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7 February 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 comprising them, combinations and therapeutic uses thereof. More particularly, the invention relates to glucocorticosteroids that are derivatives of isoxazolidine.



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INTERNATIONAL SEARCH REPORT

International application No
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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 <table border="1"> <thead> <tr> <th>Category*</th> <th>Citation of document, with indication, where appropriate, of the relevant passages</th> <th>Relevant to claim No.</th> </tr> </thead> <tbody> <tr> <td>X,P</td> <td>WO 2011/029547 A2 (CHIESI FARMA SPA [IT]; ARMANI ELISABETTA [IT]; GHIDINI ELEONORA [IT];) 17 March 2011 (2011-03-17) the whole document in particular examples 73 for the 1st group, 171 for the 8th group, 10, 20, 25-27, 29, 30, 33, 38-44, 47, 50, 53, 55, 57, 61, 62, 64, 66-72, 77, 78 and 85 for the 10th group and claim 1 -----</td> <td>1-6,8-15</td> </tr> <tr> <td>X</td> <td>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 examples 1-3, 6 and 7 ----- -/-</td> <td>1-6,8-15</td> </tr> </tbody> </table>			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) the whole document in particular examples 73 for the 1st group, 171 for the 8th group, 10, 20, 25-27, 29, 30, 33, 38-44, 47, 50, 53, 55, 57, 61, 62, 64, 66-72, 77, 78 and 85 for the 10th group and claim 1 -----	1-6,8-15	X	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 examples 1-3, 6 and 7 ----- -/-	1-6,8-15
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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									
28 November 2012		07/12/2012									
Name and mailing address of the ISA/ European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016		Authorized officer Papathoma, Sofia									

INTERNATIONAL SEARCH REPORT

International application No

PCT/EP2012/054439

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	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 the whole document in particular abstract and table 1: examples 16-19 -----	1-6,8-15
X	US 3 631 033 A (NATHANSOHN GIANGIACOMO ET AL) 28 December 1971 (1971-12-28) the whole document -----	1-6,8-15
Y	JOURNAL OF THE CHEMICAL SOCIETY. PERKIN TRANSACTIONS 1 20020321 ROYAL SOCIETY OF CHEMISTRY GB, no. 6, 21 March 2002 (2002-03-21), pages 831-839, XP002656701, page 833; figures 4,5; compounds 16-21 -----	1-6,8-15
Y	JOURNAL OF MEDICINAL CHEMISTRY, vol. 44, no. 4, 15 February 2001 (2001-02-15), pages 602-612, XP002656702, ISSN: 0022-2623 page 603; figure 1; compounds 9b,11b -----	1-6,8-15
X	WO 2005/028495 A1 (GLAXO GROUP LTD [GB]; BIGGADIKE KEITH [GB]; WEINGARTEN GORDON GAD [GB]) 31 March 2005 (2005-03-31) the whole document in particular examples 10-15, 20, 21, 30, 31, 34, 35 and claims 1, 4, 5 and 8 -----	1-6,8-15
X	WO 2009/108118 A1 (ASTRAZENECA AB [SE]; BURKAMP FRANK [SE]; MUSSIE TESFALEDET [SE]; ANDER) 3 September 2009 (2009-09-03) the whole document in particular examples 3, 6, 7, 11-15, 17, 18, 21, 22, 29, 30, 32-35, 38, 40 and 43 -----	1-6,8-15

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP2012/054439

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.:
1-6, 8-15(all partially)
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.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/EP2012/054439

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			RU	2010133722 A		10-04-2012

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

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

1. claims: 1-6, 8-15(all partially)

Compounds of the formula (I) for which R2 is an (C1-C8)alkyl group, their pharmaceutical compositions and uses.

2. claims: 1-3, 8-15(all partially)

Compounds of the formula (I) for which R2 is an (C1-C6)alkoxy group, their pharmaceutical compositions and uses.

3. claims: 1-3, 8-15(all partially)

Compounds of the formula (I) for which R2 is an halo(C1-C6)alkyl group, their pharmaceutical compositions and uses.

4. claims: 1-3, 6, 8-15(all partially)

Compounds of the formula (I) for which R2 is an -(CH2)mR6 group, m is 0 and R6 is a (C3-C8)cycloalkyl group, their pharmaceutical compositions and uses.

5. claims: 1-5, 8-15(all partially)

Compounds of the formula (I) for which R2 is an -(CH2)mR6 group, m is 0 and R6 is a (C3-C8)heterocycloalkyl or heteroaryl group, their pharmaceutical compositions and uses.

6. claims: 7(completely); 1-5, 8-15(partially)

Compounds of the formula (I) for which R2 is an -(CH2)mR6 group, m is 0 and R6 is an aryl group, their pharmaceutical compositions and uses.

7. claims: 1-3, 8-15(all partially)

Compounds of the formula (I) for which R2 is an -(CH2)mR6 group, m is 0 and R6 is an aryloxy or arylthio group, their pharmaceutical compositions and uses.

8. claims: 1-6, 8-15(all partially)

Compounds of the formula (I) for which R2 is an -(CH2)mR6

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

group, m is other than 0 (i.e. 1-3) and R6 is an (C3-C8)cycloalkyl group, their pharmaceutical compositions and uses.

9. claims: 1-5, 8-15(all partially)

Compounds of the formula (I) for which R2 is an $-(CH_2)_mR_6$ group, m is other than 0 (i.e. 1-3) and R6 is an (C3-C8)heterocycloalkyl or heteroaryl group, their pharmaceutical compositions and uses.

10. claims: 1-5, 8-15(all partially)

Compounds of the formula (I) for which R2 is an $-(CH_2)_mR_6$ group, m is other than 0 (i.e. 1-3) and R6 is an aryl group and compounds of the formula (I) for which R2 is a (C1-C6)arylalkyl (with m being 0-3), their pharmaceutical compositions and uses.

11. claims: 1-3, 8-15(all partially)

Compounds of the formula (I) for which R2 is an $-(CH_2)_mR_6$ group, m is other than 0 (i.e. 1-3) and R6 is an aryloxy or arylthio group, their pharmaceutical compositions and uses.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/EP2012/054439

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
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		WO 2009108118 A1	03-09-2009
