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

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
8 January 2009 (08.01.2009)

PCT

(10) International Publication Number
WO 2009/006130 A3

(51) International Patent Classification:
A61K 9/08 (2006.01) *A61K 31/195* (2006.01)
A61K 31/535 (2006.01) *A61K 31/155* (2006.01)

(21) International Application Number:
PCT/US2008/068090

(22) International Filing Date:
25 June 2008 (25.06.2008)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/946,801 28 June 2007 (28.06.2007) US

(71) Applicant *(for all designated States except US)*: **BAUSCH & LOMB INCORPORATED** [US/US]; One Bausch & Lomb Place, Rochester, NY 14604-2701 (US).

(72) Inventors; and
(75) Inventors/Applicants *(for US only)*: **VENKATESH, Srini** [US/US]; 9 Lusk Farm Circle, Pittsford, NY 14534 (US). **XIA, Erning** [US/US]; 93 Chippenham Drive, Penfield, NY 14526 (US).

(74) Agents: **SMITH, Glenn, D.** et al.; Bausch & Lomb Incorporated, One Bausch & Lomb Place, Rochester, NY 14604-2701 (US).

(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, 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, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, 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, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Declarations under Rule 4.17:

— *as to the identity of the inventor (Rule 4.17(i))*

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:
17 September 2009

(54) Title: SALT FREE HYALURONATE OPHTHALMIC SOLUTION

(57) Abstract: The present invention is directed to an ophthalmic composition in the form of a topical aqueous solution consisting essentially of an ophthalmologically active agent, an ion sensitive, hydrophilic polymer in an amount a of 0.004 to 1.5% by weight, at least one salt selected from the group of inorganic salts and buffers in a total amount of from 0.01 to 2.0% by weight, a wetting agent in an amount of 0 to 3.0% by weight, a preservative in an amount of 0 to 0.02% by weight, water, and optionally a pH regulating agent in an amount sufficient to give a pH of 4.0 to 8.0 to the composition, the ratio between salt and polymer components being such that the solution exhibits a viscosity of less than 1000 mPas. The composition contains a sufficient amount of polymer to provide for a controlled absorption of the drug into the eye, its viscosity having been reduced to provide for better handling characteristics.

WO 2009/006130 A3

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2008/068090

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61K9/08 A61K31/535 A61K31/195 A61K31/155

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, 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 2005/110439 A (S K PHARMACEUTICALS INC [US]; KARAGEOZIAN HAMPAR L [US]; PARK JOHN [US) 24 November 2005 (2005-11-24) example 1	1,4,5
X	US 2003/143274 A1 (VIEGAS TACEY X [US] ET AL) 31 July 2003 (2003-07-31) example 18	4,5
X	EP 0 976 407 A (SENJU PHARMA CO [JP]) 2 February 2000 (2000-02-02) examples 3,4,6	3-5
X	US 2002/183279 A1 (TANAKA KOICHIRO [JP]) 5 December 2002 (2002-12-05) example 3	1,4,5

-/--

[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

"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
14 July 2009	21/07/2009

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	Boulois, Denis

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2008/068090

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DATABASE WPI Week 200429 Thomson Scientific, London, GB; AN 2004-305270 XP002529081 & CN 1 437 947 A (LIU J) 27 August 2003 (2003-08-27) abstract	1,4,5
X	DATABASE WPI Week 200241 Thomson Scientific, London, GB; AN 2002-376193 XP002529082 & JP 2002 037746 A (FUJI YAKUHIN KK) 6 February 2002 (2002-02-06) abstract	4,5
X	DATABASE WPI Week 200425 Thomson Scientific, London, GB; AN 2004-258093 XP002529083 & CN 1 456 157 A (LIU J) 19 November 2003 (2003-11-19) abstract	1,4,5
X	WO 99/59543 A (HIGHCHEM COMPANY LTD [JP]; CHARNA CHEMICALS LTD [CN]; MA XIN FANG [CN]) 25 November 1999 (1999-11-25) example 3	2,4,5
X	DATABASE WPI Week 200239 Thomson Scientific, London, GB; AN 2002-355876 XP002536837 & JP 2002 020279 A (TAISHO PHARM CO LTD) 23 January 2002 (2002-01-23) abstract	2,4,5
X	EP 0 807 440 A (SENJU PHARMA CO [JP]) 19 November 1997 (1997-11-19) example 2	2,4,5
X	WO 2007/003481 A (SIGMA TAU IND FARMACEUTI [IT]; KOVERECH ALEARDO [IT]; PESCOSOLIDO NICO) 11 January 2007 (2007-01-11) example 1	2,4,5
A	WO 2006/110482 A (ADVANCED MEDICAL OPTICS INC [US]; YU ZHI-JIAN [US]; CRONER DIANE M [US) 19 October 2006 (2006-10-19) claims; examples	2,4,5
X	WO 2007/039201 A (BERLIN CHEMIE AG [DE]; WIHSMANN MARC [DE]; SCHMITZ REINHARD [DE]) 12 April 2007 (2007-04-12) examples 3,4,6	3-5

-/--

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2008/068090

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 02/49611 A (ALCON UNIVERSAL LTD [CH]; DOSHI UDAY [US]; WANG PAO-LI [US]; JAFARI MA) 27 June 2002 (2002-06-27) claims; examples	4,5
X	US 2005/080043 A1 (SHAHINIAN LEE [US]) 14 April 2005 (2005-04-14) claims; examples	4,5
X	US 5 166 331 A (DELLA VALLE FRANCESCO [IT] ET AL) 24 November 1992 (1992-11-24) example 14	4,5

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2008/068090

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 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.

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 (entirely),4 (part.),5 (part.)

   Composition comprising levofloxacine
   ---

2. claims: 2 (ent.), 4 and 5 (part.)

   Composition comprising taurine
   ---

3. claims: 3 (ent.), 4 and 5 (part.)

   Composition comrprising chlorhexidine
   ---

4. claims: 4,5 (all part.)

   Composition salt and buffer free

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/US2008/068090

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2005110439 A	24-11-2005	AU 2005244059 A1	24-11-2005
		CA 2565944 A1	24-11-2005
		EP 1746884 A2	31-01-2007
		JP 2007536277 T	13-12-2007
US 2003143274 A1	31-07-2003	NONE	
EP 0976407 A	02-02-2000	CA 2290461 A1	26-11-1998
		WO 9852612 A1	26-11-1998
		JP 11060505 A	02-03-1999
US 2002183279 A1	05-12-2002	NONE	
CN 1437947 A	27-08-2003	NONE	
JP 2002037746 A	06-02-2002	NONE	
CN 1456157 A	19-11-2003	NONE	
WO 9959543 A	25-11-1999	AU 3055099 A	06-12-1999
		EP 1079801 A1	07-03-2001
		US 6623732 B1	23-09-2003
JP 2002020279 A	23-01-2002	NONE	
EP 0807440 A	19-11-1997	CA 2204067 A1	13-11-1997
		JP 9301858 A	25-11-1997
		US 5908865 A	01-06-1999
WO 2007003481 A	11-01-2007	AU 2006265248 A1	11-01-2007
		CA 2611909 A1	11-01-2007
		CN 101242825 A	13-08-2008
		JP 2009500369 T	08-01-2009
		KR 20080030077 A	03-04-2008
		US 2007265338 A1	15-11-2007
WO 2006110482 A	19-10-2006	AU 2006235114 A1	19-10-2006
		CA 2604813 A1	19-10-2006
		CN 101155605 A	02-04-2008
		EP 1871432 A2	02-01-2008
		JP 2008538823 T	06-11-2008
		US 2006229219 A1	12-10-2006
WO 2007039201 A	12-04-2007	AR 056551 A1	10-10-2007
		AU 2006299115 A1	12-04-2007
		CA 2624111 A1	12-04-2007
		CN 101272765 A	24-09-2008
		DE 102005046769 A1	05-04-2007
		EC SP088310 A	30-05-2008
		EP 1940353 A2	09-07-2008
		JP 2009509993 T	12-03-2009
		KR 20080053319 A	12-06-2008
		US 2008249061 A1	09-10-2008
WO 0249611 A	27-06-2002	AU 3243702 A	01-07-2002
US 2005080043 A1	14-04-2005	NONE	

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/US2008/068090

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 5166331	A 24-11-1992	NONE	