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Class Update: Cough & Cold Preparations

Date of Review: May 2016

Date of Last Review: May 2013; Codeine DUE July 2015

Current Status of Preferred Drug List (PDL) Class:

See **Appendix 1**.

Purpose for Class Update: Four reviews^{1,2,3,4} that help to clarify the available evidence for cough treatments, new United States Food and Drug Administration (FDA) safety warnings on codeine in children,^{5,6} and new treatment guidelines⁷ were published since the last class update.

Research Questions:

1. What is the comparative evidence for available cough and cold treatments (including over-the-counter [OTC]) to reduce the severity or frequency of cough and cold?
2. What is the comparative evidence for available cough and cold treatments for safety?
3. Are there specific populations (e.g. children) where cough and cold treatments are safer or more effective?

Conclusions:

- The evidence is limited by few direct comparisons of the multiple combination products available, heterogeneous cough etiologies and small study sizes.
- There is insufficient evidence for efficacy of expectorants for cough¹ and expectorants are not recommended for cough secondary to any cause.⁸
- There is low quality evidence that various opioids (primarily codeine) and dextromethorphan reduce cough severity and cough frequency compared to placebo in patients with unexplained or refractory cough symptoms.¹ Comparisons of opioids to dextromethorphan had mixed results.¹ There was insufficient evidence of efficacy for benzonatate or antihistamines.¹
- There is low quality evidence that various combinations of antihistamines and decongestants have limited effect on “global effectiveness” for the common cold in adults and older children.⁹ There is no evidence of benefit in young children.⁹
- There is insufficient comparative safety evidence.
- There is low quality evidence that OTC cough products provide no benefit in children with acute cough.²
- There is low quality evidence of increased risk of death in young children associated with the use over-the-counter (OTC) cough and cold products^{3,10} and codeine cough remedies.⁵

Recommendations:

- Prefer no expectorants and remove all guaifenesin single ingredient products (HSN = 000271) from the PDL.
- Ensure there is a minimum of 1 product with codeine and 1 with dextromethorphan preferred on the PDL for refractory cough as these have the strongest evidence of efficacy.
- After executive session, also make benzonatate products non-preferred.

- Expand the pediatric restriction (children 13 years of age and older) to all cough and cold products (with or without codeine) (**Appendix 4**).
- Restrict codeine cough products to adults 19 years of age and older (**Appendix 4**).

Previous Conclusions:

- The level of comparative evidence of efficacy and safety is insufficient to identify differences between products.
- The overall evidence of efficacy of over-the-counter cough remedies to suppress cough was poor quality and showed conflicting results.
- The FDA recommended cough and cold preparations not be used to treat infants and children under 2 years old in 2008.
- The FDA issued a black box warning restricting the use of codeine in children under 13 for post-operative pain.⁶
- FDA warns about potential risk of serious side effects of using codeine-containing medicines to treat cough and colds in children under 18 years old.⁵

Previous Recommendations:

- Create a PDL class for Cough & Cold Preparations (May 2013)
- Prefer: guaifenesin liquid 100 mg/5 mL, guaifenesin/dextromethorphan syrup, guaifenesin/codeine phosphate liquid, pseudoephedrine HCL tablets 30 mg and 60 mg, benzonatate capsules (May 2013)
- Mucinex™ made preferred (July 2015).
- Age restriction (<18 years) added to all codeine cough products (July 2015).

Background: Symptomatic treatment of common upper respiratory infections (URI) (Line 617) and rhinitis (Line 564) are not funded diagnoses on the Oregon Health Plan List of Prioritized Services.¹¹ The Cough & Cold PDL class includes antitussives, expectorants, oral decongestants and combinations of all 3 with or without antihistamines.¹² This class ranked 36 of 110 classes by number of prior authorization (PA) requests during Q1 2016. A total of 29 requests for non-preferred drugs were made (12 approved, 16 denied, 1 cancelled).¹³ The most commonly requested product was promethazine-codeine (9 requests) followed by hydrocodone-homatropine (8 requests).¹³ All other drugs had 2 or fewer requests.¹³ The Codeine Age Limit PA was not yet implemented in Q1-2016.

There is low quality evidence that various combinations of antihistamines and decongestants have limited effect on “global effectiveness” for the common cold in adults and older children.⁹ There is no evidence of benefit in young children.⁹

The effectiveness of cough treatments is often evaluated for subjective severity rating and cough frequency. Cough can also be experimentally induced in patients using varying concentrations of inhaled capsaicin to cause 2 – 5 coughs (C2 – C5). This model has been called into question as to its predictive accuracy of disease.¹⁴ It is also recognized there is a significant placebo effect associated with cough treatments for young children.^{4,15}

The American College of Chest Physicians published evidence-based clinical practice guidelines for diagnosis and management of cough in 2006.⁸ The recommendations scale was as follows: A-strong; B-moderate; C-weak; D-negative.⁸ Acute cough (<3 week) is most frequently associated with the URI, acute bronchitis, allergic rhinitis or community-acquired pneumonia.⁸ Cough occurs sub-acutely (3-8 weeks) post-infectiously or with pertussis.⁸ Chronic cough (> 8 weeks) in adults is likely secondary to angiotensin-converting enzyme use, smoking, gastroesophageal reflux, asthma, chronic obstructive pulmonary disease, environmental irritant exposure, chronic sinusitis or allergic rhinitis.^{8,16} The primary cause of the cough should be addressed first in each case.^{8,16} Antitussives and expectorants have a very limited role. Antitussives, antihistamines or zinc containing products are not recommended for URI associated cough (Recommendation Grade D).⁸ Ipratropium is recommended for cough suppression for URI or chronic bronchitis (Recommendation Grade A). Hydrocodone, dihydrocodeine, codeine or dextromethorphan are recommended for short-term symptomatic relief of cough due to chronic bronchitis in adults

(Recommendation Grade B).⁸ Hypertonic saline is recommended to increase cough clearance for patients with bronchitis or cystic fibrosis.⁸ Expectorants are *not* recommended for chronic bronchitis (Recommendation Grade D).⁸ Benzonatate is not mentioned in the guidelines.

Methods:

A Medline literature search for new systematic reviews and randomized controlled trials (RCTs) assessing clinically relevant outcomes to active controls, or placebo, was conducted. The Medline search strategy used for this review is available in **Appendix 3**, which includes dates, search terms and limits used. The OHSU Drug Effectiveness Review Project, Agency for Healthcare Research and Quality (AHRQ), Cochrane Collection, National Institute for Health and Clinical Excellence (NICE), Department of Veterans Affairs, BMJ Clinical Evidence, and the Canadian Agency for Drugs and Technologies in Health (CADTH) resources were manually searched for high quality and relevant systematic reviews. When necessary, systematic reviews are critically appraised for quality using the AMSTAR tool and clinical practice guidelines using the AGREE tool. The FDA website was searched for new drug approvals, indications, and pertinent safety alerts. Finally, the AHRQ National Guideline Clearinghouse (NGC) was searched for updated and recent evidence-based guidelines.

The primary focus of the evidence is on high quality systematic reviews and evidence-based guidelines. Randomized controlled trials (RCTs) will be emphasized if evidence is lacking or insufficient from those preferred sources

New Systematic Reviews:

There have been 3 high quality systematic reviews¹ or updates^{2,4} of cough treatments and 1 “short-cut review”³ of the safety of OTC cough and cold preparations published since the last scan in May 2013.

Yancey et al.¹ compared treatments (pharmacologic and nonpharmacologic) for unexplained or refractory cough. The review was commissioned by the Agency for Health Research and Quality. It contained a meta-analysis of the English language medical literature through June 2012.¹ The overall strength of evidence was limited by inconsistent and imprecise results, small numbers of direct comparisons and small studies.¹ Forty-nine studies (n=3067) met inclusion criteria. There were 11 comparisons of opioids (primarily codeine) with placebo with 8 showing the opioid more effective for decreasing cough frequency and cough severity. Standardized mean differences for cough severity for opioids were 0.55 (95% CI, 0.38-0.72) and for rate ratios for cough frequency 0.57 (95% CI, 0.36-0.91).¹ No one opioid was superior to another although codeine had a dose-response improvement.¹ Comparisons of codeine to dextromethorphan were mixed. Six studies of dextromethorphan compared to placebo provided mean difference in cough severity of 0.37 (95% CI, 0.19-0.56) and rate ratios for cough frequency of 0.40 (95% CI, 0.18-0.85).¹ Benzonatate effectiveness was mixed in 3 low quality studies; one placebo-controlled study was negative and 2 studies found it more effective than opioids.¹ Two studies evaluated antihistamines (one of diphenhydramine and one of loratadine) but were limited by extremely small samples (<20). There were 6 negative studies comparing various expectorants (oral N-acetylcysteine, inhaled N-acetylcysteine, bromhexime, ambroxol, inhaled 2-mercaptoethan sulfonate, narcotine-glycerol) to placebo. One good quality study (n=60) for guaifenesin showed improvement over placebo in a subgroup of patients who produced a high volume of sputum.¹ Only 3 studies address cough in children and none of these evaluated antitussives or expectorants.¹

Cochrane published an updated review of OTC cough medications for acute cough in children and adults in 2014.² The literature was searched through March 2014. The evidence was limited by few trials for each comparison as well as heterogeneous participants, interventions and outcomes such that pooling could not be done. There were 19 adult trials (n=3799) and 10 pediatric trials (n=1036) included.² The adult placebo controlled trials included: 2 comparing codeine with non-significant results, 4 comparing dextromethorphan with mixed results, and 3 comparing guaifenesin with mixed results.² In the pediatric studies, antitussives, antihistamines, antihistamine-decongestants and antitussive-bronchodilator combinations were no more effective than placebo.² Adverse effects were reported in 21 studies with higher rates for those taking antihistamines or dextromethorphan.²

Cochrane published an updated review of honey for acute cough in children 1 to 18 years old.⁴ The search was current through November 2014 and identified 3 RCTs (n=568). The authors conclude honey was better than: no treatment in reducing the frequency of cough (mean difference [MD] -1.05; 95% confidence interval [CI] -1.48 to -0.62; I² statistic 23%; two studies, 154 participants), placebo at reduction of cough frequency (MD -1.85; 95% CI -3.36 to -0.33; one study, 300 participants) and diphenhydramine in reducing cough frequency (MD -0.57; 95% CI -0.90 to -0.24; one study, 80 participants).⁴ Honey was no different than dextromethorphan at reducing cough frequency (MD -0.07; 95% CI -1.07 to 0.94; two studies, 149 participants).⁴ Honey should not be given to infants because of their poor immunity against *Clostridium botulinum* that may be present in honey.⁴

A “short-cut review” identified 3 case-series (n=214) reporting deaths associated with OTC cough and cold preparations in children under the age of 12 years old from 1950 to 2007.³

New Treatment Guidelines: The American College of Chest Physicians updated treatment guidelines for treatment of unexplained cough in January 2016.⁷ The guidelines were based upon a high quality systematic review evaluating the efficacy of treatments on cough severity and frequency for adults and adolescents 12 years or older with chronic cough of more than 8 weeks duration and unexplained after systematic workup. The review included the previously mentioned Yancy et al.¹ The authors concluded the evidence was limited by the heterogeneity of therapeutic interventions with few studies available in each category, inconsistent outcome assessment tools and differing definitions of unexplained cough. The treatment algorithm adds empiric trials of speech therapy and gabapentin as last resort options.

New FDA Safety Alerts: The FDA is investigating the safety of codeine containing products to treat cough and cold in children under 18 years old. This was in reaction to the European Medicines Agency recommendation that codeine use is contraindicated in children under 12 years old and is not recommended in older children between 12 and 18 who have breathing problems.⁶

New FDA Drug Approvals: No new molecular entities approved by the FDA for cough treatment were identified from 2013 to date.

New Formulations: Unable to report because of unclear tracking of over-the-counter formulations on the FDA website.

Randomized Controlled Trials:

A total of 30 citations were reviewed from the literature search (**Appendix 3**). After further review, 25 citations were excluded because the population, intervention or outcomes were not of interest. The search identified 4 recent reviews^{1,2,3,4} and 1 new treatment guideline⁷ that were included. No RCTs were included.

References:

1. Yancy WS, McCrory DC, Coeytaux RR, et al. Efficacy and tolerability of treatments for chronic cough. *Chest*. 2013;144(6):1827-1838. doi:10.1378/chest.13-0490.
2. Smith SM, Schroeder K, Fahey T. Over-the-counter (OTC) medications for acute cough in children and adults in community settings. In: *The Cochrane Library*. John Wiley & Sons, Ltd; 2014. <http://onlinelibrary.wiley.com.liboff.ohsu.edu/doi/10.1002/14651858.CD001831.pub5/abstract>. Accessed April 19, 2016.
3. Deschler D, Judge B. BET 3: Paediatric deaths associated with over the counter cough and cold medicines. *Emerg Med J*. 2014;31(2):171-172. doi:10.1136/emmermed-2013-203506.3.
4. Oduwole O, Meremikwu MM, Oyo-Ita A, Udoh EE. Honey for acute cough in children. In: The Cochrane Collaboration, ed. *Cochrane Database of Systematic Reviews*. Chichester, UK: John Wiley & Sons, Ltd; 2014. <http://doi.wiley.com/10.1002/14651858.CD007094.pub4>. Accessed April 21, 2016.
5. Safety Alerts for Human Medical Products - Codeine cough-and-cold medicines in children: Drug Safety Communication - FDA Evaluating Potential Risk of Serious Side Effects. <http://www.fda.gov/safety/medwatch/safetyinformation/safetyalertsforhumanmedicalproducts/ucm453379.htm>. Accessed April 19, 2016.
6. Safety Alerts for Human Medical Products - Codeine use in certain children after tonsillectomy and/or adenoidectomy: Drug Safety Communication - Risk of Rare, But Life-Threatening Adverse Events or Death. <http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm315627.htm>. Accessed April 19, 2016.
7. Gibson P, Wang G, McGarvey L, Vertigan AE, Altman KW, Birring SS. Treatment of unexplained chronic cough. *Chest*. 2016;149(1):27-44. doi:10.1378/chest.15-1496.
8. Irwin RS, Baumann MH, Bolser DC, et al. Diagnosis and management of cough executive summary. *Chest*. 2006;129(1):1S-23S. doi:10.1378/chest.129.1_suppl.1S.
9. De Sutter AI, van Driel ML, French L. Oral antihistamine-decongestant-analgesic combinations for the common cold. In: The Cochrane Collaboration, ed. *Cochrane Database of Systematic Reviews*. Chichester, UK: John Wiley & Sons, Ltd; 2011. <http://doi.wiley.com/10.1002/14651858.CD004976.pub2>. Accessed April 21, 2016.
10. United States Food and Drug Administration. 2008 - Public Health Advisory: FDA recommends that over-the-counter (OTC) cough and cold products not be used for infants and children under 2 years of age. <http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/2008/ucm051137.htm>. Accessed April 21, 2016.
11. Oregon Health Plan Prioritized List of Health Services. Oregon Health Authority - Health Evidence Review Commission. <http://www.oregon.gov/oha/herc/Pages/PrioritizedList.aspx>. Published January 1, 2016. Accessed April 21, 2016.
12. Oregon Health Plan Drug Class List - Cough and Cold. OHA-Medical Assistance Program: OSU Drug Use Research & Management. <http://orpd.org/drugs/drugclass.php?cid=1110>. Accessed April 21, 2016.

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13. OSU Drug Use Research & Management. OHA FFS Drug PA Report (Internal Report). Q1 2016.
 14. Hilton ECY, Baverel PG, Woodcock A, Van Der Graaf PH, Smith JA. Pharmacodynamic modeling of cough responses to capsaicin inhalation calls into question the utility of the C5 end point. *J Allergy Clin Immunol*. 2013;132(4):847-855.e5. doi:10.1016/j.jaci.2013.04.042.
 15. Paul IM, Beiler JS, Vallati JR, Duda LM, King TS. Placebo effect in the treatment of acute cough in infants and toddlers: a randomized clinical trial. *JAMA Pediatr*. 2014;168(12):1107. doi:10.1001/jamapediatrics.2014.1609.
 16. Metersky M (ed), Miner DS (ed). Chronic cough in adults. In: *Dynamed (on-Line Database)*. 2016th ed. USA: EBSCO Information Services; 2015. <http://web.b.ebscohost.com.liboff.ohsu.edu/dynamed/>. Accessed April 14, 2016.

Appendix 1: Preferred Alternatives:

HSN	Generic Drug Name
001929	Benzonatate
000271	Guaifenesin
000206	Guaifenesin/Codeine PHOS
000223	Guaifenesin/D-methorphan HB
002091	Pseudoephedrine HCL

Appendix 2: Abstracts of Included Clinical Trials

No RCTs included in this review

Appendix 3: Medline Search Strategy

Database: Ovid MEDLINE(R) <1946 to April Week 1 2016> Search Strategy:

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- 1 exp Cough/ (13323)
 - 2 exp Antitussive Agents/ (21643)
 - 3 exp Expectorants/ (14917)
 - 4 2 or 3 (36207)
 - 5 1 and 4 (1458)
 - 6 limit 5 to (English language and humans and yr="2013 -Current" and (clinical trial, all or controlled clinical trial or meta analysis or randomized controlled trial or systematic reviews))

30 text results returned

1. Ternesten-Hasseus E, Johansson EL, Millqvist E. Cough reduction using capsaicin. *Respir Med.* 2015;109(1):27-37. doi:10.1016/j.rmed.2014.11.001
EXCLUDED: INTERVENTION NOT FDA APPROVED
2. Barth A, Hovhannisyan A, Jamalyan K, Narimanyan M. Antitussive effect of a fixed combination of *Justicia adhatoda*, *Echinacea purpurea* and *Eleutherococcus senticosus* extracts in patients with acute upper respiratory tract infection: A comparative, randomized, double-blind, placebo-controlled study. *Phytomedicine.* 2015;22(13):1195-200. doi:10.1016/j.phymed.2015.10.001
EXCLUDED: INTERVENTION NOT FDA APPROVED
3. O'Donnell K, Mansbach JM, LoVecchio F, et al. Use of Cough and Cold Medications in Severe Bronchiolitis before and after a Health Advisory Warning against Their Use. *J Pediatr.* 2015;167(1):196-8.e1-2. doi:10.1016/j.jpeds.2015.03.037
EXCLUDED: OUTCOME NOT OF INTEREST
4. Murphy GS, Szokol JW, Avram MJ, et al. Intraoperative Methadone for the Prevention of Postoperative Pain: A Randomized, Double-blinded Clinical Trial in Cardiac Surgical Patients. *Anesthesiology.* 2015;122(5):1112-22. doi:10.1097/ALN.0000000000000633
EXCLUDED: OUTCOME/POPULATION NOT OF INTEREST
5. Abdulqawi R, Dockry R, Holt K, et al. P2X3 receptor antagonist (AF-219) in refractory chronic cough: a randomised, double-blind, placebo-controlled phase 2 study. *Lancet.* 2015;385(9974):1198-205. doi:10.1016/S0140-6736(14)61255-1
EXCLUDED: INTERVENTION NOT FDA APPROVED
6. Garaiova I, Muchova J, Nagyova Z, et al. Probiotics and vitamin C for the prevention of respiratory tract infections in children attending preschool: a randomised controlled pilot study. *Eur J Clin Nutr.* 2015;69(3):373-9. doi:10.1038/ejcn.2014.174
EXCLUDED: OUTCOME NOT OF INTEREST

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7. Boulet LP, Coeytaux RR, McCrory DC, et al. Tools for assessing outcomes in studies of chronic cough: CHEST guideline and expert panel report. *Chest*. 2015;147(3):804-14. doi:10.1378/chest.14-2506
EXCLUDED: OUTCOME NOT OF INTEREST
8. Dicipinigaitis PV, Canning BJ, Garner R, Paterson B. Effect of memantine on cough reflex sensitivity: translational studies in guinea pigs and humans. *J Pharmacol Exp Ther*. 2015;352(3):448-54. doi:10.1124/jpet.114.221218
EXCLUDED: POPULATION NOT OF INTEREST
9. Oduwole O, Meremikwu MM, Oyo-Ita A, Udoh EE. Honey for acute cough in children. *Cochrane Database Syst Rev*. 2014;12:CD007094. doi:10.1002/14651858.CD007094.pub4
INCLUDED
10. Paul IM, Beiler JS, Vallati JR, Duda LM, King TS. Placebo effect in the treatment of acute cough in infants and toddlers: a randomized clinical trial. *Jama, Pediatr*. 2014;168(12):1107-13. doi:10.1001/jamapediatrics.2014.1609
EXCLUDED: INTERVENTION NOT OF INTEREST
11. Smith SM, Schroeder K, Fahey T. Over-the-counter (OTC) medications for acute cough in children and adults in community settings. *Cochrane Database Syst Rev*. 2014;11:CD001831. doi:10.1002/14651858.CD001831.pub5
EXCLUDED; UPDATE WITH NO NEW TRIALS OR CONCLUSIONS
12. Faruqi S, Wright C, Thompson R, Morice AH. A randomized placebo controlled trial to evaluate the effects of butamirate and dextromethorphan on capsaicin induced cough in healthy volunteers. *Br J Clin Pharmacol*. 2014;78(6):1272-80. doi:10.1111/bcp.12458
EXCLUDED: POPULATION NOT OF INTEREST
13. Lee JH, Choi SH, Choi YS, Lee B, Yang SJ, Lee JR. Does the type of anesthetic agent affect remifentanyl effect-site concentration for preventing endotracheal tube-induced cough during anesthetic emergence? Comparison of propofol, sevoflurane, and desflurane. *J Clin Anesth*. 2014;26(6):466-74. doi:10.1016/j.jclinane.2014.02.002
EXCLUDED: POPULATION NOT OF INTEREST
14. Fassoulaki A, Chassiakos D, Melemeni A. Intermittent epidural vs continuous wound infusion of ropivacaine for acute and chronic pain control after hysterectomy or myomectomy: a randomized controlled trial. *PAIN MED*. 2014;15(9):1603-8. doi:10.1111/pme.12523
EXCLUDED: OUTCOME/POPULATION NOT OF INTEREST

15. Guenin E, Armogida M, Riff D. Pharmacokinetic profile of dextromethorphan hydrobromide in a syrup formulation in children and adolescents. *Clin Drug Invest.* 2014;34(9):609-16. doi:10.1007/s40261-014-0210-5
EXCLUDED: OUTCOME NOT OF INTEREST
16. Khalid S, Murdoch R, Newlands A, et al. Transient receptor potential vanilloid 1 (TRPV1) antagonism in patients with refractory chronic cough: a double-blind randomized controlled trial. *J Allergy Clin Immunol.* 2014;134(1):56-62. doi:10.1016/j.jaci.2014.01.038
EXCLUDED: INTERVENTION NOT FDA APPROVED
17. Canciani M, Murgia V, Caimmi D, Anapurapu S, Licari A, Marseglia GL. Efficacy of Grintuss pediatric syrup in treating cough in children: a randomized, multicenter, double blind, placebo-controlled clinical trial. *Ital. J. Pediatr.* 2014;40:56. doi:10.1186/1824-7288-40-56
EXCLUDED: INTERVENTION NOT FDA APPROVED
18. Chang CC, Cheng AC, Chang AB. Over-the-counter (OTC) medications to reduce cough as an adjunct to antibiotics for acute pneumonia in children and adults. *Cochrane Database Syst Rev.* 2014;3:CD006088. doi:10.1002/14651858.CD006088.pub4
EXCLUDED: UPDATE OF PREVIOUS REVIEW- NO NEW STUDIES IDENTIFIED
19. Wise PM, Breslin PA, Dalton P. Effect of taste sensation on cough reflex sensitivity. *Lung.* 2014;192(1):9-13. doi:10.1007/s00408-013-9515-z
EXCLUDED: INTERVENTION NOT OF INTEREST
20. Deschler D, Judge B. Towards evidence-based emergency medicine: best BETs from the Manchester Royal Infirmary. BET 3: Paediatric deaths associated with over the counter cough and cold medicines. *Emerg Med J.* 2014;31(2):171-2. doi:10.1136/emmermed-2013-203506.3
INCLUDED
21. Zanasi A, Mazzolini M, Tursi F, Morselli-Labate AM, Paccapelo A, Lecchi M. Homeopathic medicine for acute cough in upper respiratory tract infections and acute bronchitis: a randomized, double-blind, placebo-controlled trial. *Pulm Pharmacol Ther.* 2014;27(1):102-8. doi:10.1016/j.pupt.2013.05.007
EXCLUDED: INTERVENTION NOT OF INTEREST
22. Yancy WS Jr, McCrory DC, Coeytaux RR, et al. Efficacy and tolerability of treatments for chronic cough: a systematic review and meta-analysis. *Chest.* 2013;144(6):1827-38. doi:10.1378/chest.13-0490
INCLUDED
23. Bhattacharya M, Joshi N, Yadav S. To compare the effect of dextromethorphan, promethazine and placebo on nocturnal cough in children aged 1-12 y with upper respiratory infections: a randomized controlled trial. *Indian J Pediatr.* 2013;80(11):891-5. doi:10.1007/s12098-013-1002-2
EXCLUDED: NOT AVAILABLE (INCLUDED IN COCHRANE REVIEW OF OTC ANTITUSSIVES)
24. Hilton EC, Baverel PG, Woodcock A, Van Der Graaf PH, Smith JA. Pharmacodynamic modeling of cough responses to capsaicin inhalation calls into question the utility of the C5 end point. *J Allergy Clin Immunol.* 2013;132(4):847-55.e1-5. doi:10.1016/j.jaci.2013.04.042
EXCLUDED: OUTCOME NOT OF INTEREST

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25. Raeessi MA, Aslani J, Raeessi N, Gharaie H, Karimi Zarchi AA, Raeessi F. Honey plus coffee versus systemic steroid in the treatment of persistent post-infectious cough: a randomised controlled trial. *Prim. care respir. j.*. 2013;22(3):325-30. doi:10.4104/pcrj.2013.00072
EXCLUDED: INTERVENTION NOT OF INTEREST
26. Chalumeau M, Duijvestijn YC. Acetylcysteine and carbocysteine for acute upper and lower respiratory tract infections in paediatric patients without chronic broncho-pulmonary disease. *Cochrane Database Syst Rev.* 2013;5:CD003124. doi:10.1002/14651858.CD003124.pub4
EXCLUDED: OUTCOME NOT OF INTEREST
27. Gavliakova S, Biringerova Z, Buday T, et al. Antitussive effects of nasal thymol challenges in healthy volunteers. *Respir Physiol Neurobiol.* 2013;187(1):104-7. doi:10.1016/j.resp.2013.02.011
EXCLUDED: POPULATION NOT OF INTEREST
28. Johnstone KJ, Chang AB, Fong KM, Bowman RV, Yang IA. Inhaled corticosteroids for subacute and chronic cough in adults. *Cochrane Database Syst Rev.* 2013;3:CD009305. doi:10.1002/14651858.CD009305.pub2
EXCLUDED:INTERVENTION NOT OF INTEREST
29. Millqvist E, Ternesten-Hasseus E, Bende M. Inhalation of menthol reduces capsaicin cough sensitivity and influences inspiratory flows in chronic cough. *Respir Med.* 2013;107(3):433-8. doi:10.1016/j.rmed.2012.11.017
EXCLUDED: OUTCOME NOT OF INTEREST
30. Faruqi S, Wright C, Thompson R, Morice AH. A randomized placebo controlled trial to evaluate the effects of butamirate and dextromethorphan on capsaicin induced cough in healthy volunteers. *Br J Clin Pharmacol.* 2014;78(6):1272-80. doi:10.1111/bcp.12458
EXCLUDED: POPULATION NOT OF INTEREST

Appendix 4: Current Prior Authorization Criteria

Cough and Cold Preparations

Goal(s):

- Limit use of cough and cold preparations to OHP-funded diagnoses.
- Symptomatic treatment of upper respiratory tract infections is not funded by the OHP.

Length of Authorization:

Up to 12 months

Requires PA:

- All drugs (expectorants, antitussives, oral decongestants and combinations) in TC = 16, 17 except those listed below.
- All products for patients under 13 years of age.
- All codeine-containing products for patients under 19 years of age (see Codeine PA criteria).

Covered Alternatives:

- Current PMPDP preferred drug list per OAR 410-121-0030 at www.orpdl.org
- Searchable site for Oregon FFS Drug Class listed at www.orpdl.org/drugs/

HSN	Generic Drug Name
000206	Guaifenesin/codeine
000223	Guaifenesin/Dextromethorphan
002091	Pseudoephedrine

Approval Criteria

1. What diagnosis is being treated?	Record ICD10 code.	
2. Is the diagnosis an OHP-funded diagnosis? All indications need to be evaluated to see if funded on the Oregon Health Plan list of prioritized services.	Yes: Go to #3	No: Pass to RPh. Deny; not funded by the OHP.
3. Has the patient tried and failed, or have contraindications to, one of the covered alternatives listed above?	Yes: document failure. Approve for up to 1 year.	No: Pass to RPh. Deny; cost-effectiveness

P&T Review: 5/16 (KK); 5/13; 2/06
Implementation: TBD; 1/10/08

Author: Ketchum

Date: May 2016

Codeine

Goal(s):

- Promote safe use of codeine in pediatric patients for analgesia or cough.

Length of Authorization:

Up to 3 days

Requires PA:

- All codeine products for patients under 19 years of age

Covered Alternatives:

- Current PMPDP preferred drug list per OAR 410-121-0030 at www.orpdl.org
- Searchable site for Oregon FFS Drug Class listed at www.orpdl.org/drugs/

Approval Criteria		
4. What diagnosis is being treated?	Record ICD10 code.	
5. What is the age of the patient?	Ages 0-12 years: Pass to RPh. Deny; medical appropriateness	Ages 13-18 years: Go to #3
6. Is the prescription for an OHP-funded condition?	Yes: Go to #4	No: Pass to RPh. Deny; not funded by the OHP
7. Has the patient recently undergone tonsillectomy or adenoidectomy?	Yes: Pass to RPh. Deny; medical appropriateness	No: Go to #5
8. Does the dose exceed 240 mg per day?	Yes: Pass to RPh. Deny; medical appropriateness	No: Approve no more than 3-day supply

P&T Review: 5/16; 9/15; 7/15
 Implementation: TBD; 8/25/15