(19) World Intellectual Property Organization International Bureau





(43) International Publication Date 17 July 2003 (17.07.2003)

PCT

(10) International Publication Number WO 03/057135 A3

(51) International Patent Classification⁷: A61K 31/724, 31/455, 31/4174

TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

(21) International Application Number: PCT/US02/36063

(22) International Filing Date:

7 November 2002 (07.11.2002)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

10/033,835

24 December 2001 (24.12.2001) US

(71) Applicant (for all designated States except US): DOW PHARMACEUTICAL SCIENCES [US/US]; 1330A Redwood Way, Petaluma, CA 94954-6542 (US).

(72) Inventors; and

- (75) Inventors/Applicants (for US only): CHANG, Yunik [US/US]; 814 Third Street West, Sonoma, CA 95476 (US). DOW, Gordon, J. [US/US]; 4189 Chaparral Court, Santa Rosa, CA 95409 (US).
- (74) Agent: EISENBERG, Howard; 601 SW Second Avenue, Suite 1600, Portland, OR 97204 (US).
- (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, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, 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, IE, IT, LU, MC, NL, PT, SE, SK,

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, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, 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, IE, IT, LU, MC, NL, PT, SE, 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, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, 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, IE, IT, LU, MC, NL, PT, SE, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG)
- of inventorship (Rule 4.17(iv)) for US only

Published:

with international search report

(88) Date of publication of the international search report:

18 December 2003

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.

57135

(54) Title: AQUEOUS COMPOSITIONS CONTAINING METRONIDAZOLE

(57) Abstract: An aqueous solution of metronidazole in which the concentration of metronidazole is higher than 0.75%. The solution contains a combination of solubility-enhancing agents, one of which is a cyclodextrin such as beta-cyclodextrin and the second is a compound other than a cyclodextrin. Methods of manufacture and therapeutic use of the solution are disclosed.

International application No. INTERNATIONAL SEARCH REPORT CLASSIFICATION OF SUBJECT MATTER A61K 31/724, 31/455, 31/4174 IPC(7) US CL 514/58, 356, 398 According to International Patent Classification (IPC) or to both national classification and IPC FIELDS SEARCHED Minimum documentation searched (classification system followed by classification symbols) U.S.: 514/58, 356, 398 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 practicable, search terms used) Please See Continuation Sheet C. DOCUMENTS CONSIDERED TO BE RELEVANT Citation of document, with indication, where appropriate, of the relevant passages Relevant to claim No. Category * US 6,468,989 B1 (CHANG et al) 22 October 2002 (22.10.2002), col 5, lines 59-67 and 1-4, 9, 10, 15, 22 X, P examples 9 and 10. 5-8, 11-14, 16-21, 23-Y, P 44 WO 99/09988 (HEXAL AG) 04 March 1999 (04.03.1999), Example IV/10; Table 11; and X 1, 9 page 5, last paragraph. 5, 6, 11, 15, 17, 18, Y 20-23 KATA, M. et al, "Increasing the Solubility Characteristics of Pharmaca with Cyclodextrins" 1-44 Y Pharm. Ind., 1987, Vol. 49, No. 1, pages 98-100. See entire reference. Y CHIEN, Y. "Solubilization of Metronidazol by Water-Miscible Multi-cosolvents and Water-1-44 Soluble Vitamins" J. Parenteral Sci. Tech. January-February 1984, Vol. 38, No. 1, pages 32-36. See entire reference. US 5,646,131 A (BADWAN et al) 08 July 1997 (08.07.1007), col 4. 12-14 Y US 4,837,378 A (BORGMAN) 06 June 1989 (06.06.1989), see abstract. 33-44 Y Further documents are listed in the continuation of Box C. See patent family annex. 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 Special categories of cited documents: "A' document defining the general state of the art which is not considered to be of particular relevance document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step "X" "E" earlier application or patent published on or after the international filing date when the document is taken alone 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 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 referring to an oral disclosure, use, exhibition or other means document published prior to the international filing date but later than the u g, n document member of the same patent family priority date claimed Date of the actual completion of the international search Date of mailing of the international search report 18 SEP 2003 10 March 2003 (10.03.2003) Authorized officer Name and mailing address of the ISA/US

Leigh C. Maier

Telephone No. (703) 308-1235

Form PCT/ISA/210 (second sheet) (July 1998)

Washington, D.C. 20231

Box PCT

Facsimile No. (703)305-3230

Commissioner of Patents and Trademarks

INTERNATIONAL SEARCH REPORT

PCT/LS02/36063

C. (Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT			
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.	
Y Y	Citation of document, with indication, where appropriate, of the relevant passages US 5,324,718 A (LOFTSSON) 28 June 1994 (24.06.1994), see entire reference, especially col 11, lines 20-28.	Relevant to claim No.	

INTERNATIONAL SEARCH REPORT	PCT/UDD / 36063
1	
Continuation of B. FIELDS SEARCHED Item 3:	
EAST, Derwent, Caplus: metronidazole, cyclodextrin, niacin?, nicotinamide, nicot	tinic, solubil?, soluble, rosacea, aqueous, gel?
Form PCT/ISA/210 (second sheet) (July 1998)	