



US008163723B2

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

(10) **Patent No.:** **US 8,163,723 B2**
(45) **Date of Patent:** **Apr. 24, 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 77 days.
- (21) Appl. No.: **12/879,515**
- (22) Filed: **Sep. 10, 2010**
- (65) **Prior Publication Data**
US 2010/0331289 A1 Dec. 30, 2010
- Related U.S. Application Data**
- (62) Division of application No. 10/518,016, filed as application No. PCT/GB03/02557 on Jun. 13, 2003.
- (30) **Foreign Application Priority Data**
Jun. 14, 2002 (GB) 0213739.6
- (51) **Int. Cl.**
A61K 31/55 (2006.01)
- (52) **U.S. Cl.** **514/171**
- (58) **Field of Classification Search** None
See application file for complete search history.

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	Longnecker 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.
5,972,920 A	10/1999	Seidel
5,981,517 A	11/1999	Bodor
6,017,963 A	1/2000	Alfonso et al.
6,057,307 A	5/2000	Sequeira et al.
6,127,353 A	10/2000	Yuen et al.
6,136,294 A	10/2000	Adjei et al.
6,197,761 B1	3/2001	Biggadike et al.
6,261,539 B1	7/2001	Adjei et al.
6,294,153 B1	9/2001	Modi
6,319,513 B1	11/2001	Dobrozi
6,330,938 B1	12/2001	Herve et al.
6,391,340 B1	5/2002	Malmqvist-Granlund et al.
6,395,300 B1	5/2002	Straub et al.
6,416,743 B1	7/2002	Fassberg et al.
6,525,228 B2	2/2003	Chauvin et al.

(Continued)

FOREIGN PATENT DOCUMENTS

AU 2003244799 B2 12/2003

(Continued)

OTHER PUBLICATIONS

Office Action (Final) dated Feb. 18, 2011 (23 pages), U.S. Appl. No. 12/508,388, filed Jul. 23, 2009.

(Continued)

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

(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 pharmaceutical acceptable salt, solvate or physiologically functional derivative thereof, preferably the product or formulation being in a form suitable for nasal or ocular administration.

28 Claims, No Drawings

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

2,837,464 A	6/1958	Nobile
3,067,197 A	12/1962	Agnello et al.
3,312,590 A	4/1967	Elks 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.
3,828,080 A	8/1974	May et al.
3,856,828 A	12/1974	Phillipps et al.
3,891,631 A	6/1975	Phillipps et al.
3,981,894 A	9/1976	Phillipps et al.
3,989,686 A	11/1976	Phillipps et al.
4,093,721 A	6/1978	Phillipps 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.
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	Phillipps et al.
4,377,575 A	3/1983	Stache et al.
4,472,393 A	9/1984	Shapiro

U.S. PATENT DOCUMENTS

6,537,983	B1	3/2003	Biggadike et al.
6,583,180	B2	6/2003	Link et al.
6,787,532	B2	9/2004	Biggadike et al.
6,921,757	B2	7/2005	Cuenoud et al.
7,101,866	B2	9/2006	Biggadike et al.
7,244,742	B2	7/2007	Pieper et al.
7,776,315	B2	8/2010	Pairet et al.
2002/0061281	A1	5/2002	Osbakken et al.
2002/0076382	A1	6/2002	Kaplan et al.
2002/0081266	A1	6/2002	Woolfe et al.
2002/0103392	A1	8/2002	Stache et al.
2002/0165211	A1	11/2002	Biggadike et al.
2002/0173496	A1	11/2002	Biggadike
2002/0177581	A1	11/2002	Biggadike
2003/0018019	A1	1/2003	Meade et al.
2003/0073676	A1	4/2003	Biggadike et al.
2003/0109511	A1	6/2003	Biggadike et al.
2003/0144257	A1	7/2003	Biggadike et al.
2003/0158163	A1	8/2003	Cuenoud et al.
2004/0053904	A1	3/2004	Komoto et al.
2004/0136918	A1	7/2004	Garrett et al.
2004/0204399	A1	10/2004	Osbakken et al.
2004/0235807	A1	11/2004	Weinrich et al.
2004/0242638	A1	12/2004	Yanni et al.
2005/0163724	A1	7/2005	Miyadia et al.
2005/0192261	A1	9/2005	Jost-Price et al.
2006/0025391	A1	2/2006	Lulla et al.
2006/0110331	A1	5/2006	Dang et al.
2006/0228306	A1	10/2006	Lane
2007/0020330	A1	1/2007	Dang et al.
2009/0286762	A1	11/2009	Myles et al.
2009/0291143	A1	11/2009	Lulla et al.
2009/0318397	A1	12/2009	Lulla et al.
2010/0152147	A1	6/2010	Fuge et al.

FOREIGN PATENT DOCUMENTS

BE	889563	A	11/1981
DE	1059906		6/1959
DE	3836579	A1	5/1989
DE	19947234	A1	9/1999
DE	10152369	A1	5/2002
EP	0004773		10/1979
EP	0057401		8/1982
EP	0179583		4/1986
EP	0393658		10/1990
EP	0416951		3/1991
EP	0780127		6/1997
EP	0780127	A1	6/1997
EP	1519731	B1	4/2009
EP	2072051	A1	6/2009
GB	1191965		5/1970
GB	1296458		11/1972
GB	1384372		2/1975
GB	1438940		6/1976
GB	1517278		7/1978
GB	2079755		1/1982
GB	2088877		6/1982
GB	2140800		12/1984
GB	2389530	A	12/2003
IL	109656		2/1998
JP	04208267		7/1992
JP	8291072		11/1996
JP	8291073		11/1996
JP	2002-053485		2/2002
WO	8903390		4/1989
WO	9015816		12/1990
WO	9104252		4/1991
WO	9214472		9/1992
WO	9531964		11/1995
WO	9619199		6/1996
WO	9632151		10/1996
WO	9701337	A1	1/1997
WO	9705136		2/1997
WO	9715298		5/1997
WO	9721721		6/1997

WO	9740836		11/1997
WO	9746243	A1	12/1997
WO	9817676		4/1998
WO	9834596		8/1998
WO	9848839	A1	11/1998
WO	9901467		1/1999
WO	9925359		5/1999
WO	9932089		7/1999
WO	0016814		3/2000
WO	0033892		6/2000
WO	0038811		7/2000
WO	0048587		8/2000
WO	0049993		8/2000
WO	0066522		11/2000
WO	0104118		1/2001
WO	0120331		3/2001
WO	0154481		8/2001
WO	0154664		8/2001
WO	0157025		8/2001
WO	0162722		8/2001
WO	0178736		10/2001
WO	0178739		10/2001
WO	0178741		10/2001
WO	0178745		10/2001
WO	0200199		1/2002
WO	0200679		1/2002
WO	0202565		1/2002
WO	0207767		1/2002
WO	0208243		1/2002
WO	0212265		2/2002
WO	0212266		2/2002
WO	0213868		2/2002
WO	0226723		4/2002
WO	0236106		5/2002
WO	02051422		7/2002
WO	02053186		7/2002
WO	02066422		8/2002
WO	02070490		9/2002
WO	02076933		10/2002
WO	02085296		10/2002
WO	02088167		11/2002
WO	02100879		12/2002
WO	03000241		1/2003
WO	03013427		2/2003
WO	03033000		4/2003
WO	03035668		5/2003
WO	03040691		5/2003
WO	03042229		5/2003
WO	03042230		5/2003
WO	03048181		6/2003
WO	03062259		7/2003
WO	03064445		8/2003
WO	03066033		8/2003
WO	03066036		8/2003
WO	03066656		8/2003
WO	03072592		9/2003
WO	03086399		10/2003
WO	03105856	A1	12/2003
WO	2004013156		2/2004
WO	2004019955	A1	3/2004
WO	2008012338	A2	1/2008
ZA	872389		4/1987

OTHER PUBLICATIONS

Office Action (Final) dated Feb. 24, 2011 (20 pages), U.S. Appl. No. 12/508,393, filed Jul. 23, 2009.

Office Action dated Feb. 16, 2011, (22 pages), U.S. Appl. No. 10/518,016, filed Jul. 6, 2005.

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.

Schmidt, M. W., "The new topical steroid ciclesonide is effective in the treatment of allergic rhinitis," *Journal of Clinical Pharmacology*, 1999, vol. 39, pp. 1062-1069.

- Nielsen, et al., "Intranasal corticosteroids for allergic rhinitis: superior relief?" *Drugs*, 2001, vol. 61, No. 11, pp. 1535-1691.
- Opponent's R116 Submission for EP1519731, 2011.
- CIPLA's response to Statement of Opposition for EP1519731, 2011.
- Shenfield, "Fixed drug combinations: which ones can be recommended?" *Current Therapeutics*, 1986, pp. 15-29.
- Opponent's Statement of Opposition for EP1519731, 2011.
- Result of oral proceedings dated Oct. 12, 2011 of EP Patent No. 1519731.
- Opponent's submission dated Oct. 6, 2011 to EP Patent No. 1519731.
- Patentee's submission dated Oct. 5, 2011 to EP Patent No. 1519731.
- Patentee's submission dated Sep. 29, 2011 regarding list of attendees at oral proceedings on EP Patent No. 1519731.
- Opponent's submission dated Sep. 23, 2011 regarding list of attendees at oral proceedings on EP Patent No. 1519731.
- Opponent's submission dated Sep. 23, 2011 regarding additional documents on EP Patent No. 1519731.
- Patentee's submission dated Sep. 19, 2011 on EP Patent No. 1519731.
- Patentee's response of Sep. 6, 2010 of EP Patent No. 1519731.
- Hampel, Frank C., et al., Double-blind, placebo-controlled study of azelastine and fluticasone in a single nasal spray delivery device, *Annals of Allergy, Asthma & Immunology*, Aug. 2010, vol. 105, pp. 168-173.
- Biggadike, Keith, Letter to the Editor, "Fluticasone furoate/fluticasone propionate—different drugs with different properties," *The Clinical Respiratory Journal*, 2011, pp. 183-184.
- Rapid response report: summary with critical appraisal, fluticasone furoate versus fluticasone propionate for seasonal allergic rhinitis: a review of the clinical and cost-effectiveness, Jun. 13, 2011, Fluticasone Furoate for Seasonal Allergic Rhinitis.
- Office Action dated Sep. 9, 2011 of U.S. Appl. No. 12/508,388, filed Jul. 23, 2009.
- Office Action dated Sep. 15, 2011 of U.S. Appl. No. 12/508,393, filed Jul. 23, 2009.
- Search Report dated May 12, 2009 of EP 09075101.
- Search Report dated May 12, 2009 of EP 09075100.
- Mealy, N. E., et al., "Ciclesonide: treatment of allergic rhinitis anti-allergy/antiasthmatic," *Drugs of the Future*, Prous Science, ES, vol. 26, No. 11, Nov. 2001, pp. 1033-1039.
- Office Action dated Jul. 11, 2011—20632 IL.
- Office Action dated Aug. 31, 2010 (6 pages), U.S. Appl. No. 12/374,523, filed Jan. 21, 2009.
- Applicants' response dated Oct. 6, 2010 (8 pages) in U.S. Appl. No. 12/374,523, filed Jan. 21, 2009.
- Office Action dated Nov. 30, 2010 (16 pages), U.S. Appl. No. 12/374,523, filed Jan. 21, 2009.
- Applicants' response dated Feb. 24, (2010) 2011 (8 pages) in U.S. Appl. No. 12/374,523, filed Jan. 21, 2009.
- Office Action (Final) dated May 3, 2011 (8 pages), U.S. Appl. No. 12/374,523, filed Jan. 21, 2009.
- Applicants' response dated Jun. 22, 2011 (9 pages) in U.S. Appl. No. 12/374,523, filed Jan. 21, 2009.
- Notice of Non-responsive Amendment dated Jul. 6, 2011 (3 pages), U.S. Appl. No. 12/374,523, filed Jan. 21, 2009.
- Applicants' response dated Sep. 6, 2011 (8 pages) in U.S. Appl. No. 12/374,523, filed Jan. 21, 2009.
- Spector, Sheldon, "Ideal pharmacotherapy for allergic rhinitis," *J Allergy Clin Immunol*, vol. 103, No. 3, Part 2, pp. S386-S387, 1999.
- Duonase Data Sheet, "The complete rhinitis control," 6 pages, Cipla Limited, Mumbai, India, 2004.
- Product Specification Bulletin, Avicel® RC-591, Bulletin AVC591-SPEC-02/09.RS, 2 pages, FMC BioPolymer, Feb. 2009.
- Product Specification Bulletin, Avicel® CL-611, Bulletin AVC611-SPEC02/09.RS, 2 pages, FMC BioPolymer, Feb. 2009.
- File history of Brazilian Patent Application No. PI 0312128-3, 27 pages, Apr. 2011.
- File history of Canadian Patent Application No. 2,489,427, 19 pages, Dec. 2010.
- File history of Polish Patent Application No. P-373001, 95 pages, May 2011.
- Notice of Allowance dated Oct. 3, 2011 (33 pages) in U.S. Appl. No. 10/518,016, filed Jul. 6, 2005.
- Salib, et al.; "Safety and Tolerability Profiles of Intranasal Antihistaminase and Intranasal Corticosteroids in the Treatment of Allergic Rhinitis;" *Drug Safety*; 2003; vol. 26, No. 12, pp. 829-911.
- Office Action dated Apr. 7, 2011 (3 pages) from counterpart application, AU2009243420.
- Product Information, Nasonex®, Aug. 2001, 22 pages, Schering Corporation, Kenilworth, NJ, US.
- Product Specification Bulletin, Avicel® RC-591, Bulletin AVC591-SPEC-02/09.RS, 2 pages, FMC BioPolymer.
- Product Specification Bulletin, Avicel® CL-611, Bulletin AVC611-SPEC-02/09.RS, 2 pages, FMC BioPolymer.
- Ratner, Paul H., et al., "Combination therapy with azelastine hydrochloride nasal spray and fluticasone propionate nasal spray in the treatment of patients with seasonal allergic rhinitis," *Annals of Allergy, Asthma & Immunology*, Jan. 2008, vol. 100, Cover page, publishing page, pp. 74-81.
- Ratner, Paul H., et al., "A Comparison of the Efficacy of Fluticasone Propionate Aqueous Nasal Spray and Loratadine, Alone and in Combination, for the Treatment of Seasonal Allergic Rhinitis," *The Journal of Family Practice*, Aug. 1998, vol. 47, No. 2, pp. 118-125, Appleton & Lange.
- 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.
- 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.
- Salib Rami Jean, et al., "Safety and Tolerability Profiles of Intranasal Antihistamines and Intranasal Corticosteroids in the Treatment of Allergic Rhinitis," *Drug Safety* 2003, vol. 26, No. 12, Cover page, publication page, pp. 863-893, ADIS Data Information BV.
- Simpson, Richard J., "Budesonide and terfenadine, separately and in combination, in the treatment of hay fever," *Annals of Allergy*, Dec. 1994, vol. 73, Cover page, publication page, pp. 497-502.
- Spector, Sheldon, "Ideal pharmacotherapy for allergic rhinitis," *J Allergy Clin Immunol*, 1999, vol. 103, No. 3, Part 2, pp. S386-S387, Mosby, Inc..
- Wang, De-Yun, "Treatment of Allergic Rhinitis: H1-Antihistamines and Intranasal Steroids," *Current Drug Targets—Inflammation & Allergy*, 2002, vol. 1, pp. 215-220, Bentham Science Publishers Ltd.
- 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, IMC Health, 2001, cover, preface, and copyright pages plus pp. 4-42 and 5-1 through 5-11, IMS A.G.
- Applicant Response to foreign communication EP Patent 1519731, Aug. 11, 2011, 252 pages.
- "Azelastine," STN Registry No. 58581-89-8, STN Registry File, Retrieved Nov. 23, 2010, p. 1.
- "Fluticasone Furoate," STN Registry No. 397864-44-7, STN Registry File, Retrieved Nov. 23, 2010, p. 1.
- Astepro (azelastine HCl) Nasal Spray 0.15%, Meda Pharmaceuticals Inc., 2009, Press Release, pp. 1-4.
- Aigbirhio, Franklin I., et al., "Automated radiosynthesis of no-carrier-added [S-fluoromethyl-18F]Fluticasone propionate as a radiotracer for lung deposition studies with PET," *Journal of Labelled Compounds and Radiopharmaceuticals*, vol. 39, No. 7, 1997, pp. 569-584.
- Austin, et al., "Mometasone furoate is a less specific glucocorticoid than fluticasone propionate," *Eur. Respir. J.*, 2002, vol. 20, pp. 1386-1392.
- Banov, et al., "Once daily intranasal fluticasone propionate is effective for perennial allergic rhinitis," *Annals of Allergy*, 1994, vol. 73, pp. 240-246.
- Baumgarten, C., et al., "Initial treatment of symptomatic mild to moderate bronchial asthma with the salmeterol/fluticasone

- Berstein, et al., "Treatment with intranasal fluticasone propionate significantly improves ocular symptoms in patients with seasonal allergic rhinitis," *Clin. Exp. Allergy*, 2004, vol. 34, pp. 952-957.
- Brooks, et al., "Spectrum of seasonal allergic rhinitis symptom relief with topical corticoid and oral antihistamine given singly or in combination," *American Journal of Rhinology*, 1996, vol. 10, No. 3, pp. 193-199.
- Bryson, et al., "Intranasal fluticasone propionate: a review of its pharmacodynamic and pharmacokinetic properties, and therapeutic potential in allergic rhinitis," *Drugs*, 1992, vol. 43, No. 5, pp. 760-775.
- Busse, William, et al., "Steroid-sparing effects of fluticasone propionate 100µg and salmeterol 50 µg administered twice daily in a single product in patients previously controlled with fluticasone propionate 250 µg administered twice daily," *J. Allergy Clin. Immunol.*, vol. 111, No. 1, Jan. 2003, pp. 57-65.
CAS Registry No. 102113-40-6, 2004.
- CAS Registry No. 90566-53-3, "Fluticasone," Nov. 16, 1984.
- Chapman, et al., "Anti-inflammatory activity of inhaled mometasone furoate in allergic mice," *Arzneimittelforschung ("Drug Research")*, 1998, vol. 48, No. 4, pp. 384-391.
- Daley-Yates, et al., "Systemic bioavailability of fluticasone propionate administered as nasal drops and aqueous nasal spray formulations," *Br. J. Clin. Pharmacol.*, 2001, vol. 51, pp. 103-105.
- Derby, et al., "Risk of cataract among users of intranasal corticosteroids," *J. Allergy Clin. Immunol.*, 2000, vol. 105, No. 5, pp. 912-916.
- Dewester, et al., "The efficacy of intranasal fluticasone propionate in relief of ocular symptoms associated with seasonal rhinitis," *Allergy and Asthma Proc.*, 2003, vol. 24, No. 5, pp. 331-337.
- Dictionary of Organic Compounds, 6th Ed., vol. 1, p. 3234, definition of "fluticasone," Chapman & Hall, 1996.
- Dolovich, et al., "Multicenter trial of fluticasone propionate aqueous nasal spray in ragweed allergic rhinitis," *Annals of Allergy*, 1994, vol. 73, No. 2, pp. 147-153.
- Fowler, Stephen J., et al., "Step-down therapy with low-dose fluticasone-salmeterol combination or medium-dose hydrofluoroalkane 134a-beclomethasone alone," *J. Allergy Clin. Immunol.*, vol. 109, No. 6, Jun. 2002, pp. 929-935.
- Garner, R. C., et al., "A validation study comparing accelerator MS and liquid scintillation counting for analysis of ¹⁴C-labelled drugs in plasma, urine and faecal extracts," *Journal of Pharmaceutical and Biomedical Analysis*, vol. 24, 2000, pp. 197-209.
- Gawchik, et al., "Comparison of intranasal triamcinolone acetonide with oral loratadine in the treatment of seasonal ragweed-induced allergic rhinitis," *Am. J. Man. Care*, 1997, vol. 3, No. 7, pp. 1052-1058.
- Harding, "The human pharmacology of fluticasone propionate," *Respiratory Medicine*, 1990, vol. 84, Suppl. A, pp. 25-29.
- Howland, "Fluticasone propionate: topical or systemic effects?" *Clinical and Experimental Allergy*, 1996, vol. 26, Suppl. 3, pp. 18-22.
- Isogai, et al., "Binding affinities of mometasone furoate and related compounds including its metabolites for the glucocorticoid receptor of rat skin tissue," *J. Steroid Biochem. Mol. Biol.*, 1993, vol. 44, pp. 141-145.
- Johansson, Gunnar, et al., "Comparison of salmeterol/fluticasone propionate combination with budesonide in patients with mild-to-moderate asthma," *Clin. Drug Invest.*, vol. 21, No. 9, 2001, pp. 633-642, 11 pages.
- Juniper, Elizabeth F., et al., "Impact of inhaled salmeterol/fluticasone propionate combination product versus budesonide on the health-related quality of life of patients with asthma," *Am. J. Respir. Med.*, vol. 1, No. 6, 2002, pp. 435-440.
- Kenley, Richard A., et al., "An automated, column-switching HPLC method for analyzing active and excipient materials in both cream and ointment formulations," *Drug Development and Industrial Pharmacy*, vol. 11 (9 & 10), 1985, pp. 1781-1796.
- Kertesz, Denis J., et al., "Thiol esters from steroid 17β-carboxylic acids: carboxylate activation and internal participation by 17 α-acylates," *J. Org. Chem.*, vol. 51, 1986, 14 pages.
- Kooreman, et al., "The synthesis of 17-esters of corticosteroids pro-
- Laforce, et al., "Fluticasone propionate: an effective alternative treatment for seasonal allergic rhinitis in adults and adolescents," *J. Fam. Pract.*, 1994, vol. 38, No. 2, pp. 145-152.
- Lane, S. J., et al., "Evaluation of a new capillary electrochromatography/mass spectrometry interface using short columns and high field strengths for rapid and efficient analyses," *Rapid Communications in Mass Spectrometry*, vol. 10, 1996, pp. 733-736.
- Lewis, Sarah A., et al., "Association of specific allergen sensitization with socioeconomic factors and allergic disease in a population of Boston women," *J. Allergy Clin. Immunol.*, vol. 107, No. 4, Apr. 2001, pp. 615-622.
- Li, et al., "Synthesis of aryl 5-(2-chlorophenyl)-2-furoates under phase transfer catalysis," *Synthetic Communications*, vol. 32, No. 20, pp. 3081-3086, 2002.
- Linder, "Symptom scores as measurements of the severity of rhinitis," *Clinical Allergy*, 1988, vol. 18, pp. 29-37.
- Lutsky, et al., "A novel class of potent topical antiinflammatory agents: 17-benzoylated, 7α-halogeno substituted corticosteroids," *Arzneimittelforschung ("Drug Research")*, 1978, vol. 29, No. 11, pp. 1662-1667.
- Lyseng-Williamson, Katherine A., et al., "Inhaled salmeterol/fluticasone propionate combination in chronic obstructive pulmonary disease," *Am. J. Respir. Med.*, vol. 1, No. 4, 2002, pp. 273-282.
- Mahoney, Janette M., et al., "Drug effects on the neovascularization response to silver nitrate cauterization of the rat cornea," *Current Eye Research*, vol. 4, No. 5, 1985, pp. 531-535.
- Millard, Jeffrey W., et al., "Solubilization by cosolvents establishing useful constants for the log-linear model," *Int'l Journal of Pharmaceutics*, vol. 245, 2002, pp. 153-166.
- Mistry, Nisha, et al., "Characterisation of impurities in bulk drug batches of fluticasone propionate using directly coupled HPLC-NMR spectroscopy and HPLC-MS," *Journal of Pharmaceutical and Biomedical Analysis*, vol. 16, 1997, pp. 697-705.
- Mistry, Nisha, et al., "Impurity profiling in bulk pharmaceutical batches using 19F NMR spectroscopy and distinction between monomeric and dimeric impurities by NMR-based diffusion measurements," *Journal of Pharmaceutical and Biomedical Analysis*, vol. 19, 1999, pp. 511-517.
- Moreno-Vargas, et al., "Synthesis and glycosidase inhibitory activities of 5-(1',4'-dideoxy-1',4'-imino-D-erythrosyl)-2-methyl-3-furoic acid (=5-[(3S,4R)-3,4-dihydroxypyrolidin-2-yl]-2-methylfuran-3-carboxylic acid) derivatives: new leads as selective alpha-L-fucosidase and beta-galactosidase inhibitors," *Helvetica Chimica Acta*, vol. 86, pp. 1894-1913, 2003.
- Nathan, et al., "A once daily fluticasone propionate aqueous nasal spray is an effective treatment for seasonal allergic rhinitis," *Annals of Allergy*, 1991, vol. 67, pp. 332-338.
- Nelson, Harold S., et al., "Fluticasone propionate-salmeterol combination provides more effective asthma control than low-dose inhaled corticosteroid plus montelukast," *J. Allergy Clin. Immunol.*, vol. 106, No. 6, Dec. 2000, pp. 1088-1095.
- Ong, John T. H., et al., "Micellar solubilization of timobesone acetate in aqueous and aqueous propylene glycol solutions of nonionic surfactants," *Pharmaceutical Research*, vol. 5, No. 11, 1988, pp. 704-708.
- Ong, John T. H., et al., "Intrinsic potencies of novel thiol ester corticosteroids RS-85095 and RS-21314 as compared with clobetasol 17-propionate and fluocinonide," *Arch Dermatol*, vol. 125, Dec. 1989, pp. 1662-1665.
- Onrust, et al., "Mometasone furoate, a review of its intranasal use in allergic rhinitis," *Drugs*, vol. 56, No. 4, Oct. 1998, pp. 725-745, vol. 21.
- Pettersson, Bertil, et al., "Re-evaluation of the classical mycoplasma lipophilum cluster (Weisburg, et al., 1989) and description of two new clusters in the hominis group based on 16S rDNA sequences," *Int'l Journal of Systematic & Evolutionary Microbiology*, 2001, vol. 51, pp. 633-643.
- Phillips, G. H., et al., "Synthesis and structure activity relationships in a series of anti-inflammatory corticosteroid analogues, halomethyl androstane—17B-carbothioates and—17B-carboselenoates," *Journal of Medicinal Chemistry*, 1994, vol. 37, pp. 3717-3729.

- Product Information Rhinocort Aqua (budesonide) Nasal Spray 32 mcg, 2005, pp. 1-2.
- Sakagami, et al., "Mucoadhesive BDP microspheres for powder inhalation—their unique pharmacokinetic-pharmacodynamic profiles," *Respiratory Drug Delivery*, vol. VI, pp. 193-199, 1998.
- Sandham, et al., "Synthesis and biological properties of novel glucocorticoid androstene C-17 furoate esters," *Bioorganic & Medicinal Chemistry*, 2004, vol. 12, pp. 5213-5224.
- Scadding, et al., "Clinical and physiological effects of fluticasone propionate aqueous nasal spray in the treatment of perennial rhinitis," *Rhinology*, 1991, Suppl. 11, pp. 37-43.
- Settipane, et al., "Triamcinolone acetonide aqueous nasal spray in patients with seasonal ragweed allergic rhinitis: a placebo-controlled, double-blind study," *Clin. Ther.*, 1995, vol. 17, No. 2, pp. 252-263.
- Shapiro, et al., "17-esters and 17,21-diester of 9-alpha, 11-beta-dichlorocorticoids. Synthesis and anti-inflammatory activity," *Steroids*, vol. 9, No. 2, pp. 143-156, 1967.
- Shapiro, et al., "Synthesis and structure-activity studies of corticosteroid 17-heterocyclic aromatic esters. 1. 9-alpha, 11-beta dichloro series," *Journal of Medicinal Chemistry*, vol. 30, No. 6, pp. 1068-1073, 1987.
- Shapiro, et al., "17 heteroaryl esters of corticosteroids 2. 11 beta hydroxy series," *Journal of Medicinal Chemistry*, American Chemical Society, Washington, US, vol. 30, No. 9, 1987, pp. 1581-1588.
- Smith, et al., "In vitro glucocorticoid receptor binding and transcriptional activation by topically active glucocorticoids," *Arzneimittelforschung*, 1998, 48(II)(9), pp. 956-959.
- Smith, N., et al., "Comparison of the electroosmotic flow profiles and selectivity of stationary phases used in capillary electrochromatography," *Journal of Chromatography A.*, vol. 832, 1999, pp. 41-54.
- Souness, et al., "Immunosuppressive and anti-inflammatory effects of cyclic AMP phosphodiesterase (PDE) type 4 inhibitors," *Immunopharmacology*, 2000, vol. 47, Nos. 2/3, pp. 127-162.
- Stempel, et al., "Treatment of allergic rhinitis: an evidence-based evaluation of nasal corticosteroids versus non-sedating antihistamines," *Am. J. Man. Care*, 1998, vol. 4, pp. 89-96.
- Study No. 03DMW062—"Pharmacokinetics of GW685698X and CC118781 (fluticasone propionate) when co-administered by the intratracheal or intravenous route to the anaesthetised white pig," 2004.
- Study No. B30947—"The Pharmacokinetics of GW685698X and CC118781 following intratracheal co-administration to the anaesthetised white pig," 2003.
- Szefler, Stanley J., et al., Chapter 21, "Glucocorticoids in severe asthma: mechanisms of action and route of administration," *Difficult Asthma*, pp. 371-375, Martin Dunitz Ltd., Informa Health Care, 1999.
- Togashi, et al., 9-fluoro-11B, 17, 21-trihydroxy-16a-methyl-1,4-pregnadiene-3, 20-dione 21-cyclohexanecarboxylate 17-cyclopropanecarboxylate (ST126); Oyo Yakuri, 2002, vol. 63, No. 5/6, pp. 61-77.
- Udem, et al., "Neural integration and allergic disease," *J. Allergy Clin. Immunol.*, 2000, vol. 106, No. 5, pp. S213-S220.
- The United States Pharmacopoeia, 23rd Ed., US Pharmacopoeia Convention, Inc., Rockville MD, 1995, pp. 1843-1844, "Physical Tests / (941) X-Ray Diffraction."
- Van AS, et al., "Once daily fluticasone propionate is as effective for perennial allergic rhinitis as twice daily beclomethasone dipropionate," *J. Allergy Clin. Immunol.*, 1993, vol. 91, No. 6, pp. 1146-1154.
- Van Bavel, et al., "Ocular efficacy and clinician overall evaluation of intranasal fluticasone propionate (FP) versus loratadine (LOR) in seasonal allergic rhinitis (SAR)," *Annals of Allergy, Asthma, & Immunology*, 1997, vol. 78, p. 128, Abstract P101.
- Wenkert, et al., "Short syntheses of furan and catechol derivatives. A synthesis of hydroureshiol.2," *Journal American Chemical Society*, vol. 105, pp. 2021-2029, 1983.
- Westlund, et al., "Fluticasone propionate aqueous nasal spray 200 mg once daily provides relief of ocular symptoms associated with seasonal allergic rhinitis," 57th Annual Meeting of the American Acad-
- Woodford, et al., "Activity and bioavailability of a new steroid (Timobesone acetate) in cream and ointment compared with Lidex and Dermovate creams and ointments and Betnovate cream," *Int'l Journal of Pharmaceutics*, 1985, vol. 26, pp. 145-155.
- Observations on patentability of the object of the patent application PV 2003-352 (Czech Republic), 2003.
- Notice of Opposition to the grant of patent on Patent Application No. 762/2001 (140397) (Pakistan), 2010.
- CIPLA Annual Report Extract; 2010; (report shows that they launched an FF+azelastine product in 2010).
- Declaration of Geena Malhotra for EP1519731 dated Aug. 11, 2011.
- Declaration of Joachim Maus for EP1519731 dated Aug. 10, 2011.
- Vanrell, "Preservatives in ophthalmic formulations: an overview," *Arch. Soc. Esp. Oftalmol.*, 2007, vol. 82, pp. 531-532.
- Malhotra Exhibit A, Aug. 2011.
- ABPI Data Sheet Compendium, 1995-96, cover page plus pp. 38-39, Datapharm Publications Limited, London, Great Britain.
- Akerlund, Anders, et al., "Clinical trial design, nasal allergen challenge models, and considerations of relevance to pediatric, nasal polyposis, and different classes of medication," *J. Allergy Clin. Immunol.*, Mar. 2005, vol. 115, No. 3, pp. S460-S482.
- Applicants response to foreign communication—KR10-2004-7020819, Dec. 27, 2010, 18 pages.
- Applicants response to foreign communication—EP 03738280.1 (EP Patent 1519731), Sep. 6, 2010, 15 pages.
- Applicants response to foreign communication—CA 2489427, Dec. 20, 2010, 10 pages.
- 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.
- Opposition to EP 1518731, Aug. 8, 2011, 19 pages.
- 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>.
- Baena-Cagnani, Carlos E., "Safety and Tolerability of Treatments for Allergic Rhinitis in Children," *Drug Safety* 2004, vol. 27, No. 12, pp. 883-898, ADIS Data Information BV.
- Barnes, M. L., et al., "Effects of levocetirizine as add-on therapy to fluticasone in seasonal allergic rhinitis," *Clinical and Experimental Allergy*, Jan. 27, 2006, vol. 36, pp. 676-684, Blackwell Publishing Ltd.
- Berge, Stephen M., et al., "Pharmaceutical Salts," *Journal of Pharmaceutical Sciences*, vol. 66, No. 1, Jan. 1977, pp. 1-19.
- 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.
- Di Lorenzo, G., et al., "Randomized Placebo-controlled Trial Comparing fluticasone aqueous nasal spray in mono-therapy, fluticasone plus cetirizine, fluticasone plus montelukast and cetirizine plus montelukast for seasonal allergic rhinitis," *Clin. Exp. Allergy*, 2004, vol. 34, pp. 259-267., Blackwell Publishing Ltd.
- Duonase Data Sheet, "The Complete Rhinitis Control," 6 pages, Cipla Limited, Mumbai, India.
- 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.
- File history of Australian Patent Application No. AU2003244799, 38 pages.
- File history of Brazilian Patent Application No. PI 0312128-3, 27 pages.
- File history of Canadian Patent Application No. 2,489,427, 19 pages.
- File history of Korean Patent Application No. 10-2004-7020819, 89 pages.
- File history of Mexican Patent Application No. PA/a/2004/01266 (now Patent No. 265349), 86 pages.
- File history of Polish Patent Application No. P-373001, 95 pages.

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.