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2777/MUM/2011 30 September 2011 (30.09.2011) IN(71) Applicant (for all designated States except US): **CADILA HEALTHCARE LIMITED** [IN/IN]; Zydus Tower, Satellite Cross Roads, Ahmedabad - 380 015, Gujarat (IN).

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Declarations under Rule 4.17:

— as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))

Published:

— with international search report (Art. 21(3))
— 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:
14 March 2013

(54) Title: NOVEL SALTS OF DPP-IV INHIBITOR

(57) Abstract: The present invention discloses new salts of (2R)-4-oxo-4-[3-(trifluoromethyl)-5,6-dihydro[1,2,4]-triazolo[4,3-a]pyrazin-7(8H)-yl]-1-(2,4,5-trifluorophenyl)butan-2-amine i.e. gentisate, adipate and trifluoro acetic acid salts. The invention also describes the new, crystalline and amorphous forms of (2R)-4-oxo-4-[3-(trifluoromethyl)-5,6-dihydro[1,2,4]-triazolo[4,3-a]pyrazin-7(8H)-yl]-1-(2,4,5-trifluorophenyl)butan-2-amine gentisate. The present invention also discloses novel crystalline salt form of (2R)-4-oxo-4-[3-(trifluoromethyl)-5,6-dihydro[1,2,4]-triazolo[4,3-a]pyrazin-7(8H)-yl]-1-(2,4,5-trifluorophenyl)butan-2-amine hydrochloride and novel crystalline and amorphous salt forms of besylate and process for their preparation and isolation.



WO 2012/147092 A3

INTERNATIONAL SEARCH REPORT

International application No
PCT/IN2012/000148

A. CLASSIFICATION OF SUBJECT MATTER
INV. C07D487/04
ADD.

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)
C07D

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)

EPO-Internal, CHEM ABS Data, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	"SITAGLIPTIN SALTS, PROCESSES FOR THEIR PREPARATION AND THEIR USE FOR THE PREPARATION OF PHARMACEUTICAL DOSAGE FORMS", IP.COM JOURNAL, IP.COM INC., WEST HENRIETTA, NY, US, 21 October 2010 (2010-10-21), XP013143473, ISSN: 1533-0001 page 1, line 1 - page 1, line 14	1-44
X	WO 2009/085990 A2 (REDDYS LAB LTD DR [IN]; REDDYS LAB INC DR [US]; PADI PRATAP REDDY [IN]) 9 July 2009 (2009-07-09) cited in the application examples 9-23 ----- -/-	1-44



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

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31/01/2013

Name and mailing address of the ISA/

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INTERNATIONAL SEARCH REPORT

International application No
PCT/IN2012/000148

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2005/072530 A1 (MERCK & CO INC [US]; FERLITA RUSSELL R [US]; HANSEN KARL [US]; VYDRA V) 11 August 2005 (2005-08-11) cited in the application examples 1-5	1-44
X	WO 2010/117738 A2 (TEVA PHARMA [IL]; TEVA PHARMA [US]; PILARSKI GIDEON [IL]; PERLMAN NURI) 14 October 2010 (2010-10-14) cited in the application examples 2-56	1-12
A	KIM B H ET AL: "Pharmacodynamic (Hemodynamic) and pharmacokinetic comparisons of S-amlodipine gentisate and racemate amlodipine besylate in healthy Korean male volunteers: Two double-blind, randomized, two-period, two-treatment, two-sequence, double-dummy, single-dose crossover studies", CLINICAL THERAPEUTICS, EXCERPTA MEDICA, PRINCETON, NJ, US, vol. 32, no. 1, 1 January 2010 (2010-01-01), pages 193-205, XP026908537, ISSN: 0149-2918, DOI: 10.1016/J.CLINTHERA.2010.01.017 [retrieved on 2010-02-08] the whole document	1-12
A	EP 2 019 113 A1 (ANADYS PHARMACEUTICALS INC [US]) 28 January 2009 (2009-01-28) claim 1	1-12
E	WO 2013/001457 A1 (RANBAXY LAB LTD [IN]; JAYACHANDRA SURESH BABU [IN]; SHAH JIGAR BHASKAR) 3 January 2013 (2013-01-03) example 5	13-17
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X	WO 03/004498 A1 (MERCK & CO INC [US]; EDMONDSON SCOTT D [US]; FISHER MICHAEL H [US]; KI) 16 January 2003 (2003-01-16) cited in the application example 7	1-44
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INTERNATIONAL SEARCH REPORT

International application No

PCT/IN2012/000148

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	LEE H Y ET AL: "Clinic blood pressure responses to two amlodipine salt formulations, adipate and besylate, in adult Korean patients with mild to moderate hypertension: A multicenter, randomized, double-blind, parallel-group, 8-week comparison", CLINICAL THERAPEUTICS, EXCERPTA MEDICA, PRINCETON, NJ, US, vol. 27, no. 6, 1 June 2005 (2005-06-01), pages 728-739, XP027641221, ISSN: 0149-2918 [retrieved on 2005-06-01] the whole document -----	13-17, 31-44
A	WO 2010/004231 A2 (UNIV NANCY 1 HENRI POINCARÉ [FR]; DUVAL RAPHAEL EMMANUEL [FR]; GRARE M) 14 January 2010 (2010-01-14) example 2 -----	18-25

INTERNATIONAL SEARCH REPORT

International application No.
PCT/IN2012/000148

Box No. 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. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:
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:
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 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:

see additional sheet

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 fees, this Authority did not invite payment of additional fees.
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 and, where applicable, the payment of a protest fee.
- ☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- ☒ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-12

Gentisate salt of sitagliptin

2. claims: 13-17

Adipate salt of sitagliptin

3. claims: 18-25

Trifluoroacetic acid salt of sitagliptin

4. claims: 26-30

Hydrochloride salt of sitagliptin

5. claims: 31-44

Besilate salt of sitagliptin

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/IN2012/000148

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International application No

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