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(54) Title: S-ALKYLISOTHIOURONIUM DERIVATIVES FOR THE TREATMENT OF INFLAMMATORY DISEASES

(57) Abstract: The present invention relates to uses of S-alkylisothiouronium derivatives for treating inflammation. In particular, the present invention provides extended release pharmaceutical dosage forms of S-alkylisothiouronium derivatives and methods of use thereof for the treatment of inflammatory diseases or conditions.

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INTERNATIONAL SEARCH REPORT

International application No
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A. CLASSIFICATION OF SUBJECT MATTER
INV. A61K31/155 A61K9/00 A61K9/20 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)
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 practical, search terms used)
EPO-Internal, CHEM ABS Data, BIOSIS, EMBASE, 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	WO 94/12165 A (WELLCOME FOUND [GB]; GARVEY EDWARD PATRICK [US]; TANOURY GERALD JOSEPH) 9 June 1994 (1994-06-09) abstract page 3, last paragraph page 12, paragraph 1 page 13, paragraph 2; claims 1,8,14; examples ----- -/--	1-3,5-7, 10, 13-16, 18-20, 23-28, 31,32

[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 document but published on or after the international filing date

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"P" document published prior to the international filing date but later than the priority date claimed

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"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
29 October 2007	08/11/2007

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, Tx. 31 651 epo nl, Fax: (+31–70) 340–3016	Hoff, Philippe

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

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 00/51623 A (TRUSTEES OF UNIVERSITY TECHNOL [US]) 8 September 2000 (2000-09-08) abstract page 13, line 33 - page 15, line 10 page 22, line 6 - line 8; claims 31-33	1,2,5,6, 10, 13-15, 18,19, 23-31
X	DATABASE CA [Online] CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; GHICAVII, VICTOR ET AL: "Remedy for nasal congestion treatment" XP002456848 retrieved from STN Database accession no. 2007:61004 abstract & MD 2 875 F1 (UNIVERSITATEA DE STAT DE MEDICINA SI FARMACIE "NICOLAE TESTEMITANU" DI) 31 October 2005 (2005-10-31)	1,2,5,6, 10,11, 13-15, 18,19, 23-28,31
X	WO 02/19961 A (MEDITOR PHARMACEUTICALS LTD [IL]; BARKAN RAPHAEL [IL]; MIRIMSKY ALEXAN) 14 March 2002 (2002-03-14) cited in the application abstract page 18, line 7 - line 25 page 19, line 30 - page 20, line 2 page 20, line 30 - page 21, line 6; claims	1-13
X	DATABASE CA [Online] CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; KONG, QINGZHONG ET AL: "Implants for local antitumor treatment containing angiogenesis inhibitors and antitumor drugs and biodegradable polymers" XP002456849 retrieved from STN Database accession no. 2006:316453 abstract & CN 1 736 486 A (PEOP. REP. CHINA) 22 February 2006 (2006-02-22)	1,2,5,6, 10,13
X	TANAKA SUMIKO ET AL: "Immunological abnormality associated with the augmented nitric oxide synthesis in adjuvant-induced arthritis" INTERNATIONAL JOURNAL OF IMMUNOPHARMACOLOGY, vol. 20, no. 1-3, January 1998 (1998-01), pages 71-84, XP002456846 ISSN: 0192-0561 the whole document	14,15, 18,24, 25, 27-29,31

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C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	SOUTHEY ANGELA ET AL: "Pathophysiological role of nitric oxide in rat experimental colitis" INTERNATIONAL JOURNAL OF IMMUNOPHARMACOLOGY, vol. 19, no. 11-12, 1997, pages 669-676, XP002456847 ISSN: 0192-0561 the whole document	14,15, 18,24, 25, 27-29,31
X	JANG D ET AL: "S-SUBSTITUTED ISOTHIOUREAS ARE POTENT INHIBITORS OF NITRIC OXIDE BIOSYNTHESIS IN CARTILAGE" EUROPEAN JOURNAL OF PHARMACOLOGY, AMSTERDAM, NL, vol. 312, no. 3, 1996, pages 341-347, XP000910850 ISSN: 0014-2999 the whole document	14,15, 18,19, 24,25, 27-29,31
X	SZABÓ C ET AL: "Beneficial effects and improved survival in rodent models of septic shock with S-methylisothiourea sulfate, a potent and selective inhibitor of inducible nitric oxide synthase" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA, NATIONAL ACADEMY OF SCIENCE, WASHINGTON, DC, US, vol. 91, no. 26, 20 December 1994 (1994-12-20), pages 12472-12476, XP002410960 ISSN: 0027-8424 abstract page 12476, left-hand column, paragraph 1	14,15, 18,19, 24,25, 27-29,31
X	SOUTHAN G J ET AL: "ISOTHIOUREAS: POTENT INHIBITORS OF NITRIC OXIDE SYNTHASE WITH VARIABLE ISOFORM SELECTIVITY" BRITISH JOURNAL OF PHARMACOLOGY, BASINGSTOKE, HANTS, GB, vol. 114, no. 2, 1995, pages 510-516, XP000575068 ISSN: 0007-1188 the whole document	14,15, 18,19, 24,25, 27,28,31
A	WO 98/13036 A (AMINOLAB LTD [IL]; MIZRAKH I LEV [IL]; GIKAVY I VICTOR [MD]; ZNAMENSKY) 2 April 1998 (1998-04-02) cited in the application abstract; claims; examples	1-32

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INTERNATIONAL SEARCH REPORT

International application No.
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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. [X] Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claims 14-30 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 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:

1. [ ] As all required additional search fees were timely paid by the applicant, this international search report covers allsearchable 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 reportcovers 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.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/IL2007/000385

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