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(71) Applicant and

(72) Inventor: SHARMA, Anant [GB/GB]; 37 Pemberley Avenue, Bedford MK40 2LE (GB).

(74) Agent: BANFORD, Jonathan; TM Gregory & Co, Carlton House, 26 Billing Road, Northampton NN1 5AT (GB).

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(54) Title: A MEDICAMENT COMPRISING A PARASYMPATHETIC AGONIST AND A SYMPATHETIC ANTAGONIST OR A SYMPATHETIC AGONIST

(57) Abstract: A medicament for topical administration to a human or animal eye comprises at least two pharmacologically active agents. One of the active agents is a parasympathetic agonist, such as pilocarpine, and the other active agent is either a sympathetic antagonist such as dapiprazole or thymoxamine, or a sympathetic agonist such as brimonidine or iopidine. The medicament is preferably in the form of a liquid composition, such as eye drops, or a gel or ointment and may comprise a slow-release composition. The medicament acts to improve visual acuity for a period of several hours, and may be beneficial in cases of presbyopia, myopia, hypermetropia, astigmatism and/or impaired night vision.



WO 2009/077736 A3

INTERNATIONAL SEARCH REPORT

International application No
PCT/GB2008/004129

A. CLASSIFICATION OF SUBJECT MATTER
 INV. A61K31/138 A61K31/4178 A61K31/496 A61K31/498 A61K31/385
 A61K31/4168 A61P27/02

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

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, EMBASE, BIOSIS, CHEM ABS 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	GEYER ORNA ET AL: "The additive miotic effects of dapiprazole and pilocarpine" GRAEFE'S ARCHIVE FOR CLINICAL AND EXPERIMENTAL OPHTHALMOLOGY, SPRINGER VERLAG, XX, vol. 233, no. 7, 1 July 1995 (1995-07-01), pages 448-451, XP008107292 ISSN: 0721-832X [retrieved on 2004-11-29] abstract page 450 <div style="text-align: center;">----- -/--</div>	1,4-9, 17,22,23

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 of other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
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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.
- *8* document member of the same patent family

Date of the actual completion of the international search

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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

Leherte, Chantal

INTERNATIONAL SEARCH REPORT

International application No
PCT/GB2008/004129

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>MASTROPASQUA L ET AL: "The usefulness of dapiprazole, an alpha-adrenergic blocking agent, in pigmentary glaucoma" OPHTHALMIC SURGERY AND LASERS, SLACK, INC., THOROFARE, NJ, US, vol. 27, no. 9, 1 September 1996 (1996-09-01), pages 806-809, XP008107290 ISSN: 1082-3069 page 806, column 1 - column 2, paragraph 4 page 808, column 2, paragraph 3 -----</p>	1,2,4-7, 9,17,22, 23
X	<p>MAPSTONE R: "Closed angle glaucoma. Experimental results" BRITISH JOURNAL OF OPHTHALMOLOGY, LONDON, GB, vol. 58, no. 1, 1 January 1974 (1974-01-01), pages 41-45, XP008107340 ISSN: 0007-1161 abstract -----</p>	1,2,4-7, 10,11, 17,22,23
Y	<p>DOUGHTY M J ET AL: "A REVIEW OF THE CLINICAL PHARMACOKINETICS OF PILOCARPINE MOXISYLYTE THYMOXAMINE AND DAPIPRAZOLE IN THE REVERSAL OF DIAGNOSTIC PUPILLARY DILATION" OPTOMETRY AND VISION SCIENCE, vol. 69, no. 5, 1992, pages 358-368, XP008107658 ISSN: 1040-5488 abstract page 364, column 2, paragraph 3 - page 366 -----</p>	1-11, 17-23
Y	<p>US 6 410 544 B1 (GWON ARLENE [US] ET AL) 25 June 2002 (2002-06-25) claims -----</p>	1-11, 17-23
Y	<p>ABRAMSON D H ET AL: "PILOCARPINE IN THE PRESBYOPE. DEMONSTRATION OF AN EFFECT ON THE ANTERIOR CHAMBER AND LENS THICKNESS" ARCHIVES OF OPHTHALMOLOGY, AMERICAN MEDICAL ASSOCIATION, US, vol. 89, no. 2, 1 February 1973 (1973-02-01), pages 100-102, XP000866126 ISSN: 0003-9950 abstract -----</p>	1-11, 17-23
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INTERNATIONAL SEARCH REPORT

International application No

PCT/GB2008/004129

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	<p>GILMARTIN B ET AL: "Reversal of tropicamide mydriasis with single instillations of pilocarpine can induce substantial pseudo-myopia in young adults" OPTHALMIC AND PHYSIOLOGICAL OPTICS, PERGAMON PRESS, OXFORD, GB, vol. 15, no. 5, 1 September 1995 (1995-09-01), pages 475-479, XP008107296 ISSN: 0275-5408 [retrieved on 2002-02-25] abstract</p>	1-11, 17-23
Y	<p>MANDELL A I ET AL: "REDUCED CYCLIC MYOPIA WITH PILOCARPINE GEL" ANNALS OF OPHTHALMOLOGY, vol. 20, no. 4, 1988, pages 133-135, XP008107341 ISSN: 0003-4886 abstract</p>	1-11, 17-23
Y	<p>IUGLIO N.: "Ocular effects of topical application of dapiprazole in man" GLAUCOMA, vol. 6, 1984, pages 110-116, XP008107656 abstract page 116, column 1, paragraph 2 - paragraph 3</p>	1-11, 17-23

INTERNATIONAL SEARCH REPORT

International application No.
PCT/GB2008/004129

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.:

see annex

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.

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, 17-23 (all partially), 7-11

A medicament adapted for topical administration to a human or animal eye, comprising a parasympathetic agonist and a sympathetic antagonist adapted to act as an alpha-receptor blocker

2. claims: 1-6, 17-23 (all partially), 12

A medicament adapted for topical administration to a human or animal eye, comprising a parasympathetic agonist and a sympathetic antagonist, wherein the sympathetic antagonist comprises a beta-blocker

3. claims: 1-6, 17-23 (all partially), 13- 16

A medicament adapted for topical administration to a human or animal eye, comprising a parasympathetic agonist and a sympathetic antagonist

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

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Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 6410544	B1	25-06-2002	
		AT 250412 T	15-10-2003
		AU 754588 B2	21-11-2002
		AU 5216099 A	21-02-2000
		BR 9912599 A	02-05-2001
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		DE 69911620 T2	29-07-2004
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