILLY AND COMPANY) 6 December 1995 (1995-12-06) example 4	1-24
A	US 4 719 228 A (RAWLINS ET AL) 12 January 1988 (1988-01-12) example 3	1-24
A	US 4 863 720 A (BURGHART ET AL) 5 September 1989 (1989-09-05) examples 1-6	1-24
X,P	WO 2005/018611 A (K.U. LEUVEN RESEARCH & DEVELOPMENT; VAN DEN MOOTER, GUY; MARTENS, JOHA) 3 March 2005 (2005-03-03) example 2	1-4, 13-16

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2006/005224

Box 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 claims 13-24 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 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 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:

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.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/US2006/005224

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 6207178	B1	27-03-2001	NONE
US 2004185003	A1	23-09-2004	NONE
WO 03041693	A	22-05-2003	NONE
EP 0685233	A	06-12-1995	AU 684924 B2 08-01-1998
		AU 2042495 A 14-12-1995	
		CA 2150517 A1 04-12-1995	
		CN 1119101 A 27-03-1996	
		DE 69528109 D1 17-10-2002	
		HU 71598 A2 29-01-1996	
		IL 113912 A 11-04-1999	
		JP 7330608 A 19-12-1995	
		NO 952130 A 04-12-1995	
		NZ 272231 A 25-05-2001	
		US 5457101 A 10-10-1995	
		ZA 9504358 A 29-11-1996	
US 4719228	A	12-01-1988	AU 589561 B2 19-10-1989
		AU 4280085 A 28-11-1985	
		CA 1255222 A1 06-06-1989	
		DE 3580304 D1 06-12-1990	
		EP 0163178 A2 04-12-1985	
		ES 8800039 A1 01-01-1988	
		GR 851254 A1 25-11-1985	
		IE 57732 B1 24-03-1993	
		JP 2096181 C 02-10-1996	
		JP 7072128 B 02-08-1995	
		JP 60258113 A 20-12-1985	
		MX 163564 B 01-06-1992	
		NZ 212148 A 06-01-1989	
		US 4859709 A 22-08-1989	
		ZA 8503823 A 30-04-1986	
US 4863720	A	05-09-1989	WO 8705210 A1 11-09-1987
		AU 601176 B2 06-09-1990	
		AU 7127887 A 28-09-1987	
		EP 0259383 A1 16-03-1988	
		JP 2573275 B2 22-01-1997	
		JP 63503303 T 02-12-1988	
WO 2005018611	A	03-03-2005	EP 1658052 A1 24-05-2006