

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
21 October 2004 (21.10.2004)

PCT

(10) International Publication Number
WO 2004/089380 A3

- (51) International Patent Classification⁷: **A61K 31/5513**, 31/519, 31/4985, 31/4745, A61P 3/04
- (21) International Application Number: PCT/DK2004/000251
- (22) International Filing Date: 6 April 2004 (06.04.2004)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data:
PA 2003 00571 11 April 2003 (11.04.2003) DK
60/467,284 2 May 2003 (02.05.2003) US
PA 2003 00776 22 May 2003 (22.05.2003) DK
60/475,157 2 June 2003 (02.06.2003) US
- (71) Applicant (for all designated States except US): **NOVO NORDISK A/S** [DK/DK]; Novo Allé, Bagsværd, 2880 (DK).
- (72) Inventors; and
- (75) Inventors/Applicants (for US only): **ANDERSEN, Henrik, Sune** [DK/DK]; Gustav Adolphs Vej 2, Kgs. Lyngby, 2800 (DK). **KAMPEN, Gita, Camilla, Tejlgaard** [DK/DK]; Gærdebuen 18, Nærum, 2850 (DK). **CHRISTENSEN, Inge, Thøger** [DK/DK]; Kulsviertofte 52, Kgs. Lyngby, 2800 (DK). **MOGENSEN, John, Patrick** [DK/DK]; Rørløkken 96, Herlev, 2730 (DK). **LARSEN, Annette, Rosendal** [DK/DK]; Hallingdal 5, Kgs. Lyngby, 2800 (DK).
- (74) Common Representative: **NOVO NORDISK A/S**; Corporate Patents, Novo Allé, Bagsværd, 2880 (DK).
- (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, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, 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 (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, 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, IT, LU, 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).
- 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: 23 December 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.

(54) Title: PHARMACEUTICAL USE OF FUSED 1,2,4-TRIAZOLES

(57) Abstract: The use of fused 1,2,4-triazoles for modulating the activity of 11 β -hydroxysteroid dehydrogenase type 1 (11 β HSD1) and the use of these compounds as pharmaceutical compositions has been described. Also a novel class of fused 1,2,4-triazoles, their use in therapy, pharmaceutical compositions comprising the compounds, as well as their use in the manufacture of medicaments has been described. The present compounds are modulators and more specifically inhibitors of the activity of 11 β HSD1 and may be useful in the treatment, prevention and/or prophylaxis of a range of medical disorders where a decreased intracellular concentration of active glucocorticoid is desirable.



WO 2004/089380 A3

INTERNATIONAL SEARCH REPORT

International Application No
PCT/DK2004/000251

A. CLASSIFICATION OF SUBJECT MATTER IPC 7 A61K31/5513 A61K31/519 A61K31/4985 A61K31/4745 A61P3/04		
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) EPO-Internal, CHEM ABS Data, EMBASE, BIOSIS, MEDLINE, SCISEARCH, 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	GB 825 514 A (BAYER AG) 16 December 1959 (1959-12-16)	23, 34, 36-38, 40, 41, 47-57, 59
X	column 1, paragraph 1	1-17, 23, 25-28, 34, 58, 59, 65
X	columns 5, 6; examples IV, V, VI, VII, VIII, XIX, XXI claims 5-13, 20-28 example XVII ----- -/--	47
<input checked="" type="checkbox"/> Further documents are listed in the continuation of box C. <input checked="" type="checkbox"/> 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	Date of mailing of the international search report	
15 July 2004	- 3. 11. 2004	
Name and mailing address of the ISA	Authorized officer	
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 840-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Bonzano, C	

INTERNATIONAL SEARCH REPORT

International Application No

PCT/DK2004/000251

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2 913 454 A (WOLFGANG WIRTH ET AL) 17 November 1959 (1959-11-17) column 1, paragraph 1 columns 5,6; examples IV,V,VI,VII,VIII,XXIII	23,34, 36-38, 40,41, 48-57,59
X	claims 5-10	1-17,23, 25-28, 34,58, 59,65
X	----- DEMCHENKO, A. M.: "Derivatives of 1,4-diaryl-5,6,7,8-tetrahydro-2,2a,8a- triazacyclopenta[c,d]azulene" CHEMISTRY OF HETEROCYCLIC COMPOUNDS (NEW YORK)(TRANSLATION OF KHIMIYA GETEROTSIKLICHESKIKH SOEDINENII) , VOLUME DATE 2000, 36(8), 985-988 CODEN: CHCCAL; ISSN: 0009-3122, 2001, XP008032860 page 986; examples 6a,6b,6c,6g	36-38, 40,41, 48-54
X	US 5 932 569 A (JANSSENS FRANS EDUARD ET AL) 3 August 1999 (1999-08-03) column 19, line 22 - line 29 column 21, lines 34,55; example 2 claim 1 sentence 52; example 8 column 22, line 24; example 3	1-17, 24-28, 36-38, 40,41, 48-59,65
P,A	----- WO 03/065983 A (WADDELL SHERMAN T ; ASTER SUSAN D (US); GRAHAM DONALD W (US); MALETIC) 14 August 2003 (2003-08-14) claims 1,12,14-23	1-17
X	----- US 5 426 105 A (MANNING ROBERT E ET AL) 20 June 1995 (1995-06-20) claims 20,23,24 examples 3221-3225	1,2,66

INTERNATIONAL SEARCH REPORT

International application No.
PCT/DK2004/000251

Box 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:

Although claims 1,3-16,27-35,65,66 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
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 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 fee, this Authority did not invite payment of any additional fee.
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.:

1-38, 40, 41, 47-66 (all partially)

Remark on Protest

The additional search fees were accompanied by the applicant's protest.

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: 1-38,40,41,47-66 (partially)

Use of a fused 1,2,4-triazole of formula (I), where the triazole is fused with an azepine for the modulation of the activity of 11betaHSD1 in a patient, and new compounds thereof.

2. claims: 1-38,40,41,47-66 (partially)

Use of a fused 1,2,4-triazole of formula (I), where the triazole is fused with an isoquinoline, for the modulation of the activity of 11betaHSD1 in a patient, and new compounds thereof.

3. claims: 1-38,40,41,47-66 (partially)

Use of a fused 1,2,4-triazole of formula (I), where the triazole is fused with a pyridazine for the modulation of the activity of 11betaHSD1 in a patient, and new compounds thereof.

4. claims: 1-38,40,41,47-66 (partially)

Use of a fused 1,2,4-triazole of formula (I), where the triazole is fused with a quinazoline for the modulation of the activity of 11betaHSD1 in a patient, and new compounds thereof.

5. claims: 1-38,40,41,47-66 (partially)

Use of a fused 1,2,4-triazole of formula (I), where the triazole is fused with a pyrimidine for the modulation of the activity of 11betaHSD1 in a patient, and new compounds thereof.

6. claims: 1-15,17-41, 48-66 (partially), 39,42-46

Use of a fused 1,2,4-triazole of formula (I), according to formula (III) for the modulation of the activity of 11betaHSD1 in a patient, and new compounds thereof.

7. claims: 1-41,47-66 (partially)

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Use of a fused 1,2,4-triazole of formula (I), excluding the above mentioned inventions, for the modulation of the activity of 11betaHSD1 in a patient, and new compounds thereof.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/DK2004/000251

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
GB 825514	A	16-12-1959	DE 1025881 B	13-03-1958
			FR 1231625 A	30-09-1960
			US 2852525 A	16-09-1958

US 2913454	A	17-11-1959	NONE	

US 5932569	A	03-08-1999	AT 236164 T	15-04-2003
			AU 676701 B2	20-03-1997
			AU 5627894 A	04-07-1994
			CA 2150806 A1	23-06-1994
			DE 69332830 D1	08-05-2003
			DE 69332830 T2	29-01-2004
			WO 9413671 A1	23-06-1994
			EP 0675887 A1	11-10-1995
			ES 2196020 T3	16-12-2003
			FI 952722 A	02-06-1995
			HU 71811 A2	28-02-1996
			JP 8503952 T	30-04-1996
			JP 3572074 B2	29-09-2004
			KR 251893 B1	15-04-2000
			NO 952198 A	03-08-1995
NZ 258551 A	A	25-06-1996	PL 309253 A1	02-10-1995
			RU 2126802 C1	27-02-1999

WO 03065983	A	14-08-2003	CA 2474168 A1	14-08-2003
			WO 03065983 A2	14-08-2003

US 5426105	A	20-06-1995	US 5674879 A	07-10-1997
