(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
25 January 2007 (25.01.2007)

PCT

(10) International Publication Number
WO 2007/010559 A3

(51) International Patent Classification:
A61K 9/20 (2006.01) *A61K 31/415* (2006.01)
A61K 9/48 (2006.01) *A61K 31/192* (2006.01)
A61K 31/18 (2006.01) *A61P 29/00* (2006.01)

(21) International Application Number:
PCT/IN2006/000258

(22) International Filing Date: 19 July 2006 (19.07.2006)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
1899/DEL/2005 20 July 2005 (20.07.2005) IN

(71) Applicant *(for all designated States except US)*: **PANACEA BIOTEC LTD.** [IN/IN]; B-1 Extn./A-27, Mohan Co-operative Industrial Estate, Mathura Road, New Delhi 110 044 (IN).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: **JAIN, Rajesh** [IN/IN]; Panacea Biotec Limited, B-1 Extn. A-27, Mohan Co-operative Industrial Estate, Mathura Road, New Delhi 110 044 (IN). **JINDAL, Kour, Chand** [IN/IN]; Panacea Biotec Limited, B-1 Extn.A-27, Mohan Co-operative Industrial Estate, Mathura Road, New Delhi 110 044 (IN). **SINGH, Sukhjeet** [IN/IN]; Panacea Biotec Limited, B-1 Extn.A-27, Mohan Co-operative Industrial Estate, Mathura Road, New Delhi 110 044 (IN). **TALWAR, Munish** [IN/IN]; Panacea Biotec Limited, B-1 Extn.A-27, Mohan Co-operative Industrial Estate, Mathura Road, New Delhi 110 044 (IN).

(74) Agent: **GUPTA, Bhartee**; Panacea Biotec Limited, B-1 Extn./A-27, Mohan Co-operative Industrial Estate, Mathura Road, New Delhi 110 044 (IN).

(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, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, 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, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Declarations under Rule 4.17:
— *as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))*
— *as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii))*
— *of inventorship (Rule 4.17(iv))*

Published:
— *with international search report*
— *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments*

(88) Date of publication of the international search report:
20 September 2007

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: NOVEL PHARMACEUTICAL MODIFIED RELEASE DOSAGE FORM CYCLOOXYGENASE ENZYME INHIBITOR

(57) Abstract: Pharmaceutical modified release dosage form comprising at least one cyclooxygenase enzyme inhibitor or its pharmaceutically acceptable salts, esters, prodrugs, solvates, hydrates, or derivatives thereof as active agent, with a pharmaceutically acceptable carrier for controlling the release of the cyclooxygenase enzyme inhibitor is provided. The dosage form preferably provides a release of not more than about 60 % of the cyclooxygenase enzyme inhibitor in 1 hour and not less than about 75 % of the cyclooxygenase enzyme inhibitor after 12 hours when tested in accordance with the dissolution method (I) described herein employing Distilled water with 2.0 % Sodium lauryl sulphate as the dissolution medium or in accordance with the dissolution method (II) described herein employing pH 7.0 Phosphate buffer with 2.0% Sodium lauryl sulphate as the dissolution medium or in accordance with the dissolution method (III) described herein employing 0.001 N Hydrochloric acid with 1.0 % Sodium lauryl sulphate as dissolution medium. Further, the pharmaceutical composition of the present invention when tested in a group of healthy humans preferably achieves a mean peak plasma concentration (C_{max}) after at least about 1 hour of administration of the dosage form,. The present invention also provides process of preparing such dosage form compositions and prophylactic and/or therapeutic methods of using such dosage form.

WO 2007/010559 A3

INTERNATIONAL SEARCH REPORT

International application No
PCT/IN2006/000258

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61K9/20 A61K9/48 A61K31/18 A61K31/415 A61K31/192
A61P29/00

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)
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, EMBASE, BIOSIS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 01/22791 A2 (PANACEA BIOTEC LTD [IN]; SINGH AMARJIT [IN]; JAIN RAJESH [IN]) 5 April 2001 (2001-04-05) examples pages 1-4,6 table 1 pages 8-12	1-7,9, 10,12-30
X	US 2002/012702 A1 (KESHARLAL BIYANI MILIND [IN] ET AL) 31 January 2002 (2002-01-31) examples paragraphs [0005] - [0009], [0017] - [0025] table 1	1-7,9, 10, 12-16, 18-27, 29,30

-/--

[X] Further documents are listed in the continuation of Box C.

[X] 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	Date of mailing of the international search report
3 July 2007	20/07/2007

Name and mailing address of the ISA/
European Patent Office, P.B. 5818 Patentlaan 2
NL – 2280 HV Rijswijk
Tel. (+31–70) 340–2040, Tx. 31 651 epo nl,
Fax: (+31–70) 340–3016

Authorized officer
Sproll, Susanne

INTERNATIONAL SEARCH REPORT

International application No
PCT/IN2006/000258

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 6 258 816 B1 (SINGH AMARJIT [IN] ET AL) 10 July 2001 (2001-07-10) example V	1-7,9, 10, 12-27, 29,30
X	US 6 187 343 B1 (GOLD OSCAR [AR]) 13 February 2001 (2001-02-13) examples column 6 column 1, line 15 - line 22	1-7,9, 10, 12-16, 18-30
X	NAGOJI K E V ET AL: "RELEASE STUDIES OF NIMESULIDE FROM ETHYL CELLULOSE AND ETHYL CELLULOSE AND HYDROXY PROPYL METHYL CELLULOSE MATRICES" INDIAN JOURNAL OF PHARMACEUTICAL SCIENCES, vol. 62, no. 6, November 2000 (2000-11), pages 482-484, XP001063992 ISSN: 0250-474X the whole document	1-7,9, 10, 12-16, 18,20-30
X	US 2003/170303 A1 (HEDDEN DAVID B [US] ET AL) 11 September 2003 (2003-09-11) cited in the application examples, esp. M5, M9, M12, M13, M17 paragraphs [0102], [0103], [0257], [0267] - [0281], [0291]	1-10, 12-18, 20-30
X	WO 00/04879 A (ANDRIX PHARMACEUTICALS INC [US]) 3 February 2000 (2000-02-03) the whole document	1-7,9, 12, 14-16, 18-27, 29,30
X	EP 0 438 249 A1 (ELAN CORP PLC [IE]) 24 July 1991 (1991-07-24) examples page 3, line 6 - line 7 page 15, line 55 - line 56	1-7,9, 12, 14-16, 18-30
X	US 6 599 529 B1 (SKINHOEJ ANNETTE [DK] ET AL) 29 July 2003 (2003-07-29) cited in the application examples 12-14	1-10, 12-27, 29,30

-/--

INTERNATIONAL SEARCH REPORT

International application No
PCT/IN2006/000258

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2005/129764 A1 (VERGEZ JUAN A [AR] ET AL) 16 June 2005 (2005-06-16). paragraphs [0002], [0052], [0056], [0062], [0107]; example 2	1-6,9, 11,12, 14-16, 18,20-30
X	EP 1 462 098 A (SPRL FRANPHARMA [BE]) 29 September 2004 (2004-09-29) the whole document	1-7,9, 12,14-30
Y	WO 01/22917 A2 (PANACEA BIOTEC LTD [IN]; SINGH AMARJIT [IN]; JAIN RAJESH [IN]) 5 April 2001 (2001-04-05) page 4, second paragraph	27-29
Y	EP 1 002 531 A1 (PANACEA BIOTEC LTD [IN]) 24 May 2000 (2000-05-24) paragraph [0001]	27-29

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box II.1

Although claims 27-28 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.

Continuation of Box II.2

Claims Nos.: 1-30 (in part)

Present claims 1-30 relate to a product which has a given desired property or effect, namely a pharmaceutical dosage form having specific release characteristics. However, the description does not provide support and disclosure in the sense of Article 6 and 5 PCT for any such product having the said property or effect and there is no common general knowledge of this kind available to the person skilled in the art. This non-compliance with the substantive provisions is to such an extent, that the search was performed taking into consideration the non-compliance in determining the extent of the search of the claim (PCT Guidelines 9.19 and 9.20).

The search of claims 1-30 was consequently restricted to the specifically disclosed products having the desired property or effect, see description pages 26-32, namely an oral solid dosage form comprising nimesulid, celecoxib or naproxen, and a release controlling polymer, wherein the dosage form shows a modified release profile.

The applicant's attention is drawn to the fact that 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. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guideline C-VI, 8.5), should the problems which led to the Article 17(2) declaration be overcome.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/IN2006/000258

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. [X] Claims Nos.: 1-30 (in part)
because they relate to subject matter not required to be searched by this Authority, namely:

Although claims 27-28 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. [X] Claims Nos.: 1-30 (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 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/IN2006/000258

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 0122791 A2	05-04-2001	AU 774099 B2	17-06-2004
		AU 2879901 A	30-04-2001
		BG 106605 A	29-12-2002
		BR 0014383 A	22-10-2002
		CA 2385890 A1	05-04-2001
		CN 1399543 A	26-02-2003
		CZ 20021076 A3	14-08-2002
		EP 1218889 A2	03-07-2002
		HU 0204451 A2	28-06-2003
		JP 2003534236 T	18-11-2003
		MX PA02003321 A	10-09-2004
		NO 20021540 A	28-05-2002
		NZ 518052 A	29-04-2005
		PL 358369 A1	09-08-2004
		RU 2238087 C2	20-10-2004
		US 2007128276 A1	07-06-2007
		ZA 200202411 A	26-06-2003
US 2002012702 A1	31-01-2002	AU 8438201 A	02-01-2002
		BR 0111879 A	24-06-2003
		EP 1406635 A2	14-04-2004
		WO 0197775 A2	27-12-2001
		IN 190963 A1	06-09-2003
US 6258816 B1	10-07-2001	AU 729581 B2	01-02-2001
		CA 2253061 A1	06-05-1999
		IN 188720 A1	02-11-2002
US 6187343 B1	13-02-2001	ES 2129010 A1	16-05-1999
		IT MI972893 A1	02-07-1998
		PT 102095 A	31-07-1998
US 2003170303 A1	11-09-2003	US 2004062803 A1	01-04-2004
		US 2003219488 A1	27-11-2003
		US 2002015735 A1	07-02-2002
WO 0004879 A	03-02-2000	AU 5134699 A	14-02-2000
		US 2001001658 A1	24-05-2001
EP 0438249 A1	24-07-1991	AT 126055 T	15-08-1995
		AU 639519 B2	29-07-1993
		AU 6933291 A	18-07-1991
		CA 2034096 A1	16-07-1991
		DE 69111832 D1	14-09-1995
		DE 69111832 T2	14-03-1996
		DK 438249 T3	18-09-1995
		ES 2075338 T3	01-10-1995
		GR 3017633 T3	31-01-1996
		IE 900149 A1	17-07-1991
		IL 96900 A	31-12-1995
		JP 3157182 B2	16-04-2001
		JP 4217918 A	07-08-1992
		NZ 236762 A	23-12-1992
		PH 30694 A	16-09-1997
		ZA 9100274 A	30-10-1991
US 6599529 B1	29-07-2003	AT 252892 T	15-11-2003
		AU 9062998 A	29-03-1999

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/IN2006/000258

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 6599529 B1		CA 2301883 A1	18-03-1999
		CN 1277550 A	20-12-2000
		DE 69819351 D1	04-12-2003
		WO 9912524 A1	18-03-1999
		EA 2806 B1	31-10-2002
		EP 1017370 A1	12-07-2000
		JP 2001515854 T	25-09-2001
		NO 20001290 A	28-04-2000
US 2005129764 A1	16-06-2005	AR 047731 A1	15-02-2006
		WO 2006056144 A2	01-06-2006
EP 1462098 A	29-09-2004	NONE	
WO 0122917 A2	05-04-2001	AU 2879801 A	30-04-2001
		IN 190018 A1	31-05-2003
EP 1002531 A1	24-05-2000	AU 718356 B2	13-04-2000
		AU 7308998 A	29-07-1999
		CN 1240646 A	12-01-2000
		JP 3242622 B2	25-12-2001
		JP 11228448 A	24-08-1999