

# Cough and Cold Review

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## Cough and Cold Review

### FDA-Approved Indications<sup>1</sup>

Drug	Manufacturer	Common Cold	Sinusitis	Allergies	Cough
<i>Cold Formulations</i>					
Alahist-D, Alahist LQ	Poly Pharm	X	X	X	--
Atuss DS tannate	Atley Pharm	X	--	X	X
Aldex AN Aldex D	Pernix Therapeutics	X*	--	X*	--
Aldex CT BroveX PEB BroveX PSB	Pernix Therapeutics	X	X	X	--
Aldex DM BroveX PEB DM liq BroveX PSB DM liq	Pernix Therapeutics	X	X	X	X
Allantan Allanvan-S	Allan Pharm	X	X	X	--
BroveX ADT BroveX PD	MCR Pharm	X	X	X	--
Allerx PM Allerx PE-PM	Cornerstone Therapeutics	X	X	X	--
Allerx AM	Cornerstone Therapeutics	X	X	--	--
Allerx DF-AM Allerx DF-PM	Cornerstone Therapeutics	X	--	X	--
Allerx PE-AM	Cornerstone Therapeutics	X	--	--	--
BPM PE DM BPM PE BPM/Pseudo C-Phen DM Dex PC Dexphen M P-Chlor GG PBM allergy syrup PDM GG PediaHist DM Phencarb GG Phenyltoloxamine PE CPM PSE Brom DM Pseudo cough	Boca pharma	X	X	X	X

**FDA-Approved Indications (continued)**

Drug	Manufacturer	Common Cold	Sinusitis	Allergies	Cough
<i>Cold Formulations</i>					
Bromhist Bromhist NR Ceron Chlor-Mes D	Cypress Pharm	X	X	X	--
Bromspiro Doxytex	Centurion Labs	X	--	X	--
Centergy C-Tan D	Centurion Labs	X	X	X	--
C-Phen CPE PSE PediaHist PSE BPM	Boca Pharmacal	X	X	X	--
Carbinoxamine	Boca Pharmacal	X	--	X	--
CoryZa DM	Larken Labs	X	X	X	X
CoryZa D	Larken Labs	X	X	X	--
Crantex Pyrichlor PE Rhinacon A Triphohist Triphohist D	Breckenridge	X	X	X	X
Deconsal Deconsal C Expectorant Deconsal pediatric Deconsal sprinkle Deconsal LA	Medeva Pharm	X	X	--	X
Deconsal CT	Cornerstone Bio	X	X	X	--
Dicel Tenar PSE	Centrix Pharm	X	X	X	X
Disophrol	S-P Healthcare	X	X	X	--
Duratuss DA	Victory Pharm	X	X	X	--
EndoCof-PD drops	Larken Labs	X	X	X	X
ExeClear-DM	Larken Labs	X	X	--	X
J-Tan D PD J-Tan D J-Tan	Jaymac pharm	X	X	X	--

**FDA-Approved Indications (continued)**

Drug	Manufacturer	Common Cold	Sinusitis	Allergies	Cough
<i>Cold Formulations</i>					
LoHist-PD drops LoHist D LoHist 12D NoHist Ext NoHist-Plus MyHist PD NoHist PE	Larken Labs	X	X	X	--
Lodrane	ECR Pharm	X	--	X	X
Lodrane 24	ECR Pharm	X	--	--	X
Lodrane D	ECR Pharm	X	X	X	X
LoHist 12 NoHist	Larken Labs	X	--	X	--
Lusair	Centurion Labs	X	X	X	X
Lusonal	Wraser Pharm	X	X	--	X
MyHist DM NoHist DMX	Larken Labs	X	--	X	X
Ny-Tannic Seradex-LA	Allegis Pharm	X	X	X	--
PE-Hist DM NoHist PDX	Larken Labs	X	X	X	X
Poly Hist PD	Poly Pharm	X	X	X	--
Poly Hist HC	Poly Pharm	X	X	X	X
Poly Tan, Poly Tan D	Poly Pharm	X	--	X	--
Poly Tan D	Poly Pharm	X	X	X	--
Poly Tan DM	Poly Pharm	X	X	X	X
Poly-Tussin AC Poly-Tussin HD Poly-Tussin DHC	Poly Pharm	X	X	X	X
Pyrlex	Athlon Pharm	X	--	X	--
Pediox-S tannate	Atley Pharm	X	--	X	--
Pyrlex PD	Athlon Pharm	X	X	X	--
Rescon Rescon MX Tekral	Capellon	X	X	X	--
Respivent D	Aristos Pharm	X	X	--	--
Respivent DF	Aristos Pharm	X	X	X	--

**FDA-Approved Indications (continued)**

Drug	Manufacturer	Common Cold	Sinusitis	Allergies	Cough
<i>Cold Formulations</i>					
Ru-Hist Forte Ru-Tuss	Carwin Assoc	X	X	X	--
Ryna 12 Ryna 12S	Meda Pharm	X	X	X	--
Rynatan	Meda Pharm	X	X	X	--
ScopoHist PE ScopoHist	Larken Labs	X	X	X	--
Sina-12 X	Meda Pharm	X	--	X	X
Sudal 12	Atley Pharm	X	X	X	--
Sudatex G	Larken Laboratories	X	--	X	X
SudaHist	Larken Labs	X	X	X	--
SudaTrate	Larken Labs	X	X	--	--
TannaHist PD	Larken Labs	X	--	X	--
Time Hist QD	Ambi Pharma	X	X	X	X
Viravan PDM	Tiber Pharm	X	X	X	--
V-Tann	Breckenridge	X	--	X	--
Zotex D Zotex PE	Vertical Pharm	X	X	X	--
Zotex -12D	Vertical Pharm	X	X	X	X

\* For use in combination with antitussives and decongestants for temporary relief of cold and allergy symptoms. Aldex AN is only indicated for use in the short term treatment of insomnia.

There are many cold formulations available as prescription generics which are combined in one of the following manners with several of the available ingredients: antihistamine-only, antihistamine-decongestant, decongestant-expectorant, and expectorant-only.

**FDA-Approved Indications (continued)**

Drug	Manufacturer	Common Cold	Sinusitis	Allergies	Cough
<i>Narcotic Formulations</i>					
Ambifed-G CD, Ambifed-G CDX	MCR/American Ph	X	--	--	X
Alahist AC, Alahist DHC	Poly Pharm	X	--	--	X
Ambifed CD, Ambifed CDX	MCR/American Ph	X	--	--	X
Baltussin	Ballay Pharm	X	X	X	X
BroveX CB BroveX CBX	MCR Pharm	X	--	X	X
BroveX PB C BroveX PB CX	MCR Pharm	X	X	X	X
Coldcough PD Duohist DH Tusscough DHC	Breckenridge	X	X	X	X
Cotab A Cotab AX	MCR/American Ph	X	--	X	X
Dextuss Gani-Tuss NR	Cypress Pharm	X	X	--	X
Duratuss HD	Victory Pharm	X	--	X	X
Dytan HC	Hawthorn Pharm	X	X	X	X
Endal CD	Tiber Labs	X	--	--	X
EndaCof-C EndaCof-AC	Larken Labs	X	--	X	X
EndaCof-DC	Larken Labs	X	X	--	X
EndaCof-DH	Larken Labs	X	X	X	X
ExeClear-C	Larken Labs	--	--	--	X
J-Max DHC	Jaymac Pharma	X	--	--	X
J-Cof DHC	Jaymac Pharma	X	X	X	X
Maxifed CD, Maxifed CDX	MCR/American Ph	X	--	--	X
Maxifed-G CD, Maxifed-G CDX	MCR/American Ph	X	--	--	X
Maxiphen CD, Maxiphen CDX	MCR/American Ph	X	--	--	X

Cough and Cold

Drug	Manufacturer	Common Cold	Sinusitis	Allergies	Cough
<i>Narcotic Formulations</i>					
M-End PE M-End WC	RA McNeil Co	X	X	X	X
Nalex AC	Blansett Pharmacal	X	--	--	X
Nalex DH	Blansett Pharmacal	X	--	--	X
Notuss AC	SJ Pharmacal	X	--	X	X
Notuss Notuss Forte Notuss PD	SJ Pharmacal	X	X	X	X
Notuss DC	SJ pharmacal	--	--	--	--
Nucofed	Monarch Pharm	X	--	--	X
Phenflu CDX Phenflu CD	MCR Pharm	X	--	X	X
PolyTussin AC, PolyTussin DHC Poly-Tussin HD	Poly Pharm	X	X	X	X
Proclear AC	Pro-Pharma LLC	X	--	X	X
ProRed AC ProRed	Pro-Pharma LLC	X	X	X	X
Tusnel C	Llorens Pharm	X	X	X	X
Tussicaps	Mallinckrodt	X	--	X	X
Tussionex	UCB Pharma	X	--	X	X
Vanacof CD	G.M. Pharm	X	X	--	X
Zotex-C	Vertical Pharm	X	--	X	X
Zotex-HC	Vertical Pharm	X	X	X	X
Z-tuss AC	Magna Pharm	X	--	X	X
Z-tuss 2	Magna Pharm	X	X	X	X

There are many narcotic cough and cold formulations available as prescription generics which are combined in one of the following manners with several of the available ingredients: antitussive-anticholinergic, antitussive-antihistamine-decongestant, antitussive-decongestant-expectorant, and antitussive-expectorant.

**FDA-Approved Indications (continued)**

<b>Drug</b>	<b>Manufacturer</b>	<b>Common Cold</b>	<b>Sinusitis</b>	<b>Allergies</b>	<b>Cough</b>
<i>Non-Narcotic Formulations</i>					
Alacol DM	Ballay Pharm	X	X	X	X
Allanhist PDX Allanvan DM	Allan Pharm	X	X	X	X
Allres G Allres PD	Allegis Pharm	X	X	--	X
Ambi	Ambi Pharma	X	--	--	X
Ambifed G Ambifed G DM	MCR	X	X	--	X
Atuss DS	Atley Pharm	X	X	X	X
Balacall DM Centergy DM	Centurion Labs	X	X	X	X
BP 8	Acella Pharm	X	X	--	X
Bromdex D Mintuss DR Quartuss DM Triplex DM Trital DM	Breckenridge	X	X	X	X
BroveX PEB DM BroveX PSE DM BroveX PSB DM	MCR/American Pharm	X	X	X	X
Deconsal DM	Cornerstone Bio	X	X	X	X
De-Chlor DM De-Chlor DR Neutrahist PDX Resperal DM Tusdec DM	Cypress Pharm	X	X	X	X
Dicel DM Tenar DM	Centrix Pharm	X	X	X	X
Indamix DM Livetan DM	Centurion Labs	X	X	X	X
Duratuss A	Victory Pharm	X	--	X	X
Duratuss AC 12	Victory Pharm	X	X	X	X
Duratuss CS	Victory Pharm	--	--	--	X
Duratuss DM 12	Victory Pharma	--	--	--	X
Duratuss PE	Victory Pharma	X	--	X	X

**FDA-Approved Indications (continued)**

<b>Drug</b>	<b>Manufacturer</b>	<b>Common Cold</b>	<b>Sinusitis</b>	<b>Allergies</b>	<b>Cough</b>
<i>Non-Narcotic Formulations</i>					
Dytan DM	Hawthorn Pharm	X	X	X	X
Dytan- AT Dytan- CS Dytan D	Hawthorn Pharm	X	X	X	--
Entre-S	Acella Pharm	X	X	X	X
Exefen DMX Exefen IR	Larken Laboratories	X	--	--	X
Expectuss	Centurion Labs	X	X	--	X
Flutabs Guidex DM	Breckenridge	X	X	--	X
Gani-Tuss DM NR Simuc DM Su-Tuss DM	Cypress Pharm	X	--	--	X
Guiadrine DX	Breckenridge	X	--	--	X
J-Max	Jaymac pharm	X	X	--	X
Maxichlor DM, Maxichlor PSE DM	MCR/American Pharm	X	--	X	X
Maxichlor PEH DM	MCR/American Pharm	X	--	--	X
Maxiphen DM	MCR/American Pharm	X	--	--	X
Phenflu DM	MCR/American Pharm	X	X	X	X
PolyTan DM	Poly Pharm	X	X	X	X
Pulmari GP	Cypress Pharm	X	X	--	X
Rynatuss	Meda Pharm	X	X	X	X
Seradex	Allegis Pharm	X	X	X	X
SudaTex-DM	Larken Labs	X	X	--	X
Trebrom	Capellon	X	X	X	X
Tusnel Ped-C	Llorens Pharm	X	--	--	X
Tussi 12	Wallace Pharm	X	X	X	X
Tussi 12D, Tussi 12DS	Meda Pharmaceuticals	X	--	X	X
Tusso XR	Everett Labs	X	--	--	X
Tusso-ZMR Tusso ZR	Everett Labs	X	X	--	X

**FDA-Approved Indications (continued)**

Drug	Manufacturer	Common Cold	Sinusitis	Allergies	Cough
<i>Non-Narcotic Formulations</i>					
Vanacof	G.M. Pharm	X	--	X	X
Vanacof DX	G.M. Pharm	X	--	--	X
Vazotan	Wraser Pharm	X	--	X	X
Y-Cof DM	Larken Pharm	X	X	X	X
Zotex -Ex	Vertical Pharm	X	--	X	X
Z-tuss DM	Magna Pharm	X	--	X	X

There are many non-narcotic cough and cold formulations available as prescription generics which are combined in one of the following manners with several of the available ingredients: antitussive-antihistamine, antitussive-antihistamine-decongestant, antitussive-antihistamine-decongestant-expectorant, antitussive-decongestant, antitussive-decongestant-expectorant, and antitussive-expectorant.

**Overview**

The common cold is a viral illness that affects persons of all ages, prompting frequent use of over-the-counter (OTC) and prescription medications and alternative remedies.<sup>2</sup> Adults in the United States experience two to four colds per year. At least 200 identified viruses are capable of causing the common cold.<sup>3</sup> The viruses often implicated include rhinoviruses, coronaviruses, parainfluenza viruses, respiratory syncytial virus, adenoviruses, and enteroviruses. Although histologic effects on the nasal epithelium may vary, any of the viruses can cause vasodilation and hypersecretion, which leads to the common cold syndrome, which includes nasal congestion, nasal discharge, postnasal drip, throat clearing, sneezing, and cough.

The 2006 ACCP Evidence-Based Clinical Practice Guidelines on the Diagnosis and Management of Cough state that patients with acute cough associated with the common cold can be treated with a first-generation antihistamine and decongestant preparation.<sup>4</sup> There are a variety of prescription and over-the-counter (OTC) cough and cold combination products. The focus of this review will be on the prescription products with emphasis on the component ingredients. There are numerous generic products available, as well. Rather than list all of the available combinations, they have been included in the above tables by a categorization of their ingredients.

**Pharmacology**

Drug Type	Mechanism of Action	Examples
Anticholinergics	Competitively blocks the muscarinic receptors, primarily M2 and M3, and causing the drying effect on mucus membranes.	homatropine, methscopolamine, scopolamine
Antihistamines (first generation)	Competitively antagonize the effects of histamine on H <sub>1</sub> -receptors in the GI tract, uterus, large blood vessels, and bronchial smooth muscle. Blockade of H <sub>1</sub> -receptors also suppresses the formation of edema, flare, and pruritus that result from histaminic activity. H <sub>1</sub> -antagonists also possess anticholinergic properties in varying degrees.	brompheniramine, carbinoxamine, chlorpheniramine, clemastine, cyproheptadine, dexbrompheniramine, dexchlorpheniramine, diphenhydramine, doxylamine, hydroxyzine, promethazine, pyrilamine, triprolidine
Antitussives (opiate)	Directly act on receptors in the cough center of the medulla. These agents may also have a drying effect on the respiratory tract and increases the viscosity of bronchial secretions. Cough suppression can be achieved at lower doses than those required to produce analgesia. The most significant adverse effect associated with opiate agonist use is respiratory depression which results from a decreased sensitivity to carbon dioxide in the brainstem. Opiates cause generalized CNS depression. Additive sedative effects are possible with other agents that can lead to CNS depression.	codeine, dihydrocodeine, hydrocodone
Antitussives (non-opiate)	Dextromethorphan is a non-competitive antagonist of N-methyl-D-aspartate (NMDA) receptors in the brain and spinal cord. It acts on the cough center in the medulla to raise the threshold for coughing by decreasing the excitability of the cough center. It is the d-isomer of levorphanol but has none of the analgesic, respiratory depressive, or sedative effects associated with opiate agonists. Carbetapentane and chlophedianol appear to work directly on the cough center of the medulla, thereby suppressing the cough reflex. Carbetapentane has atropine-like and anesthetic actions, producing a drying effect of respiratory mucus secretion. In addition, it possesses mild bronchodilatory actions, and does not affect respiratory volume.	carbetapentane, chlophedianol, dextromethorphan

**Pharmacology (continued)**

Drug Type	Mechanism of Action	Examples
Decongestants	Phenylephrine possesses both direct and indirect sympathomimetic effects, primarily as a postsynaptic alpha-adrenergic agonist, producing potent vasoconstriction. An indirect effect due to the release of norepinephrine plays a small role in the overall action of phenylephrine. Constriction of blood vessels leads to reduced blood flow to the nose, decreased amount of blood in the sinusoid vessels, and decreased mucosal edema, which relieves nasal congestion. Phenylephrine does not affect the beta receptors in the heart or lungs. Pseudoephedrine is a sympathomimetic amine that causes the release of norepinephrine, leading to vasoconstriction and a decrease in nasal and sinus congestion.	phenylephrine, pseudoephedrine*
Expectorants	Loosens and thins sputum and bronchial secretions to ease expectoration.	guaifenesin, potassium guaiacolsulfonate

\* Many products containing pseudoephedrine have been reformulated due to increased regulatory restrictions on the sale and distribution of the drug, likely due to its notable use as a precursor in the illicit synthesis of methamphetamine.

**Pharmacokinetics**

Due to the various product formulations and varying component ingredients in the cough and cold products, the specific product information should be consulted to evaluate pharmacokinetics.

**Contraindications/Warnings**

In January 2007, the Centers for Disease Control and Prevention (CDC) warned caregivers and healthcare providers of the risk for serious injury or fatal overdose from the administration of cough and cold products to children and infants less than two years of age.<sup>5</sup> This warning followed an investigation of the deaths of three infants less than six months of age that were attributed to the inadvertent inappropriate use of these products. The symptoms preceding these deaths have not been clearly defined, and there is a lack of conclusive data describing the exact cause of death. The report estimated that 1,519 children less than two years of age were treated in emergency departments during 2004 and 2005 for adverse events related to cough and cold medications.

In October 2007, the FDA Nonprescription Drug Advisory Committee and the Pediatric Advisory Committee recommended that nonprescription cough and cold products containing pseudoephedrine, dextromethorphan, chlorpheniramine, diphenhydramine, brompheniramine, phenylephrine, clemastine, or guaifenesin not be used in children less than six years of age. In January 2008, the FDA issued a Public Health Advisory recommending that OTC cough and cold products not be used in infants and children less than two years old. An official ruling regarding the use of these products in children older than two years has not yet been announced. The FDA recommends that if parents and caregivers use cough and cold products in children older than two years, labels should be read carefully, caution should be used when

administering multiple products, and only measuring devices specifically designed for use with medications should be used. While some combination cough/cold products containing these ingredients are available by prescription only and are not necessarily under scrutiny by the FDA, clinicians should thoroughly assess each patient's use of similar products, both prescription and nonprescription, to avoid duplication of therapy and the potential for inadvertent overdose.

Some pyrilamine products (e.g. Deconsal CT, V-Tann Suspension, Ryna 12, Pyrlex PD Suspension etc.) may contain phenylalanine. These products should not be used in patients with phenylketonuria (PKU).

**Drug Interactions<sup>6</sup>**

Drug Type	Anticholinergics	Antihistamines	Antitussives (opiate)	Antitussives (non-opiate)	Decongestants	Expectorants
CNS depressants (e.g. alcohol, sedatives, anxiolytics, etc.)	--	✓	--	--	--	--
MAOIs	--	✓	--	--	--	--
Tricyclic antidepressants	✓	✓	--	--	--	--
Alpha blockers	--	--	--	--	✓	--
Beta blockers	--	--	--	--	✓	--
Centrally acting antihypertensives	--	--	--	--	✓	--
Antidiabetic agents	--	--	--	--	✓	--
Ototoxic medications (e.g. aminoglycosides)	✓	✓	--	--	--	--

Concurrent administration of methscopolamine nitrate with either sildenafil or vardenafil has been shown to potentiate hypotension due to the nitrate. Therefore, the concurrent use of sildenafil or vardenafil with products containing methscopolamine nitrate is not recommended.

**Adverse Effects**<sup>7,8</sup>

Drug Type	Anticholinergics	Antihistamines	Antitussives (opiate)	Antitussives (non-opiate)	Decongestants	Expectorants
Drowsiness	✓	✓	✓	✓	✓	✓
Xerostomia	✓	✓	--	--	✓	--
Nausea	✓	--	✓	✓	✓	✓
Tachycardia/ Palpitations	✓	--	--	--	✓	--
CNS depression	✓	✓	✓	✓	✓	--
Respiratory depression	✓	--	✓	✓	--	--

✓ = Reported

Adverse effects are reported above as a class effect due to the multiple ingredients contained in the products. Adverse effects have been taken from package inserts or other reliable databases and are not meant to be comparative or all inclusive.

**Special Populations**<sup>9,10</sup>Pediatrics

Many of the products in this category are approved for use in children as young as two years of age. Please consult the individual prescribing information for specific product information.

Pregnancy

Pregnancy category depends upon the component ingredients. Many are Pregnancy Category C, but consult the individual package inserts for specific product information.

Renal Impairment

Dosage adjustment may be warranted; however, specific guidelines in renal impairment are not available. Consult the individual package inserts for additional information.

Hepatic Impairment

Specific guidelines for dosage adjustments in patients with hepatic impairment are not available. Lower doses may be warranted due to metabolism of any one of the ingredients in a given product.

Geriatrics

The elderly are more susceptible to the anticholinergic effects of antihistamines. Reduced initial dosages may be needed.

**Dosages**<sup>11,12</sup>

Drug (Products containing drug)	Maximum Recommended Daily Dose		Availability
	Adult	Child	
<i>Anticholinergics</i>			
homatropine (various generic products)	9 mg	Ages: six to twelve years: 4.5 mg	Tablet and syrup formulations
methscopolamine (various generic products)	12.5 mg	Safe and effective use has not been established in children	Tablet, chewable tablet, and syrup formulations
scopolamine (various generic products)	2.4 mg	Safe and effective use has not been established in children	Tablet and solution formulations
<i>Antihistamines</i>			
brompheniramine (various generic products, Alahist, Alahist-D, Alahist-LQ, Nalex AC, BroveX PEB DM, BroveX PSB DM, BroveX PSE DM, M-End PE, M-End WC, Seradex, Tusnel C, Polytussin AC, Polytussin DHC, Vazotan, Viravan PM)	48 mg	Ages: six to 11 years: 24 mg two to five years: 12 mg one to two years: 6 mg six to 12 months: 3 mg three to six months: 2 mg one to three months: 1 mg	Tablet, capsule, solution, syrup and suspension formulations
carbinoxamine (various generic products)	32 mg	Ages: over six years: 24 mg three to six years: 16 mg two to three years: 8 mg	Solution, suspension, syrup formulations
chlorpheniramine (various generic products, Ah-Chew Ultra, Allerx, Sudal 12, Notuss AC, Cotab A, Cotab AX, P-Chlor, Tussicaps, Tussionex, Maxichlor DM, Maxichlor PEH DM, Maxichlor PSE DM, Maxiphen DM, Phenflu DM, Rynatan Pediatric), Tussi 12, Z-Tuss AC	24 mg	Ages: over six years: 12 mg two to five years: 4 mg	Suspensions, solutions, extended-release tablets, chewable tablets  Extended release formulations are not recommended for children under age six years
clemastine (various generic products)	2 mg	Ages: 12 years and older: 2 mg less than 12 years: safe and effective use has not been established.	Tablet and caplet formulations

**Dosages (continued)**

Drug (Products containing drug)	Maximum Recommended Daily Dose		Availability
	Adult	Child	
<i>Antihistamines (continued)</i>			
cyproheptadine (e.g. various generic products)	32 mg	Ages: seven to 14 years: 16 mg two to six years: 12 mg	Syrup and tablet formulations
dexbrompheniramine (e.g. various generic products, Disophrrol, etc.)	12 mg	Ages: twelve years and older: 12 mg less than 12 years: safe and effective use has not been established	Tablets, extended-release tablets, and syrup formulations
dexchlorpheniramine (e.g. various generic products, Vanacof, Vanacof CD, etc.)	No maximum dosing information available	Available for use in patients ages two and older	Extended release tablet and oral solution formulations  Extended release tablets are not recommended for use in children three to five years of age
diphenhydramine (e.g. various generic products, Alahist, Alahist-D, Alahist-LQ, Aldex CT, Endal CD, Duratuss AC, etc.)	300 mg	Ages: six years and older: 300 mg	Tablet and suspension formulations
doxylamine (e.g. various generic products, Aldex AN, etc.)	25 mg	Ages: 12 years and older: 25 mg	Suspension and chewable tablet formulations
hydroxyzine (e.g. various generic products)	400 mg	Ages: six years and older: 100 mg less than six years: 50 mg infants: safety and efficacy have not been established	Tablets, capsules, and solution formulations
promethazine (e.g. various generic products)	100 mg	Ages: Adolescents: 100 mg two years and older: lesser of 25 mg/dose or 0.5 mg/pound/dose	Tablets and syrup formulations

**Dosages (continued)**

Drug (Products containing drug)	Maximum Recommended Daily Dose		Availability
	Adult	Child	
<i>Antihistamines (continued)</i>			
pyrilamine (e.g. various generic products, Aldex D, Deconsal CT, Pyrex, Pyrex PD, Ryna 12, V-Tann, Viravan P, ProRed AC, Zotex C, Deconsal DM, Tussi-12 D, Tussi-12 DS, etc.)	No maximum dosing information available	Available for use in patients ages two years and older	Tablet, syrup, suspension, and chewable tablet formulations
triprolidine (various generic products)	10 mg	Ages: six to twelve years: 5 mg less than six years: safe and effective use has not been established	Tablet, solution, and suspension formulations
<i>Antitussives (opiate)</i>			
codeine (e.g. various generic products, Alahist AC, Ambifed-G CD, Ambifed CD, Ambifed CDX, Maxifed-G CD, Maxifed CD, Maxifed CDX, M-End PE, M-End WC, Ambifed-G CD, Maxiphen CD, Maxiphen CDX, Nalex AC, Notuss AC, Cotab A, Cotab AX, Endal CD, Nucofed, Polytussin AC, Tusnel C, Vanacof CD, Zotex-C, Z-Tuss AC, etc.)	360 mg	Ages: Adolescents: 360 mg less than 3 years: Safe and effective use has not been established	Tablet, capsule, syrup, and solution formulations
dihydrocodeine (e.g. various generic products, Alahist DHC, J-Max DHC, Polytussin DHC, etc.)	90 mg	Ages: six to twelve years: 45 mg two to five years: 22.5 mg	Syrup and solution formulations
hydrocodone (e.g. various generic products, ProClear, ProRed AC, Tussicaps, etc.)	30 mg (as an antitussive)	Ages: six years and older: 15 mg (as an antitussive) five years and under: Safe and effective use as an antitussive has not been established.	Capsule and syrup formulations

**Dosages (continued)**

Drug (Products containing drug)	Maximum Recommended Daily Dose		Availability
	Adult	Child	
<i>Antitussives (non-opiate)</i>			
carbetapentane (e.g. various generic products, Tussi 12, Tussi 12 D, Tussi 12DS, Tusso ZMR, Vazotan, Seradex, etc.)	240 mg	Ages: six to twelve years: 120 mg four to five years: 30 mg two to three years: 15 mg	Tablets, capsules, extended-release capsules, and suspension formulations
chlorphedianol (e.g VanaCof, VanaCof DX)	100 mg	Ages: two to twelve years: 50 mg	Solution formulations
dextromethorphan (e.g. various generic products, Tusnel Ped C, Ambi, Deconsal DM, BroveX PEB DM, BroveX PSB DM, BroveX PSE DM, Dytan DM, Duratuss AC, Duratuss DM 12, Exefen DMX, Maxichlor PEH DM, Maxiphen DM, Phenflu DM, Tusso XR, Viravan PDM, etc.)	120 mg	Ages: six to twelve years: 60 mg two to five years: 30 mg	Tablet, chewable tablet, suspension, and solution formulations
<i>Decongestants</i>			
phenylephrine (e.g. various generic products, Alahist D, Alahist LQ, Allerx, BroveX PEB DM, Deconsal CT, Alahist AC, Alahist DHC, Maxiphen CD, Maxiphen CDX, M-End PE, Endal CD, V-Tann, Aldex D, Aldex AN, Aldex CT, Polytussin AC, Polytussin DHC, ProRed AC, Vanacof CD, Zotex-C, Ambi, Deconsal DM, Dytan DM, Maxiphen DM, Pyrex PD, Ryna 12, Ryna 12X, Seradex, Tussi 12, Tussi 12 D, Tussi 12 DS, Tusso XR, Vazotan, Viravan PDM, etc.)	80 mg	Ages: six to twelve years: 20 mg two to five years: 7.5 mg	Tablet, chewable tablet, solution, and syrup formulations

**Dosages (continued)**

Drug (Products containing drug)	Maximum Recommended Daily Dose		Availability
	Adult	Child	
pseudoephedrine (e.g. various generic products, Exefen DMX, Sudal 12, Viravan P, Ambifed CD, Ambifed CDX, Maxifed-G CD, Maxifed CD, Maxifed G-CDX, Maxifed CDX, Ambifed-G, Ambifed G-CDX, Nucofed, Tusnel Ped C, BroveX PSE DM, BroveX PSB DM, M-End WC, Deconsal, Maxichlor PSE DM, VanaCof, Viravan PDM, etc.)	240 mg	Ages: six to eleven years: 120 mg two to five years: 60 mg	Chewable tablet, capsule, solution, suspension, and syrup formulations
<i>Expectorants</i>			
guaifenesin (e.g. various generic products, P-Chlor, Ambifed CD, Ambifed CDX, Maxifed CD, Maxifed CDX, Maxifed-G CD, Maxifed-G CDX, Ambifed-G CD, Ambifed-G CDX, Maxiphen CD, Maxiphen CDX, J-max DHC, Robafen AC, Tusnel Ped C, Ambi, Maxiphen DM, Phenflu DM, Tusso XR, Tusso ZMR, VanaCof DX, Exefen DMX, Duratuss DM 12, Deconsal, etc.)	2,400 mg	Ages: six to twelve years: 1,200 mg four to five years: 800 mg two to three years: 400 mg	Extended-release capsule, tablet, solution, suspension, and syrup formulations
potassium guaiacolsulfonate (e.g. various generic products, ProClear)	1,800 mg	Ages: three to twelve years: 0.6 mg/kg/day	Syrup formulation

**Clinical Trials**

Studies were identified through searches performed on PubMed and review of information sent by manufacturers. Search strategy included the FDA-approved use of all drugs in this class. Randomized, comparative, controlled trials comparing agents within this class for the approved indications are considered the most relevant in this category. Studies included for analysis in the review were published in English, performed with human participants, and randomly allocated participants to comparison groups. In addition, studies must contain clearly stated, predetermined outcome measure(s) of known or probable clinical importance, use data analysis techniques consistent with the study question, and include follow-up (endpoint assessment) of at least 80 percent of participants entering the investigation. Despite some inherent bias found in all studies including those sponsored and/or funded by pharmaceutical manufacturers, the

studies in this therapeutic class review were determined to have results or conclusions that do not suggest systematic error in their experimental study design. While the potential influence of manufacturer sponsorship/funding must be considered, the studies in this review have also been evaluated for validity and importance.

This class contains a vast number of combination cough and cold products whose constituent ingredients are available both as prescription and over-the-counter medications. All of the products contained in this monograph have supporting evidence related to the safety and efficacy of their constituent ingredients. There are numerous placebo-controlled studies available, but none that are comparative to other agents within this class.

### ***Meta-analysis***

A 2005 Cochrane Review suggested caution in determining clinically significant benefits of any of the non-antibiotic treatments of the common cold other than first-dose decongestants and antihistamine-decongestant combinations.<sup>13</sup> The review included comparison of several products including Echinacea, heated humidifier air, dextromethorphan, guaifenesin, vitamin C, zinc lozenges, and two combination antihistamine-decongestant products. Dexbrompheniramine 6 mg in combination with pseudoephedrine 120 mg was administered twice daily for one week in one study. Another study evaluated loratadine 5 mg in combination with pseudoephedrine 120 mg twice daily for four days. The authors concluded that most non-antibiotic treatments for the common cold are probably not effective; however, dextromethorphan, guaifenesin, combination antihistamine-decongestants, first-dose decongestants, and possibly zinc lozenges show promise.

A 2007 meta-analysis was done to assess the efficacy of oral phenylephrine 10 mg as a nasal decongestant in the symptomatic relief from the common cold.<sup>14</sup> To be included in the analysis, studies had to have a single-dose, randomized, placebo-controlled design; involve an orally administered product in which phenylephrine 10 mg was the sole active ingredient; enroll patients with acute nasal congestion due to the common cold; evaluate nasal airway resistance as the efficacy endpoint; and have sufficient data points to allow re-analysis and/or meta-analysis of phenylephrine 10 mg and placebo. Eight studies met the inclusion criteria, involving seven cross-over studies of 113 subjects. Significant differences in favor of phenylephrine were seen in four of the eight studies ( $p \leq 0.05$ ). Phenylephrine was significantly more effective than placebo at the primary time points (45, 90, 120, and 180 minutes). This meta-analysis and re-analysis support the effectiveness of a single oral dose of phenylephrine 10 mg as a decongestant in adults with acute nasal congestion associated with the common cold.

### ***Summary***

The common cold induces acute cough by directly irritating the upper airway structures. Viral infections of the airway can produce the common cold syndrome including rhinosinusitis. Active treatment of the symptoms associated with cough and cold may include combination products containing anticholinergics, first-generation antihistamines, opiate and non-opiate antitussives, decongestants, and expectorants. The available data do not result in any differentiation among the drugs in their particular class. These products are available in various combinations and individually as both prescription and OTC products. Awareness of the active ingredients is critical in ensuring proper dosing, patient safety, and effective use of these products.

## References

- <sup>1</sup> Available at: <http://www.healthsquare.com/>. Accessed May 3, 2010.
2. Simasek M, Blandino D. Treatment of the Common Cold. American Academy of Family Physicians. 2007; 75:515-20.
3. Mossad SB, Macknin ML, Medendorp SV, et al. Zinc gluconate lozenges for treating the common cold: a randomized, double-blind, placebo-controlled study. Ann Intern Med. 1996; 125:81-88.
4. Available at: [http://chestjournal.org/cgi/content/full/129/1\\_suppl/1S/DC1](http://chestjournal.org/cgi/content/full/129/1_suppl/1S/DC1). Accessed May 3, 2010.
5. Centers for Disease Control and Prevention (CDC). Infant deaths associated with cough and cold medications - two states, 2005. MMWR Weekly. 2007; 56:1—4.
- <sup>6</sup> Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2008. URL: <http://www.clinicalpharmacology.com>. Updated July 2009. Accessed May 3, 2010.
7. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2008. URL: <http://www.clinicalpharmacology.com>. Updated July 2009. Accessed May 3, 2010.
8. Available at: <http://www.drugs.com/>. Accessed May 3, 2010.
9. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2008. URL: <http://www.clinicalpharmacology.com>. Updated July 2009. Accessed May 3, 2010.
10. Available at: <http://www.drugs.com/>. Accessed May 3, 2010.
11. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2008. URL: <http://www.clinicalpharmacology.com>. Updated July 2009. Accessed May 3, 2010.
12. Available at: <http://www.drugs.com/>. Accessed May 3, 2010.
13. Arroll B. Non-antibiotic treatments for upper respiratory tract infections (common cold). Respir Med. 2005; 99(12):1477-84.
14. Kollar C, Schneider H, Waksman J, et al. Meta-analysis of the efficacy of a single dose of phenylephrine 10 mg compared with placebo in adults with acute nasal congestion due to the common cold. Clin Ther. 2007; 29(6):1057-70.
15. DRUGDEX® Tradename list (n.d). <http://www.thomsonhc.com/>. Greenwood village, CO: Thomson Healthcare; Accessed May 3, 2010.