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— *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, SC, SD, SE, SG, SK, SL, 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)*

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Published:

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(54) Title: A NOVEL CRYSTALLINE FORM OF IRBESARTAN

(57) Abstract: The present invention relates to a novel crystalline form of irbesartan, to process for its preparation and a pharmaceutical composition containing it.

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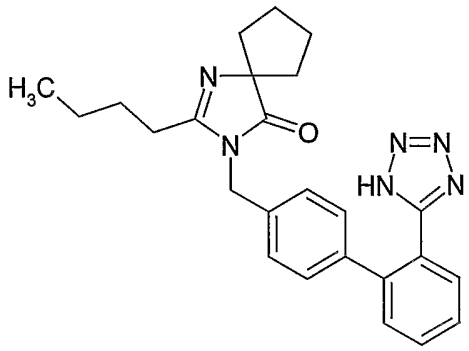
A NOVEL CRYSTALLINE FORM OF IRBESARTAN

FIELD OF THE INVENTION

The present invention relates to a novel crystalline form of irbesartan, to process for its preparation and a pharmaceutical composition containing it.

BACKGROUND OF THE INVENTION

Irbesartan or 2-Butyl-3-[[2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]-1,3-diazaspiro[4.4]non-1-en-4-one, which has the formula (1) :



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is a powerful angiotensin II receptor antagonist.

US 5,629,331 describes two crystalline forms of irbesartan (form A, B).

It has now been found that irbesartan can be prepared in a novel crystalline form (form C). The novel crystalline form is at least as stable as form A or form B and is not spontaneously converted to the previously known forms. The novel form is found to be suitable for pharmaceutical preparations.

The object of the present invention is to provide a stable novel crystalline form of irbesartan, a process for preparing it and a pharmaceutical composition containing it.

DETAILED DESCRIPTION OF THE INVENTION

According to one aspect of the present invention, there is provided a novel crystalline form of irbesartan, designated as form C, characterized by an x-ray powder diffraction pattern having peaks expressed as 2θ at about 8.3, 8.7,

10.1, 11.8, 15.0, 15.5, 16.4, 16.8, 17.5, 18.3, 19.1, 20.3, 21.1, 21.7, 23.6, 25.1, 25.5, 26.4, 26.8, 27.2, 28.1, 29.0 and 29.4 degrees. Figure 1 shows typical form C x-ray powder diffraction spectrum.

According to another aspect of the present invention, there is provided a process for preparation of the form C of irbesartan. Thus, irbesartan is mixed with a suitable solvent and irbesartan form C is isolated from the mixture. Preferably, the mixture of irbesartan and a suitable solvent is heated to reflux and the contents are filtered at about 5^0C to 25^0C. The suitable solvent is tetrahydrofuran or 1,4-dioxane; or a mixture thereof. Suitable solvent mixed with any other solvent/s like water may be used as long as irbesartan form C can be isolated from the solvent mixture. Previously known form of irbesartan or irbesartan prepared by a known method may be used in the process.

According to another aspect of the present invention there is provided a pharmaceutical composition comprising irbesartan form C. Irbesartan form C may be formulated in a form suitable for oral administration or injection.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 is a x-ray powder diffraction spectrum of irbesartan form C.

x-Ray powder diffraction spectrum was measured on a Siemens D5000 x-ray powder diffractometer having a copper-Kα radiation.

The following examples are given for the purpose of illustrating the present invention and should not be considered as limitations on the scope or spirit of the invention.

Example 1

Irbesartan (5.0 gm, obtained by the process described in example 5 of US 5,270,317) is mixed with tetrahydrofuran (350 ml), heated to reflux and maintained under reflux temperature for 30 minutes. The contents are cooled to 10^0C. The separated crystals are collected by filtration to give 4.2 gm irbesaratan form C.

Example 2

Example 1 is repeated using irbesartan form A for irbesartan to give irbesartan form C.

Example 3

Example 1 is repeated using irbesartan form B for irbesartan to give irbesartan form C.

Example 4

The mixture of Irbesartan (5.0 gm, obtained by process described in example 5 of US 5,270,317) and 1.4-dioxane (100 ml) is stirred for 5 hours at 20^0C to 25^0C. The solid is collected by filtration to give 4.7 gm irbesaratan form C.

Example 5

Irbesartan (5.0 gm, obtained by process described in example 5 of US 5,270,317) is added to a mixture of tetrahydrofuran (320 ml) and water (3 ml). The contents are heated to reflux, maintained under reflux temperature for 30 minutes and then cooled to 10^0C. The separated crystals are collected by filtration to give 3.8 gm irbesaratan form C.

We claim:

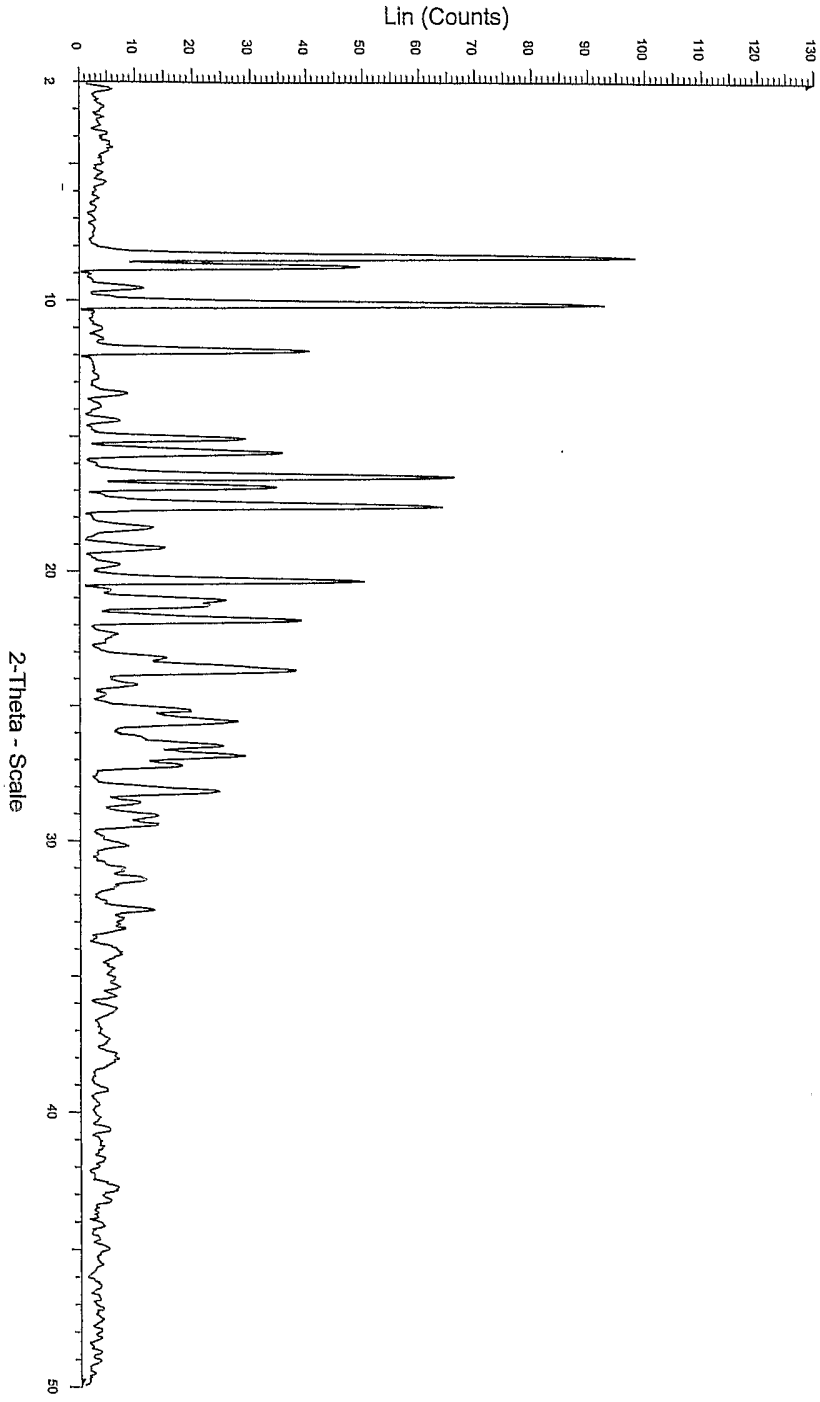
1. A crystalline irbesartan form C, characterized by an x-ray powder diffraction pattern having peaks expressed as 2θ at about 8.3, 8.7, 10.1, 11.8, 15.0, 15.5, 16.4, 16.8, 17.5, 18.3, 19.1, 20.3, 21.1, 21.7, 23.6, 25.1, 25.5, 26.4, 26.8, 27.2, 28.1, 29.0 and 29.4 degrees.
2. A crystalline irbesartan form C of claim 1, further characterized by an x-ray powder diffraction pattern as in figure 1.
3. A process for preparation of irbesartan form C of claim 1, comprising the steps of:

a) mixing irbesartan and tetrahydrofuran or 1,4-dioxane; and

b) Isolating irbesartan form C from the mixture.

4. A process according to claim 3, wherein irbesartan is mixed with tetrahydrofuran.
5. A process according to claim 3, wherein irbesartan is mixed with 1,4-dioxane.
6. A pharmaceutical composition comprising the crystalline irbesartan form C of claim 1 and a pharmaceutically acceptable carrier.

fig. 1/1


Lin (Counts)
0
10
20
30
40
50
60
70
80
90
100
110
120
130
2
10
20
30
40
50
2-Theta - Scale

INTERNATIONAL SEARCH REPORT

International application No.
PCT/IN 03/00146-0

CLASSIFICATION OF SUBJECT MATTER

IPC[7]: C07D 403/10

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]: C07D 403/10

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)

STN Karlsruhe: CAS: CAPLUS and REGISTRY databases, EPOQUE: EPODOC

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
D,A	US 5629331 A (CARON ET AL.) 13 May 1997 (13.05.97) *the whole document.*	1-6
A	EP 0420237 A1 (ESAI CO., LTD) 3 April 1991 (03.04.91) *examples 2,3.*	1-6
A	EP 0475898 A1 (CIBA-GEIGY AG) 18 March 1992 (18.03.92) *example 9.*	1-6

☐ Further documents are listed in the continuation of Box C. ☒ See patent family annex.

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INTERNATIONAL SEARCH REPORT

Information on patent family members

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PCT/IN 03/00146-0

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		IE A 903242	1991-04-10
		ZA A 9007356	1991-10-30
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