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Report

The Prescription Project promotes evidence-based prescribing and works to eliminate conflicts of interest in medicine due to pharmaceutical marketing to physicians.

It is promoting policy change by working with

- *State and Federal Policymakers*
- *Academic Medical Centers*
- *Professional Medical Societies*
- *Private Payers*

Created with The Pew Charitable Trusts, the Project is led by Community Catalyst in partnership with the Institute on Medicine as a Profession.

Risk with No Benefit: The Marketing of Over-the-Counter Cough and Cold Medications for Children

On October 18, 2007, the FDA's Nonprescription Drug Advisory Committee will convene to hear testimony on the potential dangers of over-the-counter (OTC) cough and cold medication for children. The meeting is in response to a citizen petition filed on March 1, 2007 by a group of physicians, academics, and other medical leaders.¹

The petitioners have requested that the Commissioner of the FDA take the following actions²:

1. Provide a statement to the public explaining that over-the-counter antitussive, expectorant, nasal decongestant, antihistamine and combination cough and cold products have not been shown to be safe and effective for the treatment of cough and cold in children under 6 years of age.
2. Notify manufacturers of those products whose labeling 1) uses such terms as "infant" or "baby," or 2) displays images of children under the age of 6 that:
 - a. Such marketing is not supported by scientific evidence; and
 - b. Manufacturers will be subject to enforcement action at any time.
3. Require that labeling for over-the-counter antitussive, expectorant, nasal decongestant, antihistamine, and combination cough and cold products state that:
 - a. These products have not been found to be safe or effective in children under 6 years of age for treatment of cough and cold.

¹ Sharfstein J, et al. FDA Citizen Petition 2007P-0074. March 1, 2007: 8-9

² Sharfstein et al. 1

- b. These products should not be used for treatment of cough and cold in children under 6 years of age.

The petitioners argue that given the lack of evidence of efficacy of these medications and the fact their misuse has been linked to death and injury, there is no justifiable reason to put children's safety at risk by allowing them to be sold.³ A growing number of medical organizations and agencies, including the American Academy of Pediatrics, the American Academy of Chest Physicians and the Centers for Disease Control, have echoed these concerns.⁴

In August, the FDA issued an advisory to warn parents never to give cough and cold medications to children under the age of 2 without a doctor's instruction.⁵

Industry's Response

On October 11, 2007, the Consumer Healthcare Products Association (CHPA), which represents OTC cold and cough medication manufacturers, announced manufacturers would voluntarily withdraw from the market OTC oral cold and cough medicines that refer to "infants." However, manufacturers have not offered a public position on the use of such products for children age 2 to 6.

The Problem: OTC cold and cough medications are neither safe nor effective for children age six and under

Over-the-counter cold, cough, allergy, bronchodilator, and antihistamine products (cough and cold preparations) are heavily marketed and widely used to treat children. Children are far more susceptible to colds than adults; they suffer from an average of 6-10 colds per year.⁶

Though classified under law as "generally safe and effective," there is no evidence of the safety or effectiveness of these products in treating cold and cough for children under 6 years of age.⁷ Indeed, between 1976 and September 28, 2007, when it released a statement from CHPA that the products should be labeled "do not use" for children under 2⁸, the FDA failed to conduct or present any review of evidence on the safety and efficacy of cough and cold preparations in young children,⁹ and currently there are no dosing guidelines for children under 2.¹⁰ Yet many cold and cough medications direct consumers to consult a physician for appropriate dosage information when there is no data to guide physicians in making dosage decisions.

³ Sharfstein et al. 1-8

⁴ Sharfstein et al. 5-6

⁵ FDA Public Health Advisory: Nonprescription Cough and Cold Medicine Use in Children. August 15, 2007. Available at: http://www.fda.gov/cder/drug/advisory/cough_cold.htm

⁶ Sharfstein J, et al. FDA Citizen Petition 2007P-0074. March 1, 2007: 2.

⁷ Sharfstein et al.

⁸ <http://www.fda.gov/ohrms/dockets/ac/07/briefing/2007-4323b1-01-CHPA.pdf>, page 6 of 156)

⁹ Sharfstein J, et al. FDA Citizen Petition 2007P-0074. March 1, 2007: 4.

¹⁰ Sharfstein et al.

Between 1993 and 2004, reviews of clinical trials assessing the effectiveness of OTC cough and cold preparations, published in a number of well-respected medical journals, found no evidence of the efficacy of these medications in treating children with cough or cold symptoms.¹¹

In addition, there is ample evidence that OTC cold and cough preparations carry risks for children under the age of 6. Though causality is difficult to establish, numerous case reports associate serious medical complications and deaths with the use of children's cough and cold products.

A February 2007 FDA internal review of "serious and life-threatening side effects and death in children younger than six years" found "from 1969 through the fall of 2006, there were 54 reported cases of death just with decongestants and 69 with antihistamines, the majority in children younger than two years of age."¹²

Moreover, there are numerous reports of unintentional overdose with these products. The American Association of Poison Control Centers reports that from 1985 to 1989, 72 children under age 6 had "major effects" associated with overdose of cough and cold medications that were life threatening or led to a disability; four children died.¹³ In 2004, the state of Maryland reported that 900 children under the age of 5 overdosed on OTC cough and cold medications.¹⁴ Most recently, the Centers for Disease Control and Prevention released a study that linked the deaths of three infants in 2005 to unintentional overdoses of cough and cold preparations.¹⁵ These risks are particularly unacceptable, given the lack of evidence for efficacy of these products.

"Especially when it comes to over-the-counter drugs, physicians and patients rely on the FDA to 'calculate' the benefit/risk and communicate this to the public. In this case, it appears the benefits are close to zero while the risks are significant."¹⁶

Usage and Sales

By industry's own account, companies sold 288 million units of pediatric cold and cough products in the last three years ending December 31, 2006, for an average of 95 million units annually.¹⁷ A

¹¹ Sharfstein J, et al. FDA Citizen Petition 2007P-0074. March 1, 2007: 4-5.

¹² FDA Public Health Advisory: Nonprescription Cough and Cold Medicine Use in Children. August 15, 2007.

Available at: http://www.fda.gov/cder/drug/advisory/cough_cold.htm

¹³ Litovitz T, Manoguerra A. Comparison of Pediatric Poisoning Hazards: An Analysis of 3.8 Million Exposure Incidents. A Report from the American Association of Poison Control Centers. *Pediatrics* 1992; 89(6 Pt 1): 999-1006.

¹⁴ Sharfstein J, et al. FDA Citizen Petition 2007P-0074. March 1, 2007: 6.

¹⁵ Centers for Disease Control and Prevention. Infant Deaths Associated with Cough and Cold Medications— Two States, 2005. *Morbidity and Mortality Weekly Report*. 2007;56(01):1-4.

¹⁶ Personal communication: John Santa MD, MPH is a consultant to the Prescription Project and an associate professor in the Department of Public Administration at Portland State University. Santa practices internal medicine and preventive medicine at the Portland VA. He was involved in the founding of the Drug Effectiveness Review Project and served as its medical director for several years. DERP focused on providing the public with the most comprehensive and reliable information available on the effectiveness and safety of the most common drugs prescribed in the US.

¹⁷ Consumer Healthcare Products Association Filing. <http://www.fda.gov/ohrms/dockets/ac/07/briefing/2007-4323b1-02-FDA.pdf> (p 9 of 156)

projected 39 % of all households, or 44 million buyers, purchased these products during this period.¹⁸

Including both single-ingredient and combination cough and cold market products, the FDA Office of Surveillance and Epidemiology studied the sales of eight active ingredients during the years 2002-2006.¹⁹ During that time, the vast majority of cough and cold medicines were sold over-the-counter, rather than by prescription.²⁰

Sales in terms of individual tablets, capsules and milliliters of solutions reached a high of 36 billion extended units in 2003.²¹ During 2006, nearly 33 billion extended units of products containing cough/cold ingredients were sold, and approximately 81% of those were sold over-the-counter.²²

The sales study specifically examined the following active ingredients: dextromethorphan, pseudoephedrine, guaifenesin, phenylephrine, chlorpheniramine, diphenhydramine, brompheniramine, and clemastine.²³ The most widely sold active ingredient for single-source products over the five-year period was diphenhydramine (40%) followed by guaifenesin (25%) and dextromethorphan (17%). In 2006, 15.7 billion extended units of dextromethorphan (the most widely sold ingredient in combination products) were sold in combination OTC cough/cold products.²⁴

Consumers are not the only ones paying for these drugs. States and the federal government pay for these drugs through the Medicaid program. According to a report by the Center for Medicare Advocacy, 19 states covered all cough and cold products through their Medicaid programs in 2005. An additional 16 states covered at least some cough and cold products. This report applied to coverage prescriptions for “dual-eligible” individuals – those eligible for both Medicare and for Medicaid, which would include children with disabilities.²⁵

More research is needed to determine if all Medicaid-eligible children in these states are covered for cold and cough products, since most children are not dual-eligible. A preliminary online review of several Medicaid programs shows that, for instance, Alabama²⁶, Mississippi²⁷, and Iowa²⁸ cover some or all of these products, when written with a prescription.

¹⁸ Consumer Healthcare Products Association Filing: 9

¹⁹ Governale, Laura A., Iyasu, Solomon MD MPH, Schiffenbauer, Joel M.D. “Over-the-counter and prescription use of cough/cold products.” Food and Drug Administration Office of Surveillance and Epidemiology, 2007-1022.

²⁰ Governale et al. 2

²¹ Governale et al. 3

²² Governale et al. 3

²³ Governale et al. 3

²⁴ Governale et al 3

²⁵ Center for Medicare Advocacy. Will My State Cover Drugs Excluded Under Medicare Part D? (report) Dec 1, 2005.

²⁶ Alabama Medicaid Pharmacy Services Frequently Asked Questions. Available at:

http://www.medicaid.state.al.us/documents/program-RX/FAQs-Pharmacy_8-13-07.pdf Accessed October 18, 2007

²⁷ Mississippi Envision Pharmacy FAQs. Available at: https://msmedicaid.acs-inc.com/msenvision/questionanswer.do?CATEGORY_TYPE=Pharmacy Accessed October 18, 2007

²⁸ Iowa Department of Human Services PDL for IOWA Medicaid Program. Available at:

http://www.iowamedicaidpdl.com/uploads/W/-ci/W-ciJR0lZxa-MV7ad2-jg/rt14551_covered_otc_ndcs_.pdf Accessed October 18, 2007

Marketing

In the year spanning July 1, 2006 and June 30, 2007, the pharmaceutical industry spent more than \$50 million in advertising OTC pediatric cough and cold remedies.²⁹ Many drug stores offer more than 30 different pediatric cough and cold remedies for over-the-counter sale. Manufacturers use special dosages like drops or thin strips to administer the medication to young children. Thin strips are wafer-like transparent strips of medicine that dissolve on the tongue. Special flavors, such as cherry or grape, are another key selling point.³⁰

Some products, sold as "infant" medications, feature images of babies and are sold containing oral droppers or syringes to deliver medications to children too young to drink from spoons or cups. One such product, Triaminic Infant Decongestant and Cough Thin Strips, containing both dextromethorphan and phenylephrine, has packaging that features a laughing infant. Novartis, the manufacturer of Triaminic, spent over \$2 million advertising the infant thin strips in one year.³¹

According to the citizen petitioners to the FDA, "manufacturers and trade associations justify marketing practices by referencing FDA approval of their products. In a recent letter, the Consumer Healthcare Products Association wrote that 'the U.S. Food and Drug Administration deems OTC cough and cold medicines safe and effective, provided they are used as directed.'"³² This assertion by the Consumer Healthcare Products Association is not accurate.

Conclusion

OTC cough and cold medicines are heavily marketed products. Much of the marketing is focused on children under the age of six. Millions of children in this age group have been treated with these medicines despite the documented dangers and lack of scientific evidence demonstrating their efficacy in children.

²⁹ AdSpender Report on Advertising Expenditures for Over-the-Counter Medications. Created 09/05/2007

³⁰ Kalorama "The U.S. Market for Over-the-Counter Pediatric Medication and Healthcare Products" March 2006: 182-183

³¹ AdSpender Report on Advertising Expenditures for Over-the-Counter Medications. Created 09/05/2007

³² <http://www.fda.gov/ohrms/dockets/ac/07/briefing/2007-4323b1-02-FDA.pdf> (p 13 of 156)

Charts

Top companies and brands in ad spending (all pediatric OTC medications):³³

Marketer	Ad Spend (in millions)
Johnson & Johnson	\$37.53
Wyeth Consumer Healthcare	11.30
Schering-Plough Corp.	8.31
Pfizer Inc.	8.12
Vetco Inc.	3.12
Novartis AG	2.94
Beiersdorf Inc.	1.43

Ad Spend for Children's Cold and Cough Medications:³⁴

Children's Cough & Cold Medications - Reported Time Period: 7/1/2006-6/30/2007	
Brand	Total Dollars (millions)
Benadryl Child Cold & Sinus Remedy	1119.4
Bisolvon Linctus Reg & Child Cough Syrup	\$3.50
Childrens Motrin Liquid Cold Remedy	\$0.80
Childrens Mucinex Cough Remedy	\$78.70
Childrens Mucinex Mini Melts Cough Remedy	\$19,911.90
Childrens Tylenol Cold Remedy	\$22.80
Childrens Tylenol Plus Cold Liquid	\$10,702.30
Childrens Tylenol Plus Cold & Cough Liquid	\$1,304.20
Childrens Tylenol Plus Multi-Symptom Cold	\$2,435.30
Dimetapp Child Cold & Allergy Elixir	\$3,582.20
Little Colds & Little Noses Child Cold Remedies	\$161.20
Pediacare Childrens Cough Formula	\$31.10
Pediacare Various Child Cold Products	\$2,239.90
Triaminic Children Cold Products	\$363.40
Triaminic Childrens Remedies	\$180.40
Triaminic Infant Decongestant/Cough Thin Strips	\$2,033.70
Triaminic Night Time Childrens Liquid	\$8,550.80
Totals	\$51,602.20

³³ Kalorama "The U.S. Market for Over-the-Counter Pediatric Medication and Healthcare Products" March 2006: 156

³⁴ AdSpender Report on Advertising Expenditures for Over-the-Counter Medications. Created 09/05/2007

Marketing messages for these products frequently make claims of effectiveness:

Brand	Marketer	Description
Dimetapp Children's Cold & Cough DM Elixir	Wyeth Consumer Healthcare	The medicine is said to relieve nasal congestion, runny nose, itchy watery eyes, coughing, sneezing." Ad copy for the "nasal decongestant, antihistamine, cough suppressant" states, "Making kids' medicine better." ³⁵
Children's Benadryl-D	Pfizer Inc.	The Grape Flavored Antihistamine/Nasal Decongestant is said to be alcohol and sugar free, with a banner that states, "New look!," package copy reads, "For relief of stuffy nose, runny nose, sneezing, itchy, watery eyes, itchy throat, sinus congestion." ³⁶
PediaCare® Infant Dropper Decongestant & Cough (PE)	Pfizer Inc.	Described as "Pediatrician recommended and mom-approved. PediaCare® provides effective relief for your child's cough and cold symptoms. Relieves Stuffy Noses and Coughs" ³⁷

About The Prescription Project

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³⁵ Kalorama "The U.S. Market for Over-the-Counter Pediatric Medication and Healthcare Products" March 2006: 212

³⁶ Kalorama: 212

³⁷ Pfizer Inc. <http://www.pfizerch.com/product.aspx?id=3744> Accessed 11 October 2007