

(19) World Intellectual Property  
Organization  
International Bureau



(43) International Publication Date  
26 February 2004 (26.02.2004)

PCT

(10) International Publication Number  
WO 2004/016242 A3

- (51) International Patent Classification<sup>7</sup>: A61K 9/54, 31/4439
- (21) International Application Number: PCT/IB2003/003514
- (22) International Filing Date: 4 August 2003 (04.08.2003)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data: 742/MUM/2002 16 August 2002 (16.08.2002) IN
- (71) Applicant (for all designated States except US): THEMIS LABORATORIES PRIVATE LIMITED [IN/IN]; Unit No. S-4 Khira Industrial Estate, B.M. Bhargava Road, Santacruz (West), Mumbai 400 054, Maharashtra State (IN).
- (72) Inventors; and
- (75) Inventors/Applicants (for US only): ANTARKAR, Amit, Krishna [IN/IN]; House No. C/4, Rani Laxmi Nagar, Nagpur-440 022, State of Maharashtra (IN). ABDUL SATTAR ABDUL, Javed [IN/IN]; Iqbal Nagar, Ward No. 10, Buldana-443001, State of Maharashtra (IN). LALA RAJENDRA, Ghanshlal [IN/IN]; House No. 100, ≤Guru Cottage≥, Inlaks Hospital Road, Chembur, Mumbai-400 074, State of Maharashtra (IN). JOSHI KETAKI, Kishore [IN/IN]; F/1 Nutan Sandesh Chs., Vallabh Baug Road, Ghatkopar (East), Mumbai-400 077, State of Maharashtra (IN). GADKARI PARAG, Narayan [IN/IN]; 23/703 Anant, Vasant Vihar, Pokhran Road 2, Thane (West)- 400 607, State of Maharashtra (IN). THANAWALA GAURANG, HASMUKHLAL [IN/IN]; Dhiraj Baug, L.B.S., Naupada, Thane- 400 602, State of Maharashtra (IN). SHAH MAYA, JANAK [IN/IN]; Saujanya, 3rd N. S. Road, Vallabhnagar Society, Vile Parle (West), Mumbai- 400 056, State of Maharashtra (IN). SHAH JANAK, Ramanlal [IN/IN]; Saujanya, 3rd N.S. Road, Vallabhnagar Society, Vile Parle (West), Mumbai-400 056, State of Maharashtra (IN).
- (74) Agent: GANGULI, Prabuddha; "Vision - IPR", 103B Senate, Lokhandwala Township, Akurli Road, Kandivali East, Mumbai 400 101, State of Maharashtra (IN).
- (81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.
- (84) Designated States (regional): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (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)) for the following designations AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG)
- as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii)) for the following designations AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS,

[Continued on next page]

(54) Title: A PROCESS FOR MANUFACTURE OF STABLE ORAL MULTIPLE UNITS PHARMACEUTICAL COMPOSITION CONTAINING BENZIMIDAZOLES

(57) Abstract: This invention relates to process for manufacture of a stable, oral, multiple unit pharmaceutical composition containing high concentration of benzimidazole upto about 40%w/w without the use of micronized benzimidazole, disintegrating agent and fillers. Surfactants in these compositions are in enteric polymer layer and not in contact with benzimidazole. Multiple unit pharmaceutical composition of the invention shows minimum acid degradation in 0.1 N HCl after two hours and pH 6.8 buffer release of more than 85% w/w after 45 minutes. Multiple unit pharmaceutical composition is in the form unagglomerated, uniformly shaped and sized enteric-coated pellets, which are processed continuously or in batches in single equipment such as fluid bed bottom spray processor. The invention involves sequential deposition of a) alkaline material layer on non-pariel seeds to obtain treated non-pariel seeds b) drug layer to obtain drug pellets c) sealant polymer layer to obtain sealed pellets d) enteric polymer layer to obtain enteric coated pellets. The enteric-coated pellets obtained are capable of being filled in smallest size capsule (size 5) for ease of administration and patient acceptance.



WO 2004/016242 A3



- JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG)
- as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii)) for the following designation US
  - of inventorship (Rule 4.17(iv)) for US only
  - of inventorship (Rule 4.17(iv)) for US only
  - of inventorship (Rule 4.17(iv)) for US only

— of inventorship (Rule 4.17(iv)) for US only

**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:**

8 April 2004

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.

## INTERNATIONAL SEARCH REPORT

PCT/IB 03/03514

A. CLASSIFICATION OF SUBJECT MATTER  
 IPC 7 A61K9/54 A61K31/4439

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)

WPI Data, EPO-Internal

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	EP 1 213 015 A (BYK GULDEN LOMBERG CHEMISCHE FABRIK GMBH) 12 June 2002 (2002-06-12) page 6 -page 7; example 3 ---	1-31
Y	EP 0 502 556 A (AKTIEBOLAGET HÄSSLE) 9 September 1992 (1992-09-09) page 11, line 22 - line 33 -----	1-31

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

23 January 2004

Date of mailing of the international search report

04/02/2004

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

Benz, K

## INTERNATIONAL SEARCH REPORT

PCT/IB 03/03514

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
EP 1213015	A	12-06-2002	US 5945124 A	31-08-1999
			EP 1213015 A1	12-06-2002
			SI 841903 T1	31-08-2003
			AT 232090 T	15-02-2003
			AU 6517496 A	05-02-1997
			CA 2232450 A1	23-01-1997
			DE 69626116 D1	13-03-2003
			DE 69626116 T2	23-10-2003
			DK 841903 T3	19-05-2003
			WO 9702020 A1	23-01-1997
			EP 0841903 A1	20-05-1998
			ES 2192226 T3	01-10-2003
			HK 1010836 A1	27-06-2003
			JP 11508577 T	27-07-1999
			PT 841903 T	30-06-2003
			US 6068856 A	30-05-2000
			US 6274173 B1	14-08-2001
<hr/>				
EP 502556	A	09-09-1992	GB 2189699 A	04-11-1987
			AT 84211 T	15-01-1993
			EP 0502556 A1	09-09-1992
			GR 3020501 T3	31-10-1996
			LV 5753 A4	20-12-1996
			AT 139692 T	15-07-1996
			AT 186639 T	15-12-1999
			AU 603568 B2	22-11-1990
			AU 7192287 A	05-11-1987
			CA 1302891 C	09-06-1992
			CN 87103285 A ,B	18-11-1987
			CS 8703073 A2	13-06-1989
			CY 1860 A	16-04-1987
			DD 260222 B5	09-07-1998
			DE 3751851 D1	01-08-1996
			DE 3751851 T2	31-10-1996
			DE 3783386 D1	18-02-1993
			DE 3783386 T2	06-05-1993
			DE 244380 T1	08-02-1990
			DK 215987 A	31-10-1987
			EG 18517 A	30-04-1993
			EP 0244380 A2	04-11-1987
			EP 0565210 A2	13-10-1993
			ES 2010648 T3	16-07-1994
			ES 2089277 T3	01-10-1996
			ES 2137966 T3	01-01-2000
			FI 871914 A ,B,	31-10-1987
			GR 3032639 T3	30-06-2000
			GR 89300156 T1	12-03-1990
			GR 3007448 T3	30-07-1993
			HK 55497 A	09-05-1997
			HK 104095 A	07-07-1995
			HR 920855 A1	30-06-1995
			HU 44171 A2	29-02-1988
			IE 61837 B1	30-11-1994
			JP 1946242 C	10-07-1995
			JP 6067837 B	31-08-1994
			JP 62258316 A	10-11-1987
			KR 9504886 B1	15-05-1995
			LT 2260 R3	15-12-1993

## INTERNATIONAL SEARCH REPORT

PCT/IB 03/03514

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP 502556	A	LV 5393 A3	10-03-1994
		NO 871791 A ,B,	02-11-1987
		NZ 220097 A	26-04-1990
		PH 24440 A	25-06-1990
		PL 265417 A1	21-07-1988
		PT 84786 A ,B	01-05-1987
		SI 8710680 A ,B	31-12-1996
		SU 1709894 A3	30-01-1992
		US 4853230 A	01-08-1989
		YU 68087 A1	31-08-1988

---