



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

<p>(51) International Patent Classification ⁶ : A61K 45/06, 31/57, 31/58, 31/135, 31/35, 31/245, 31/09, 31/38, 31/195, 31/47, 31/445, 31/55, 31/44, 31/615, 31/415</p>	<p>A1</p>	<p>(11) International Publication Number: WO 98/48839 (43) International Publication Date: 5 November 1998 (05.11.98)</p>
<p>(21) International Application Number: PCT/US98/06483 (22) International Filing Date: 2 April 1998 (02.04.98) (30) Priority Data: 60/044,306 30 April 1997 (30.04.97) US (71) Applicant (for all designated States except US): WARNER-LAMBERT COMPANY [US/US]; 201 Tabor Road, Morris Plains, NJ 07950 (US). (72) Inventor; and (75) Inventor/Applicant (for US only): SEGAL, Catherine, A. [US/US]; 60 Shawnee Avenue, Rockaway, NJ 07866 (US). (74) Agents: RYAN, M., Andrea; Warner-Lambert Company, 201 Tabor Road, Morris Plains, NJ 07950 (US) et al.</p>	<p>(81) Designated States: AL, AU, BA, BB, BG, BR, CA, CN, CZ, EE, GE, GW, HU, ID, IL, IS, JP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, ARIPO patent (GH, GM, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG).</p> <p>Published <i>With international search report.</i></p>	
<p>(54) Title: TOPICAL NASAL ANTIINFLAMMATORY COMPOSITIONS</p>		
<p>(57) Abstract</p> <p>The present invention provides topically applicable nasal compositions comprising a therapeutically effective amount of an antiinflammatory agent and a therapeutically effective amount of at least one agent selected from the group consisting of a vasoconstrictor, a neuramidinase inhibitor, a leukotriene inhibitor, an antihistamine, an antiallergic agent, an anticholinergic agent, an anesthetic and a mucolytic agent. The present compositions are useful as nasal sprays and nose drops for the treatment of nasal and sinus conditions.</p>		

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	ES	Spain	LS	Lesotho	SI	Slovenia
AM	Armenia	FI	Finland	LT	Lithuania	SK	Slovakia
AT	Austria	FR	France	LU	Luxembourg	SN	Senegal
AU	Australia	GA	Gabon	LV	Latvia	SZ	Swaziland
AZ	Azerbaijan	GB	United Kingdom	MC	Monaco	TD	Chad
BA	Bosnia and Herzegovina	GE	Georgia	MD	Republic of Moldova	TG	Togo
BB	Barbados	GH	Ghana	MG	Madagascar	TJ	Tajikistan
BE	Belgium	GN	Guinea	MK	The former Yugoslav Republic of Macedonia	TM	Turkmenistan
BF	Burkina Faso	GR	Greece	ML	Mali	TR	Turkey
BG	Bulgaria	HU	Hungary	MN	Mongolia	TT	Trinidad and Tobago
BJ	Benin	IE	Ireland	MR	Mauritania	UA	Ukraine
BR	Brazil	IL	Israel	MW	Malawi	UG	Uganda
BY	Belarus	IS	Iceland	MX	Mexico	US	United States of America
CA	Canada	IT	Italy	NE	Niger	UZ	Uzbekistan
CF	Central African Republic	JP	Japan	NL	Netherlands	VN	Viet Nam
CG	Congo	KE	Kenya	NO	Norway	YU	Yugoslavia
CH	Switzerland	KG	Kyrgyzstan	NZ	New Zealand	ZW	Zimbabwe
CI	Côte d'Ivoire	KP	Democratic People's Republic of Korea	PL	Poland		
CM	Cameroon	KR	Republic of Korea	PT	Portugal		
CN	China	KZ	Kazakstan	RO	Romania		
CU	Cuba	LC	Saint Lucia	RU	Russian Federation		
CZ	Czech Republic	LI	Liechtenstein	SD	Sudan		
DE	Germany	LK	Sri Lanka	SE	Sweden		
DK	Denmark	LR	Liberia	SG	Singapore		
EE	Estonia						

**TOPICAL NASAL ANTIINFLAMMATORY
COMPOSITIONS**

SPECIFICATION

BACKGROUND OF THE INVENTION

5 Topical nasal antiinflammatory preparations are known in the art for
the treatment of inflammatory conditions of the nasal mucous membranes, and in
particular for relief of the symptoms of nasal and sinus conditions such as rhinitis.
However, nasal and sinus conditions may be characterized by diverse symptoms
requiring treatment with multiple therapeutic agents. For example, allergic rhinitis
may be characterized by rhinorrhea, nasal itching, sneezing, congestion and postnasal
10 drip and treatment may require antihistamines, decongestants, antiallergics and
anesthetics in addition to antiinflammatories.

The use of multiple topical nasal preparations to administer multiple
therapeutic agents suffers from significant disadvantages. The volume of liquid that
can effectively be applied nasally is limited by the surface area of the nostril and the
15 bioadhesiveness of the liquid. In addition, a sufficient contact time between topical
preparations and the surface area of the nostril is required to assure adequate dosing
of a therapeutic agent. Further, spray formulations require a threshold surface
tension to form droplets. Accordingly, the delivery volume per actuation is limited to
the volume that will be retained in the nostril without premature drainage. Thus
20 multiple topical nasal preparations cannot be effectively administered simultaneously.

Another disadvantage of the administration of multiple topical nasal preparations is patient inconvenience. Patient compliance may be compromised by the inconvenience of applying multiple spray products or nose drops. Patients complain when excess spray drains into their throats where it can be tasted, resulting in a need for flavor masking of bitter medicaments.

Accordingly, a need exists for a convenient means of nasal administration of multiple therapeutic agents.

SUMMARY OF THE INVENTION

The present invention provides topically applicable nasal compositions comprising a therapeutically effective amount of a topical antiinflammatory agent and a therapeutically effective amount of at least one agent suitable for topical nasal administration and selected from the group consisting of a vasoconstrictor, a neuramidinase inhibitor, an anticholinergic agent, a leukotriene inhibitor, an antihistamine, an antiallergic agent, an anesthetic, and a mucolytic agent.

DETAILED DESCRIPTION OF THE INVENTION

The present invention provides topically applicable nasal compositions comprising a topical antiinflammatory agent and at least one additional therapeutic agent. The present compositions are useful for the treatment of nasal and sinus conditions, for example allergic rhinitis or the common cold.

The topical antiinflammatory agents in the compositions of the present invention are corticosteroids known in the art to suppress inflammation. In a preferred embodiment the topical antiinflammatory agent is beclomethasone dipropionate, budesonide, dexamethasone, mometasone furoate, fluticasone propionate or triamcinolone acetonide. The compositions contain a therapeutically effective amount of the selected antiinflammatory agent. Those of ordinary skill in the art can determine an amount that is therapeutically effective for the suppression of inflammation. The precise amount will depend upon the method of administration and the age, weight and condition of the subject to be treated. Generally the

antiinflammatory agents are utilized in dosages known in the art to be therapeutically effective upon nasal administration.

The compositions of the invention further comprise at least one additional therapeutic agent, and thus allow the convenient administration of an antiinflammatory agent and at least one additional therapeutic agent in a single topical nasal composition. The additional therapeutical agent is suitable for topical nasal administration and is selected from the group consisting of a vasoconstrictor, a neuramidinase inhibitor, a leukotriene inhibitor, an anticholinergic agent, an antihistamine, an antiallergic agent, a local anesthetic and a mucolytic agent. The use of an additional therapeutic agent in combination with an antiinflammatory agent provides additive and synergistic effects in the treatment of nasal and sinus conditions.

Vasoconstrictors suitable for topical nasal administration in the compositions of the present invention are oxymetazoline naphazoline, xylometazoline, and phenylephrine. Leukotriene inhibitors include zafirlukast, a selective, competitive receptor antagonist of the three leukotrienes C4, D4, and E4; pranlukast, a selective, competitive receptor antagonist of D4; and zileuton, a leukotriene inhibitor. A. neuramidinase inhibitor includes zanamivir (GG-167). Suitable antihistamines are diphenhydramine, chlorpheniramine, cetirizine terfenadine, fenofexadine, astemizole norastemizole, azelastine, and azatidine. Antiallergic agents include cromolyn sodium and nedocromil levocabastine. An anticholinergic agent useful in the compositions of the present invention is ipratropium bromide. Local topical anesthetics include dyclonine, pramoxine, and benzocaine. Mucolytic agents suitable for topical nasal administration are acetylcysteine, guaifenisin and mucocysteine. The therapeutically effect amount of foregoing agents can be determined by the ordinarily skilled artisan with regard to the known use of these agents in the art and taking into account the method of administration and the age, weight and condition of the subject to be treated.

The compositions of the present invention are formulated as aqueous solutions comprising an antiinflammatory agent and at least one additional therapeutic agent and further comprising a pharmaceutically acceptable nasal carrier.

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.