

EXHIBIT 5

U. 7521000

THE UNITED STATES OF AMERICA

TO ALL TO WHOM THESE PRESENTS SHALL COME

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office

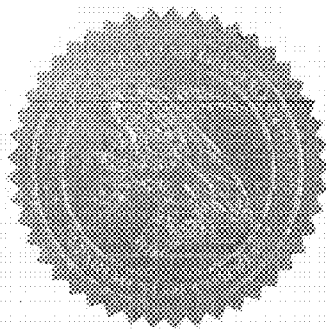
March 04, 2015

THIS IS TO CERTIFY THAT ANNEXED HERETO IS A TRUE COPY FROM
THE RECORDS OF THIS OFFICE OF:

U.S. PATENT: *8,168,620*

ISSUE DATE: *May 01, 2012*

By Authority of the
Under Secretary of Commerce for Intellectual Property
and Director of the United States Patent and Trademark Office



W. Montgomery
W. MONTGOMERY
Certifying Officer

US06816862082

(12) **United States Patent**
Lulla et al.

(10) **Patent No.:** US 8,168,620 B2
(45) **Date of Patent:** May 1, 2012

(54) COMBINATION OF AZELASTINE AND STEROIDS

(75) Inventors: Amar Lulla, Mumbai (IN); Geena Malhotra, Mumbai (IN)

(73) Assignee: CIPLA Limited, Mumbai (IN)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 987 days.

(21) Appl. No.: 10/518,916

(22) PCT Filed: Jun. 13, 2003

(86) PCT No.: PCT/GB03/02557
§ 371 (c)(1),
(2), (4) Date: Jul. 6, 2005

(87) PCT Pub. No.: WO03/105856
PCT Pub. Date: Dec. 24, 2003

(65) **Prior Publication Data**
US 2006/0025391 A1 Feb. 2, 2006

4,261,984 A 4/1981 Alvarez
4,263,289 A 4/1981 Edwards
4,267,173 A 5/1981 Draper
4,285,937 A 8/1981 Kalvoda
4,310,466 A 1/1982 Edwards
4,335,121 A 6/1982 Phillips et al.
4,377,575 A 3/1983 Stache et al.
4,477,393 A 9/1984 Shapiro
4,607,028 A 8/1986 Schmidlin
4,710,495 A 12/1987 Bodor
4,861,765 A 8/1989 Mitsukuchi et al.
4,992,474 A 2/1991 Skidmore et al.
4,994,439 A 2/1991 Longenecker et al.
4,996,335 A 2/1991 Bodor
5,063,222 A 11/1991 Komoto et al.
5,081,113 A 1/1992 Claussner et al.
5,164,194 A 11/1992 Hettche
5,202,316 A 4/1993 Claussner et al.
5,232,919 A 8/1993 Scheffler et al.
5,271,946 A 12/1993 Hettche
5,362,721 A 11/1994 Stache et al.
5,420,120 A 5/1995 Boltralik
5,608,093 A 3/1997 Stache et al.
5,658,549 A 8/1997 Akehurst et al.
5,658,919 A 8/1997 Ratnaraj et al.
5,707,984 A 1/1998 Tjoeng et al.
5,837,699 A 11/1998 Sequeira et al.
5,849,265 A 12/1998 Li-Bovet et al.
5,889,015 A 3/1999 Sequeira et al.
5,914,122 A 6/1999 Otterbeck et al.

(Continued)

(30) **Foreign Application Priority Data**
Jun. 14, 2002 (GB) 0213739.6

FOREIGN PATENT DOCUMENTS

AU 2003244799 B2 12/2003
(Continued)

(51) **Int. Cl.**
A01N 45/00 (2006.01)
A61K 31/56 (2006.01)
A61K 31/55 (2006.01)
A61K 31/57 (2006.01)
A61K 31/58 (2006.01)
A61K 9/00 (2006.01)
A61P 37/08 (2006.01)
A61P 27/14 (2006.01)
A61P 11/06 (2006.01)

OTHER PUBLICATIONS

preservative. (n.d.) Dorland's Medical Dictionary for Health Consumers. (2007). Retrieved Nov. 4, 2009 from <http://medical-dictionary.thefreedictionary.com/preservative>.*

preservative. (n.d.) The American Heritage® Medical Dictionary. (2007). Retrieved Nov. 4, 2009 from <http://medical-dictionary.thefreedictionary.com/preservative>.*

preservative. (n.d.) Mosby's Medical Dictionary, 8th edition. (2009). Retrieved Nov. 4, 2009 from <http://medical-dictionary.thefreedictionary.com/preservative>.*

Database Medline Online/ US National Library of Medicine (NLM), Bethesda, MD, US: 2000 Portmann D et al: Acceptability of local treatment of allergic rhinitis with a combination of a corticoid (beclomethasone) and an antihistaminic (azelastine), vol. 121, No. 4, 2000, pp. 273-279.

(Continued)

(52) **U.S. Cl.** 514/171

(58) **Field of Classification Search** 514/171
See application file for complete search history.

Primary Examiner — Johann Richter
Assistant Examiner — Thor Nielsen
(74) *Attorney, Agent, or Firm* — Conley Rose, P.C.; Rodney B. Carroll

(56) **References Cited**
U.S. PATENT DOCUMENTS

(57) **ABSTRACT**
A pharmaceutical product or formulation, which comprises azelastine or a pharmaceutically acceptable salt, solvate or physiologically functional derivative thereof, and a steroid, or a pharmaceutically acceptable salt, solvate or physiologically functional derivative thereof, preferably the product or formulation being in a form suitable for nasal or ocular administration.

2,837,464 A 6/1958 Nobile
3,067,197 A 12/1962 Agnello et al.
3,312,590 A 4/1967 Eiks et al.
3,506,694 A 4/1970 Oxley
3,557,162 A 1/1971 Voorschoten et al.
3,639,434 A 2/1972 Oxley et al.
3,755,302 A 8/1973 Ercoli et al.
3,823,000 A 8/1974 May et al.
3,856,328 A 12/1974 Philipps et al.
3,891,631 A 6/1975 Philipps et al.
3,981,894 A 9/1976 Philipps et al.
3,989,686 A 11/1976 Philipps et al.
4,093,721 A 6/1978 Philipps et al.
4,113,680 A 9/1978 Kamano et al.
4,187,301 A 2/1980 Edwards
4,188,385 A 2/1980 Edwards
4,198,403 A 4/1980 Alvarez
4,221,787 A 9/1980 Bodor et al.

48 Claims, No Drawings

US 8,168,620 B2

Page 2

U.S. PATENT DOCUMENTS

5,972,920	A	10/1999	Seidel		JP	8291073	11/1996
5,981,517	A	11/1999	Bodor		JP	2002-053485	2/2002
6,017,963	A *	1/2000	Alfonso et al.	514/646	WO	8903590	4/1989
6,057,367	A	5/2000	Sequeira et al.		WO	9015816	12/1990
6,127,353	A	10/2000	Yuen et al.		WO	9104252	4/1991
6,136,294	A	10/2000	Adjei et al.		WO	9214472	9/1992
6,197,761	B1	3/2001	Biggadike et al.		WO	9531964	11/1993
6,261,539	B1	7/2001	Adjei et al.		WO	9619199	6/1996
6,294,153	B1 *	9/2001	Modi	424/45	WO	9632151	10/1996
6,319,313	B1	11/2001	Dobrozai		WO	9701337	1/1997
6,330,938	B1	12/2001	Harve et al.		WO	9705136	2/1997
6,391,340	B1 *	5/2002	Malmqvist-Granlund et al.	424/489	WO	9715298	5/1997
					WO	9721721	6/1997
					WO	9721724	6/1997
6,395,300	B1	5/2002	Straub et al.		WO	9724365	7/1997
6,416,743	B1 *	7/2002	Fassberg et al.	424/45	WO	9740836	11/1997
6,525,228	B2	2/2003	Chauvin et al.		WO	9746243	A1 12/1997
6,537,983	B1	3/2003	Biggadike et al.		WO	9817676	4/1998
6,583,180	B2 *	6/2003	Link et al.	514/603	WO	9834596	8/1998
6,787,532	B2	9/2004	Biggadike et al.		WO	9848839	11/1998
6,921,757	B2	7/2005	Cuenoud et al.		WO	9901467	1/1999
7,101,866	B2	9/2006	Biggadike et al.		WO	9925359	5/1999
7,244,742	B2	7/2007	Pispor et al.		WO	9932089	7/1999
7,776,315	B2	8/2010	Pairet et al.		WO	0016814	3/2000
2002/0061281	A1	5/2002	Osbakken et al.		WO	0033892	6/2000
2002/0076382	A1	6/2002	Kaplan et al.		WO	0038811	7/2000
2002/0081266	A1	6/2002	Woolfe et al.		WO	0048587	8/2000
2002/0103392	A1	8/2002	Stache et al.		WO	0049993	8/2000
2002/0165211	A1	11/2002	Biggadike et al.		WO	0066522	11/2000
2002/0173496	A1	11/2002	Biggadike		WO	0104118	1/2001
2002/0177581	A1	11/2002	Biggadike		WO	0120331	3/2001
2003/0016019	A1	1/2003	Meade et al.		WO	0134481	8/2001
2003/0073676	A1	4/2003	Biggadike et al.		WO	0154664	8/2001
2003/0109511	A1	6/2003	Biggadike et al.		WO	0157025	8/2001
2003/0144257	A1	7/2003	Biggadike et al.		WO	0162722	8/2001
2003/0158163	A1	8/2003	Cusnoud et al.		WO	0178736	10/2001
2004/0053904	A1	3/2004	Komoto et al.		WO	0178739	10/2001
2004/0136918	A1	7/2004	Garrett et al.		WO	0178741	10/2001
2004/0204399	A1	10/2004	Osbakken et al.		WO	0178745	10/2001
2004/0235807	A1	11/2004	Weurich et al.		WO	0200199	1/2002
2004/0242638	A1	12/2004	Yanni et al.		WO	0200679	1/2002
2005/0163724	A1	7/2005	Miyadai et al.		WO	0202565	1/2002
2005/0192261	A1	9/2005	Jost-Price et al.		WO	0207767	1/2002
2006/0110331	A1	5/2006	Dang et al.		WO	0208243	1/2002
2006/0228306	A1	10/2006	Lane		WO	0212265	2/2002
2007/0020330	A1	1/2007	Dang et al.		WO	0212266	2/2002
2009/0256752	A1	11/2009	Myles et al.		WO	0213868	2/2002
2009/0291143	A1	11/2009	Lulla et al.		WO	0226723	4/2002
2009/0318397	A1	12/2009	Lulla et al.		WO	0236106	5/2002
2010/0152147	A1	6/2010	Fuge et al.		WO	02651422	7/2002

FOREIGN PATENT DOCUMENTS

BE	889563	A	11/1981		WO	02076490	9/2002
DE	1059906		6/1959		WO	02076933	10/2002
DE	19947234		4/2001		WO	02085296	10/2002
DE	10152369	A1	5/2002		WO	02088167	11/2002
DE	3836579	A1	8/2009		WO	02106879	12/2002
EP	0004773		10/1979		WO	03000241	1/2003
EP	0057401		8/1982		WO	03013427	2/2003
EP	0179583		4/1988		WO	03033006	4/2003
EP	0393658		10/1990		WO	03035668	5/2003
EP	0416951		3/1991		WO	03040691	5/2003
EP	0780127	*	6/1997		WO	03042229	5/2003
EP	0780127	*	6/1997		WO	03042230	5/2003
EP	1519731	B1	4/2009		WO	03048181	6/2003
EP	2072051	A1	6/2009		WO	03062259	7/2003
GB	1191965		5/1970		WO	03064445	8/2003
GB	1296458		11/1972		WO	03066033	8/2003
GB	1384372		2/1973		WO	03066036	8/2003
GB	1438940		6/1976		WO	03066656	8/2003
GB	1517278		7/1978		WO	03072592	9/2003
GB	2079755		1/1982		WO	03086389	10/2003
GB	2088877		6/1982		WO	03105856	A1 12/2003
GB	2140306		12/1984		WO	2004013156	2/2004
GB	2389530	A	12/2003		WO	2004019955	A1 3/2004
IL	109656		2/1998		WO	2008012338	A2 1/2008
JP	04208267		7/1992		WO	872389	4/1987
JP	9291072		11/1996		ZA		

US 8,168,620 R2

Page 3

OTHER PUBLICATIONS

- Busse W W et al: "Corticosteroid-Sparing Effect of Azelastine in the Management of Bronchial Asthma"—*American Journal of Respiratory and Critical Care Medicine*, American Lung Association, New York, NY, vol. 153, No. 1, 1996, pp. 122-172, p. 127, col. 1, paragraph 2.
- International Search Report under Section 17 UK Patent Office collections, including GB, EP, WO & US patent specifications.
- Foreign communication from the priority application—International Search Report, PCT/GB03/02557, Sep. 17, 2003, 3 pages.
- Foreign communication from the priority application—International Preliminary Examination Report, PCT/GB03/02557, Aug. 26, 2004, 6 pages.
- Foreign communication from a related counterpart application—Examination Report, EP Application 03738280.1, Nov. 10, 2005, 4 pages.
- Foreign communication from a related counterpart application—Examination Report, EP Application 03738280.1, Jul. 18, 2007, 5 pages.
- Applicants response to foreign communication—EP 03738280.1, May 22, 2006, 36 pages.
- Applicants response to foreign communication—EP 03738280.1, Jan. 18, 2008, 17 pages.
- May, Percy, et al., "May's Chemistry of Synthetic Drugs," Fifth Edition, 1964, pp. 12-17, Longmans.
- ABPI Compendium of Data Sheets and Summaries of Product Characteristics, 1999-2000, Cover page, p. 43 and Index p. 1882, Datapharm Publications Limited, London, Great Britain.
- Dykevicz, Mark S., et al., "Diagnosis and Management of Rhinitis: Complete Guidelines of the Joint Task Force on Practice Parameters in Allergy, Asthma and Immunology," *Annals of Allergy, Asthma, & Immunology*, vol. 81, November (Part II) 1998, pp. 478-518.
- Foreign communication from a related counterpart application—Notice of Opposition, EP Application 03738280.1, Feb. 22, 2010, 22 pages.
- Office Action dated Sep. 30, 2010, U.S. Appl. No. 12/508,388, filed Jul. 23, 2009, 22 pages.
- Office Action dated Sep. 30, 2010, U.S. Appl. No. 12/508,393, filed Jul. 23, 2009, 31 pages.
- Patent application entitled "Combination of azelastine and steroids," by Anas Lulla, et al., filed Sep. 10, 2010 as U.S. Appl. No. 12/879,515.
- Hodges, Norman, et al., "Antimicrobial Preservative Efficacy Testing," *Handbook of Microbiological Quality Control, Pharmaceuticals and Medical Devices*, 2000, p. 168 plus cover page and publication page, Rosamund M. Baird, et al., Editor, Taylor & Francis Publisher, USA and Canada.
- Herrero, Vanrell, R., "Preservatives in Ophthalmic Formulations: An Overview," *Arch. Soc. Esp. Ophthalmol*, 2007, vol. 82, pp. 531-532.
- Johnson, Malcolm, "Development of fluticasone propionate and comparison with other inhaled corticosteroids," *J. Allergy Clin. Immunol.*, Apr. 1998, vol. 101, No. 4, Part 2, pp. S434-S439.
- Foreign communication from a related counterpart application—CA2,489,427, Examination Report, Jun. 18, 2010, 3 pages.
- Foreign communication from a related counterpart application—CA2,489,427, Examination Report, Mar. 24, 2011, 2 pages.
- Foreign communication from a related counterpart application—Examination Report, EP Application 03738280.1, Nov. 10, 2005, 4 pages.
- Foreign communication from a related counterpart application—Examination Report, EP Application 03738280.1, Jul. 18, 2007, 5 pages.
- Foreign communication from a related counterpart application—Notice of Intent to Grant, EP Application 03738280.1, Oct. 23, 2008, 6 pages.
- Foreign communication from a related counterpart application—AI/2603244799, Examination Report, Nov. 20, 2007, 2 pages.
- Foreign communication from a related counterpart application—KR 10-2004-7020819, Examination Report, Aug. 26, 2010, 8 pages.
- Gennaro, Alfonso R., ed., et al., *Remington: The Science and Practice of Pharmacy*, 2000, 20th edition, vol. 1, pp. 785, 830, 831 plus cover page and publication page, Lippincott Williams & Wilkins.
- Gilbert, Peter, et al., "Preservation of pharmaceutical products," *Encyclopedia of Pharmaceutical Technology*, 2002, 2nd edition, vol. 3, p. 2278 plus cover page and publication page, Marcel Dekker, Inc.
- Office Action (Final) dated Feb. 18, 2011 (23 pages), U.S. Appl. No. 12/508,388, filed Jul. 23, 2009.
- Office Action (Final) dated Feb. 24, 2011 (20 pages), U.S. Appl. No. 12/508,393, filed Jul. 23, 2009.
- Reddy, Indra K., ed., *Ocular Therapeutics and Drug Delivery: A Multi-Disciplinary Approach*, 1996, pp. 382-385 plus cover page and publication page, Technomic Publishing Company, Inc.
- Foreign communication from a related counterpart application—Summons to Attend Oral Proceedings, EP Application 03738280.1, Feb. 8, 2011, 1 page.
- Foreign communication from a related counterpart application—Examination Report, RU 2005100781, Apr. 23, 2007, 6 pages.
- Foreign communication from a related counterpart application—Examination Report, RU 2005100781, May 23, 2008, 3 pages.
- Pre-Grant Opposition, Indian Patent Application 2092/KOLNP/2007 dated Jun. 8, 2007, 183 pages.
- McNeely, Wendy, et al., "Intranasal Azelastine: A Review of its Efficacy in the Management of Allergic Rhinitis," *Drugs*, 1998, vol. 56, No. 1, pp. 91-114.
- ABPI Data Sheet Compendium, 1995-96, cover page plus pp. 38-39, Datapharm Publications Limited, London, Great Britain.
- Aurora, Jack, "Nasal Delivery: Development of Nasal Delivery Systems: A Review," *Drug Delivery Technology*, vol. 2, No. 7, Oct. 2002, 8 pages, <http://www.drugdelivelytech.com/ME2/Segments/Publications:Article&id=9EB19EB2F29F462089CE081473F5F3CA>
- Block, John H., et al., "Inorganic Medicinal and Pharmaceutical Chemistry," 1986, cover, publication, and preface pages plus p. 100, Indian Edition, Varghese Publishing House, Bombay, India.
- Cipla Sixty-Ninth Annual Report 2004-2005, cover pages, information page, plus pp. 3, 5, and 44.
- Drouin, Michel A., et al., "Adding Loratadine to Topical Nasal Steroid Therapy Improves Moderately Severe Seasonal Allergic Rhinoconjunctivitis," *Advances in Therapy*, vol. 12, No. 6, Nov./Dec. 1995, pp. 340-349, Health Communications Inc.
- Foreign communication from a related counterpart application—Translation of Office Action, Israel Patent Application 165771, Jul. 11, 2011, 3 pages.
- Hodges, N. A., et al., "Preservative Efficacy Tests in Formulated Nasal Products: Reproducibility and Factors Affecting Preservative Activity," *J. Pharm. Pharmacol.*, 1996, vol. 48, pp. 1237-1242.
- Applicants response to foreign communication—KR10-2004-7020819, Dec. 27, 2010, 18 pages.
- Prescribing Information for Asteproce[®], Nov. 2010, 20 pages, Meda Pharmaceuticals Inc., Somerset, NJ, US.
- Prescribing Information for Rhinocort Aqua[™], Dec. 2010, 32 pages, AstraZeneca LP, Wilmington, DE, US.
- Product Information, Nasonex[®], Aug. 2001, 22 pages, Schering Corporation, Kenilworth, NJ, US.
- Safety Data Sheet, SDS No. 110556, Jul. 4, 2008, V14, Flonase Nasal Spray, 5 pages, GlaxoSmithKline.
- Safety Data Sheet, SDS No. 110536, Jun. 23, 2008, V13, Beconase Hayfever Allergy Spray, 5 pages, GlaxoSmithKline.
- Wiseman, Lynda R., et al., "Intranasal Fluticasone Propionate: A Reappraisal of its Pharmacology and Clinical Efficacy in the Treatment of Rhinitis," *Drugs*, 1997, vol. 53, No. 5, pp. 885-907, Adis International Limited.
- World Review 2001: The Pharmaceutical Market, vol. 1 International, IMS Health, 2001, cover, preface, and copyright pages plus pp. 4-42 and 5-1 through 5-11, IMS A.G.
- Opposition to EP 1518731, Aug. 8, 2011, 19 pages.
- Berge, Stephen M., et al., "Pharmaceutical Salts," *Journal of Pharmaceutical Sciences*, vol. 66, No. 1, Jan. 1977, pp. 1-19.
- Avicel[®] RC/CL, Microcrystalline Cellulose and Carboxymethylcellulose Sodium, NF Dispersible Cellulose, BP Specifications and Analytical Methods, RC-16 Updated Oct. 1995 (Feb. 1999), 6 pages, FMC BioPolymer.
- Baena-Cagnani, Carlos E., "Safety and Tolerability of Treatments for Allergic Rhinitis in Children," *Drug Safety* 2004, vol. 27, No. 12, pp. 863-896, ADIS Data Information BV.

Copy provided by USPTO from the PIRS Image Database on 03/04/2015

Explore Litigation Insights

Docket Alarm provides insights to develop a more informed litigation strategy and the peace of mind of knowing you're on top of things.

Real-Time Litigation Alerts



Keep your litigation team up-to-date with **real-time alerts** and advanced team management tools built for the enterprise, all while greatly reducing PACER spend.

Our comprehensive service means we can handle Federal, State, and Administrative courts across the country.

Advanced Docket Research



With over 230 million records, Docket Alarm's cloud-native docket research platform finds what other services can't. Coverage includes Federal, State, plus PTAB, TTAB, ITC and NLRB decisions, all in one place.

Identify arguments that have been successful in the past with full text, pinpoint searching. Link to case law cited within any court document via Fastcase.

Analytics At Your Fingertips



Learn what happened the last time a particular judge, opposing counsel or company faced cases similar to yours.

Advanced out-of-the-box PTAB and TTAB analytics are always at your fingertips.

API

Docket Alarm offers a powerful API (application programming interface) to developers that want to integrate case filings into their apps.

LAW FIRMS

Build custom dashboards for your attorneys and clients with live data direct from the court.

Automate many repetitive legal tasks like conflict checks, document management, and marketing.

FINANCIAL INSTITUTIONS

Litigation and bankruptcy checks for companies and debtors.

E-DISCOVERY AND LEGAL VENDORS

Sync your system to PACER to automate legal marketing.