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

REVISED VERSION

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
20 September 2012 (20.09.2012)

WIPO | PCT

(10) International Publication Number
WO 2012/123493 A9

(51) **International Patent Classification**:
C07J 71/00 (2006.01) ***A61P 11/06*** (2006.01)
A61K 31/58 (2006.01) ***A61P 37/08*** (2006.01)
A61P 5/44 (2006.01)

(21) **International Application Number**:
PCT/EP2012/054455

(22) **International Filing Date**:
14 March 2012 (14.03.2012)

(25) **Filing Language**: English

(26) **Publication Language**: English

(30) **Priority Data**:
11158243.3 15 March 2011 (15.03.2011) EP

(71) **Applicant** *(for all designated States except US)*: **CHIESI FARMACEUTICI S.P.A.** [IT/IT]; Via Palermo, 26/A, I-43100 Parma (IT).

(72) **Inventors; and**
(75) **Inventors/Applicants** *(for US only)*: **GHIDINI, Eleonora** [IT/IT]; c/o Chiesi Farmaceutici S.P.A., Via Palermo, 26/A, I-43100 Parma (IT). **CAPELLI, Anna Maria** [IT/IT]; c/o Chiesi Farmaceutici S.P.A., Via Palermo, 26/A, I-43100 Parma (IT).

(74) **Agent**: **MINOJA, Fabrizio**; Bianchetti Bracco Minoja S.r.l., Via Plinio, 63, I-20129 Milano (IT).

(81) **Designated States** *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) **Designated States** *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

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**:
10 January 2013

Date of publication of the revised international search report:
31 January 2013

(15) **Information about Correction**:
see Notice of 31 January 2013

(54) **Title**: ISOXAZOLIDINE DERIVATIVES

(57) **Abstract**: The present invention relates to novel anti-inflammatory and antiallergic compounds of the glucocorticosteroid series, methods of preparing such compounds, pharmaceutical compositions comprisingthem, combinations and therapeutic uses thereof. More particularly, the invention relates to glucocorticosteroids that are derivatives of isoxazolidine.

WO 2012/123493 A9

corrected version

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2012/054455

A. CLASSIFICATION OF SUBJECT MATTER
INV. C07J71/00 A61K31/58 A61P5/44 A61P11/06 A61P37/08
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)
C07J A61K A61P

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, WPI Data, BIOSIS, EMBASE, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X,P	WO 2011/029547 A2 (CHIESI FARMA SPA [IT]; ARMANI ELISABETTA [IT]; GHIDINI ELEONORA [IT];) 17 March 2011 (2011-03-17) cited in the application the whole document	1-15

-/--

[X] Further documents are listed in the continuation of Box C.

[X] 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
8 June 2012	16/11/2012

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Papathoma Sofia

Form PCT/ISA/210 (second sheet) (April 2005)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP2012/054455

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.:

5-8(completely); 1-4, 9-15(partially)

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.

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	GREEN M J ET AL: "Synthesis and topical antiinflammatory activity of some steroidal [16 alpha, 17 alpha-d]Isoxazolidines", JOURNAL OF MEDICINAL CHEMISTRY, AMERICAN CHEMICAL SOCIETY, US, vol. 25, no. 12, 1 December 1982 (1982-12-01), pages 1492-1495, XP002351702, ISSN: 0022-2623, DOI: 10.1021/JM00354A020 abstract page 1494; table I; compounds 17,19 page 1495; compounds 17,19	1-15
Y	US 3 631 033 A (NATHANSOHN GIANGIACOMO ET AL) 28 December 1971 (1971-12-28) abstract; claims 1-4, 9,14	1-15
Y	WO 2006/005611 A2 (NOVARTIS AG [CH]; NOVARTIS PHARMA GMBH [AT]; SANDHAM DAVID ANDREW [GB]) 19 January 2006 (2006-01-19) the whole document in particular page 6, line 8 to page 11, line 15, examples 4, 5 and 8	1-15
Y	WO 2009/069032 A2 (PFIZER LTD [GB]; GLOSSOP PAUL ALAN [GB]; MILLAN DAVID SIMON [GB]; PRIC) 4 June 2009 (2009-06-04) the whole document in particular examples 1-5, claims 1-15	1-15
Y	WO 2005/028495 A1 (GLAXO GROUP LTD [GB]; BIGGADIKE KEITH [GB]; WEINGARTEN GORDON GAD [GB]) 31 March 2005 (2005-03-31) abstract; claims 1-19; examples 32-33	1-15

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/EP2012/054455

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2011029547 A2	17-03-2011	AR 078164 A1	19-10-2011
		AU 2010294598 A1	05-04-2012
		CA 2773594 A1	17-03-2011
		CN 102482318 A	30-05-2012
		CO 6511204 A2	31-08-2012
		EP 2475676 A2	18-07-2012
		KR 20120055651 A	31-05-2012
		MA 33561 B1	01-09-2012
		PE 08942012 A1	13-08-2012
		SG 179055 A1	27-04-2012
		TW 201114776 A	01-05-2011
		US 2011065678 A1	17-03-2011
		WO 2011029547 A2	17-03-2011
US 3631033 A	28-12-1971	AT 291450 B	12-07-1971
		AT 300218 B	25-07-1972
		BE 731718 A	01-10-1969
		CH 511823 A	31-08-1971
		DE 1921778 A1	20-11-1969
		DE 1965963 A1	23-12-1970
		DK 124680 B	13-11-1972
		DK 128352 B	16-04-1974
		ES 366738 A1	16-03-1971
		ES 371991 A1	01-12-1971
		FI 46374 B	30-11-1972
		FI 46376 B	30-11-1972
		FI 46377 B	30-11-1972
		FR 2007756 A1	09-01-1970
		GB 1254487 A	24-11-1971
		IL 31997 A	14-03-1974
		LU 58451 A1	21-07-1969
		NL 6906149 A	05-11-1969
		NL 7709675 A	30-12-1977
		NO 128608 B	17-12-1973
		SE 363098 B	07-01-1974
		SE 373131 B	27-01-1975
		SE 373578 B	10-02-1975
		SE 378250 B	25-08-1975
		US 3631033 A	28-12-1971
WO 2006005611 A2	19-01-2006	AU 2005261869 A1	19-01-2006
		BR PI0513272 A	06-05-2008
		CA 2573405 A1	19-01-2006
		CN 101282987 A	08-10-2008
		EP 1809648 A2	25-07-2007
		JP 2008506649 A	06-03-2008
		US 2007185172 A1	09-08-2007
		WO 2006005611 A2	19-01-2006
WO 2009069032 A2	04-06-2009	AR 069490 A1	27-01-2010
		AU 2008331187 A1	04-06-2009
		CA 2706180 A1	04-06-2009
		CN 101878221 A	03-11-2010
		CO 6280401 A2	20-05-2011
		CR 11393 A	19-05-2010
		DO P2010000161 A	15-07-2010
		EA 201070535 A1	30-12-2010
		EC SP10010209 A	29-06-2010

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/EP2012/054455

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
		EP 2225256 A2	08-09-2010
		GT 201000153 A	27-04-2012
		JP 4686650 B2	25-05-2011
		JP 2011505350 A	24-02-2011
		KR 20100074306 A	01-07-2010
		MA 31867 B1	01-11-2010
		NZ 585434 A	29-06-2012
		PA 8805801 A1	23-07-2009
		PE 10722009 A1	23-07-2009
		SV 2010003580 A	23-03-2011
		TW 200930378 A	16-07-2009
		US 2009227548 A1	10-09-2009
		UY 31496 A1	17-07-2009
		WO 2009069032 A2	04-06-2009
WO 2005028495 A1	31-03-2005	NONE	

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

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

1. claims: 5-8(completely); 1-4, 9-15(partially)

   Steroidal isoxazolidines substituted at their 8-position by a group containing two rings, their pharmaceutical compositions, uses and methods of treatment comprising their administration.

   ---

2. claims: 1-4, 9-15(all partially)

   Steroidal isoxazolidines substituted at their 8-position by a group containing one ring, their pharmaceutical compositions, uses and methods of treatment comprising their administration (further subdivision possible).
