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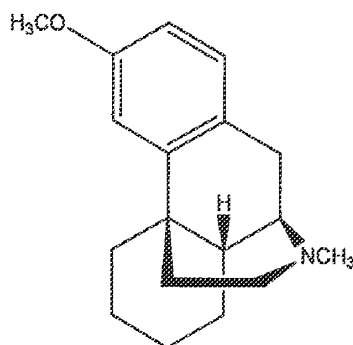
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[Continued on next page]

(54) Title: DEXTROMETHORPHAN ANTITUSSIVE COMPOSITIONS

FIG. 1



(57) Abstract: The invention provides orally administered antitussive pharmaceutical compositions comprising dextromethorphan, wherein the compositions are free of bromide, sodium and polistirex.

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DEXTROMETHORPHAN ANTITUSSIVE COMPOSITIONS

CROSS REFERENCE TO RELATED APPLICATIONS

This application claims the benefit of U.S. Provisional Appl. No.:
5 61/369,742, filed August 1, 2010. The content of the aforesaid application is
relied upon and incorporated by reference in its entirety.

FIELD OF THE INVENTION

The field of the invention relates generally to antitussive compositions
10 containing dextromethorphan, essentially free of bromide, sodium and polistirex
and methods of administering the same to subjects in need thereof.

BACKGROUND OF THE INVENTION

Dextromethorphan (racemethorphan), 3-methoxy-17-methylmorphinan, is
15 disclosed on p. 1170 in the *Merck Index, 10th Edition* (1983), M. Windholz, ed.,
No. 8009, as an antitussive agent.

Dextromethorphan hydrobromide is used extensively as an antitussive
agent in commercial products as disclosed in the *Physicians' Desk Reference for
Nonprescription Drugs*, 11th Edition (1990), E. R. Barnhardt, pub., p. 306; and in
20 *Physicians' Desk Reference*, 44th Edition (1990), E. R. Barnhardt, pub., p. 309, as
follows:

Bayer Children's Cough Syrup by Glenbrook, Benylin DM by Parke-Davis,
Benylin Expectorant by Parke-Davis, CeroSe-DM by Wyeth-Ayerst, Cheracol
D Cough Formula by Upjohn, Cheracol Plus Head Cough/Cold Formula by
25 Upjohn, Cough Formula Comtrex by Bristol-Myers Products, Comtrex Multi-
Symptom Cold Reliever Tablets/Caplets/Liquid/Liquigels by Bristol-Myers
Products, Contac Cough Formula by SmithKline Consumer, Contac Cough &
Sore Throat Formula by SmithKline Consumer, Contac Jr. Children's Cold
Medicine by SmithKline Consumer, Contac Nighttime Cold Medicine by
30 SmithKline Consumer, Contac Severe Cold Formula Caplets by SmithKline
Consumer, Dimacol Caplets by Robins, Dorcol Children's Cough Syrup by

Sandoz Consumer, Hold by SmithKline Beecham, Naldecon DX Adult Liquid by Bristol Laboratories, Naldecon DX Children's Syrup by Bristol Laboratories, Naldecon DX Pediatric Drops by Bristol Laboratories, Naldecon Senior DX Cough/Cold Liquid by Bristol Laboratories, Novahistine DMX by
5 Lakeside Pharmaceuticals, Pediacare Cough-Cold Formula Liquid and Chewable Tablets by McNeil Consumer Products, Pediacare Night Rest Cough-Cold Formula Liquid by McNeil Consumer Products, Robitussin Night Relief by Robins, Robitussin-CF by Robins, Robitussin-DM by Robins, Scot-Tussin Sugar-Free DM Cough & Cold Medicine by Scot-Tussin, Snaplets-DM
10 by Baker Cummins Pharmaceuticals, Snaplets-Multi by Baker Cummins Pharmaceuticals, St. Joseph Cough Suppressant for Children by Plough, St. Joseph Nighttime Cold Medicine by Plough, Sucrets Cough Control Formula by SmithKline Beecham, Sudafed Cough Syrup by Burroughs Wellcome, Triaminic Night Light by Sandoz Consumer, Triaminic-DM Syrup by Sandoz
15 Consumer, Triaminicol Multi-Symptom Cold Tablets by Sandoz Consumer, Triaminicol Multi-Symptom Relief by Sandoz Consumer, Tylenol Cold Medication Caplets and Tablets by McNeil Consumer Products, Tylenol Cold Medication Liquid by McNeil Consumer Products, Tylenol Cold Medication No Drowsiness Formula Caplets by McNeil Consumer Products, Vicks
20 Children's Cough Syrup by Richardson-Vicks, Inc., Vicks Children's NyQuil by Richardson-Vicks, Inc., Vicks Cough Silencers Cough Drops by Richardson-Vicks, Inc., Vicks Daycare Daytime Colds Medicine Caplets by Richardson-Vicks, Inc., Vicks Daycare Multi-Symptom Colds Medicine Liquid by Richardson-Vicks, Inc., Vicks Formula 44 Cough Control Discs by
25 Richardson-Vicks, Inc., Vicks Formula 44 Cough Medicine by Richardson-Vicks, Inc., Vicks Formula 44D Decongestant Cough Medicine by Richardson-Vicks, Inc., Vicks Formula 44M Multi-Symptom Cough Medicine by Richardson-Vicks, Inc., Vicks NyQuil Nighttime Colds Medicine-Original & Cherry Flavor by Richardson-Vicks, Inc., Vicks Pediatric Formula 44 Cough
30 Medicine by Richardson-Vicks, Inc., Vicks Pediatric Formula 44 Cough & Colds Medicine by Richardson-Vicks, Inc., Vicks Pediatric Formula 44 Cough & Congestion Medicine by Richardson-Vicks, Inc., Ambenyl-D Decongestant

5 Cough Formula by Forest Pharmaceuticals, Bromarest DX Cough Syrup by Warner Chilcott, BromFed-DM Cough Syrup by Muro, Codimal DM by Central Pharmaceuticals, Dimetane-DX Cough Syrup by Robins, Guaifenesin w/D-Methorphan Hydrobromide Syrup by Lederle, Humibid DM Tablets by Adams, IoTuss-DM Liquid by Muro, Medi-Tuss DM by Warner Chilcott, Phenergan with Dextromethorphan by Wyeth-Ayerst, Poly-Histine DM Syrup by Bock, Quelidrine Syrup by Abbott, Rondec-DM Oral Drops by Ross, Rondec DM Syrup by Ross, Tusibron-DM by RAM Laboratories, Tussar DM by Rorer Pharmaceuticals, and Tussi-Organidin DM Liquid by Wallace.

10 Delsym Cough Suppressant Syrup by McNeil Consumer contains dextromethorphan polistirex as an antitussive agent. It is believed that all of the above commercial products containing dextromethorphan are included in compositions at about neutral pH or lower.

15 Dextromethorphan Hydrobromide was approved in 1957 by the United States Food and Drug Administration, and this salt is being commercialized throughout the world due to manufacturing convenience. The salt is sparingly soluble below 20°C (about 1.5 weight percent at 20°C), while its solubility is high at higher temperature (about 25 wt. % at 85°C), which makes it easy for crystallization.

20 Bromide presents a significant health risk and is the principal limiting ingredient in antitussive over-the-counter medications. Since bromide was first introduced as a medicine, multiple clinical symptoms of bromide intoxication have been reported. Large doses of bromide cause nausea and vomiting, abdominal pain, coma and paralysis. The chronic state of bromide intoxication is reported as
25 bromism. Bromide has a long half life of about 9-12 days, which can lead to excessive accumulation. The signs and symptoms are referable to the nervous system, skin, glandular secretions, and gastrointestinal tract, as disclosed by F.X.R. van Leeuwen et al. in "1983a. Toxicity of sodium bromide in rats: effects on endocrine system and reproduction," *Food Chem. Toxicol.*, 21(4), 383-390.
30 Bromism has been associated with neurotoxic effects leading to restlessness, irritability, ataxia, confusion, hallucinations, somnolence, psychosis, seizures and

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