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11/698,253 25 January 2007 (25.01.2007) US(71) Applicant (for all designated States except US): **LEX-
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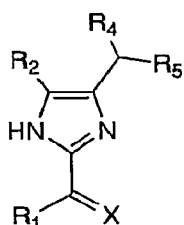
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East Winsor, NJ 08520 (US).(81) Designated States (unless otherwise indicated, for every
kind of national protection available): AE, AG, AL, AM,
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GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS,
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LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY,
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17 January 2008For two-letter codes and other abbreviations, refer to the "Guid-
ance Notes on Codes and Abbreviations" appearing at the begin-
ning of each regular issue of the PCT Gazette.

(54) Title: IMIDAZOLE-BASED COMPOUNDS, COMPOSITIONS COMPRISING THEM AND METHODS OF THEIR USE



I

(57) Abstract: Imidazole-based compounds, compositions comprising them, and methods of their use
for the treatment, prevention and management of inflammatory and autoimmune diseases and disorders
are disclosed. Particular compounds are of formula (I).

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INTERNATIONAL SEARCH REPORT

International application No

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A. CLASSIFICATION OF SUBJECT MATTER

INV. C07D233/54 A61K31/4164 A61P29/00

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 practical, search terms used)

EPO-Internal, BEILSTEIN 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	JOHN, W.: CHEM. BER., vol. 68, 1935, pages 2283-2291, XP002077052 page 2285; compound IX page 2287, paragraph 4	1-3, 8-10, 25, 30-32, 37-39, 54
X	OLIVER, J.E.; SONNET, P.E.: J. ORG. CHEM., vol. 38, no. 7, 1973, pages 1437-1438, XP002446297 page 1438, column 2; compound 3	1-3, 8-10, 25, 30-32, 37-39, 54
X	DE 21 45 456 A1 (BAYER AG) 15 March 1973 (1973-03-15) page 36; example 28	1-3, 10, 25, 30-32, 39, 54
	----- -/-	



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 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

10 August 2007

Date of mailing of the international search report

02/10/2007

Name and mailing address of the ISA/

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INTERNATIONAL SEARCH REPORT

International application No
PCT/US2007/004648

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	BELL ET AL: "2(1H)-Quinolinones with cardiac stimulant activity. 3. Synthesis and biological properties of 6-imidazol-1-yl derivatives" JOURNAL OF MEDICINAL CHEMISTRY, AMERICAN CHEMICAL SOCIETY. WASHINGTON, US, vol. 32, no. 7, 1989, pages 1552-1558, XP002200975 ISSN: 0022-2623 page 1553; table 1; compound 12 -----	1-3,6, 10,25, 30-32, 35,39,54
X	MATTHEWS, D.P.; ET AL.: J. MED. CHEM., vol. 33, no. 1, 1990, pages 317-327, XP000942263 page 318, column 1; compound 13C -----	1-3,5, 10,25, 30-32, 34,54
P,X	JAMES, D.A.; ET AL.: BIOORG. MED. CHEM. LETT., vol. 16, no. 19, 2006, pages 5164-5168, XP005611715 page 5166, column 1; compounds 10,14 -----	1-3,10, 22,25, 26, 30-32, 39,51, 54,55
X	KUJUNDZIC: PHARMAZIE, vol. 32, 1977, page 296, XP009088056 page 296; table 1; compound 2 -----	1,2,4, 8-10,17, 25,28, 30,31, 33, 37-39, 46,49, 54,57
X	GRIMMETT, M.R.; ET AL.: J. CHEM. SOC., 1975, pages 3751-3754, XP009088060 page 3753, line 7, paragraph 3 -----	1,2,4,6, 10,18, 25,30, 31,33, 39,47,54
X	CURTIS, N.J.; ET AL.: J. ORG. CHEM., vol. 45, no. 20, 1980, pages 4038-4040, XP000944041 page 4039; example 11; table 1; compound 18B ----- -/--	1-3,5, 11,13, 25, 30-32, 34,40, 42,54

INTERNATIONAL SEARCH REPORT

International application No

PCT/US2007/004648

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	HLASTA D J ET AL: "Imidazotriazinone inhibitors of the Ca ²⁺ -calmodulin sensitive phosphodiesterase (PDE I)" BIOORGANIC & MEDICINAL CHEMISTRY LETTERS, OXFORD, GB, vol. 7, no. 1, 7 January 1997 (1997-01-07), pages 89-94, XP004135972 ISSN: 0960-894X page 90; figure 1 -----	1-3,11, 13,28, 30-32, 40,42
A	HALWEG, K.M.; ET AL.: J. ORG. CHEM., vol. 50, no. 7, 1985, pages 1134-1136, XP002446300 cited in the application compound 1 -----	1-119
X	WO 97/46543 A (UNIV WOLLONGONG [AU]; PYNE STEPHEN GEOFFREY [AU]; UNG ALISON THAVARY []) 11 December 1997 (1997-12-11) cited in the application the whole document -----	59-63,65

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box II.1

Although claims 112-119 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.

Continuation of Box II.1

Claims Nos.:

Rule 39.1(iv) PCT - Method for treatment of the human or animal body by therapy

Continuation of Box II.2

Claims Nos.: -

The initial phase of the search revealed a very large number of documents relevant to the issue of novelty. So many documents were retrieved that it is impossible to determine which parts of the claims 1-58 and 109-119 may be said to define subject-matter for which protection might legitimately be sought (Article 6 PCT). For these reasons, the search was performed taking into consideration the non-compliance in determining the extent of the search of the claims. The search can only be considered complete for the subject-matter of claims 59-108, the documents cited "X" are a random selection of the documents found.

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guideline C-VI, 8.5), should the problems which led to the Article 17(2) declaration be overcome.

INTERNATIONAL SEARCH REPORT

International application No.
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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 112-119 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:

see FURTHER INFORMATION sheet PCT/ISA/210
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:

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.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/US2007/004648

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
DE 2145456	A1	15-03-1973	BE 788548 A1	08-03-1973
			CH 587604 A5	13-05-1977
			FR 2152799 A1	27-04-1973
			GB 1352100 A	15-05-1974
			IL 40319 A	30-01-1976
			IT 967280 B	28-02-1974
			JP 48034880 A	22-05-1973
			JP 48036338 A	29-05-1973
			NL 7212187 A	13-03-1973
			US 3968120 A	06-07-1976
WO 9746543	A	11-12-1997	AU 2881797 A	05-01-1998
			ZA 9704811 A	30-12-1997