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

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
15 February 2007 (15.02.2007)

PCT

(10) International Publication Number
WO 2007/017897 A3

(51) International Patent Classification:
C07D 257/04 (2006.01) *A61K 31/41* (2006.01)

(21) International Application Number:
PCT/IN2006/000175

(22) International Filing Date:
23 May 2006 (23.05.2006)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
632/MUM/2005 25 May 2005 (25.05.2005) IN

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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.

(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))*

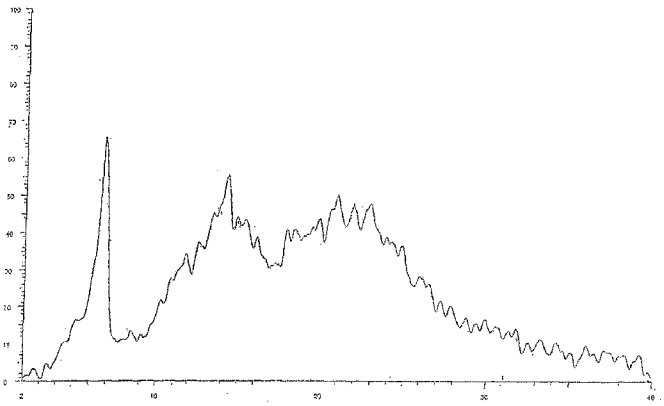
Published:

— *with international search report (Art. 21(3))*

[Continued on next page]

(54) **Title**: NOVEL CRYSTALLINE FORMS OF (S)-N-(1-CARBOXY-2-METHYL-PROP-1-YL)-N-PENTANOYL-N-[2'-(1H-TETRAZOL-5-YL)BI-PHENYL-4-YLMETHYL]-AMINE

FIG 1



(57) **Abstract**: Disclosed herein is novel crystalline forms of Valsartan namely, a crystalline form designated as Form A, and its solvates thereof, novel crystalline form of Valsartan designated as Form B and solvates thereof, novel crystalline form of Valsartan designated as Form C and solvates thereof, novel crystalline form of Valsartan designated as Form D and its solvates thereof, processes for their preparation, pharmaceutical compositions containing these polymorphs and their use in medicine. The present invention further discloses a novel process for preparing a stable amorphous form of Valsartan and in this connection to amorphous form of Valsartan produced by such processes. The present invention also discloses a novel process for obtaining stable Form I crystals of Valsartan.

WO 2007/017897 A3

— *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))*

(88) Date of publication of the international search report:
15 October 2009

INTERNATIONAL SEARCH REPORT

International application No.
PCT/IN 2006/000175

A. CLASSIFICATION OF SUBJECT MATTER
IPC[8]: C07D 257/04; ***A61K 31/41*** (AMENDED)
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[8]: C07D, A61K (amended)

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
WPI, EPODOC, PAJ, XFULL, Google, NPL

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 2004/083192 A1 (TEVA PHARMACEUTICALS INDUSTRIES INC.) 30 September 2004 (30.09.2004) .	1-3, 32-33 (partly)
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Y	WO 2003/089417 A1 (DR. REDDY'S LABORATORIES LIMITED) 30 October 2003 (30.10.2003) . *whole document, especially examples*	1-3, 32-33 (partly)
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Y	WO 2002/006253 A1 (NOVARTIS AG) 24 January 2002 (24.01.2002) *whole document*	1-3, 32-33 (partly)
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☒ 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 application or patent 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
21 July 2009 (21.07.2009)	3 August 2009 (03.08.2009)

Name and mailing address of the ISA/ AT	Authorized officer
Austrian Patent Office Dresdner Straße 87, A-1200 Vienna	PETZ-STIFTER M.
Facsimile No. +43 / 1 / 534 24 / 535	Telephone No. +36 / 1 / 474 / 5907

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,Y	CN 1763017 A (ZHEJIANG HUAHAI PHARMACEUTICAL CO.; LTD) 26 April 2006 (26.04.2006) *abstract*	1-3, 32-33 (partly)
A	US 5399578 A (BÜHLMAYER, P. et al) 21 March 1995 (21.03.1995) . *whole document*	1-3, 32-33 (partly)
A	US 2006/0149079 A1 (PADI, P.R. et al) 6 July 2006 (06.07.2006) *whole document*	1-3, 32-33 (partly)
E,Y	WO 2007/053406 A1 (NOVARTIS PHARMA GMBH) 10 May 2007 (10.05.2007) . *whole document*	1-3, 32-33 (partly)
E,Y	WO 2007/088558 A2 (ALEMBIC LIMITED) 9 August 2007 (09.08.2007) *whole document*	1-3, 32-33 (partly)

International application No.
PCT/IN 2006/000175

Continuation of first sheet

Continuation No. 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:

Group I. (Claims 1-3, 32-33 partly)

Claims are relating to a novel crystal form of Valsartan designated as Form A, to a process for preparing thereof, to a pharmaceutical composition comprising thereof and to the use thereof. The process of preparing of the Form A is based on following steps:
i) preparing a solution of amorphous or crystal Valsartan in a first solvent selected from acetone, methyl propyl ketone or their mixture thereof;
ii) bringing said solution to a temperature of about 25 to 35 deg C;
iii) mixing with a second solvent like dichloromethane till a suspension is resulted; and
iv) separating said crystal form of Valsartan (Form A) from the solvents.

Group II. (Claims 4-6, 32-33 partly)

Claims are relating to a novel crystal form of Valsartan designated as Form B, to a process for preparing thereof, to a pharmaceutical composition comprising thereof and to the use thereof. The process of preparing of the Form B is based on following steps:
i) providing an emulsion or suspension of Valsartan in an organic solvent like toluene at a first temperature characterized above 85 deg C,
ii) reducing the temperature of the emulsion or suspension to a second temperature characterized below 40 deg C,

Group III. (Claims 7-12, 24, 29, 30 partly, 32-33 partly)

Claims are relating to a novel crystal form of Valsartan designated as Form C, to a process for preparing to a pharmaceutical composition comprising thereof and to the use thereof.
The process of preparing of the Form C is based on following steps:
i) providing a suspension/emulsion of amorphous or partially crystal Valsartan in a hydrocarbon solvent especially toluene at a temperature below 60 deg C;
ii) agitating the suspension for a period of 24 hours to 110 hours; and iii) separating said new crystal Form C Valsartan.

Group IV. (Claims 13-23, 25-28, 30 partly, 31, 32-33 partly, 34)

Claims are relating to a novel crystal form of Valsartan designated as Form D, to a process for preparing thereof, to a pharmaceutical composition comprising thereof to the use thereof and method of treating.
The process of preparing of the Form D is based on following steps:
i) providing a suspension/emulsion of amorphous or partially crystal Valsartan in a

hydrocarbon solvent like toluene or its mixture with hydrocarbons such as hexane, xylene, or esters such as ethyl acetate or alcohols such as IPA or water at a temperature below 60 deg C;

ii) agitating the suspension for a period of over 115 hours; and

iii) separating said new crystal Form D Valsartan,

or

i) providing a suspension/emulsion of amorphous or partially crystal Valsartan in a hydrocarbon solvent like toluene or its mixture with hexane, xylene, ethyl acetate or water at a temperature below 60 deg C;

ii) seeding said mixture with Form D crystals of Valsartan;

iii) agitating the mixture for a period of about 24 hours; and

iv) separating said new crystal Form D Valsartan

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. Group I. (Claims 1-3, 32-33 partly)

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No.
PCT/IN2006/000175

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