Brand Names

AllFen, AllFen Jr, Altarussin , Altorant , Ambi, Amibid LA , Bidex, Chest Congestion Relief, Cough , Diabetic Tussin, Diabetic Tussin EX, Diabetic Tussin Expectorant, Diabetic Tussin Mucus Relief, Drituss G, Duratuss G, ElixSure EX, Fenesin , Ganidin NR, GERI-TUSSIN, Gua SR , Guaidrine G, Guaifenex G, Guaifenex LA, Guiatuss, Humibid, Humibid E, Humibid LA, Iophen-NR , Liquibid, Miltuss EX, Mucinex, Mucinex Children's, Mucinex Children's Chest Congestion, Mucinex Children's Mini-Melts, Mucinex Fast-Max Chest Congestion, Mucinex Junior Strength, Muco-Fen, Mucolyte, Mucosa, Mucus + Chest Congestion, Mucus ER, Mucus Relief, Mucus Relief 12 Hour, Mucus Relief Children's, Mucus Relief ER, Naldecon, Organ-1 NR, Organidin NR, Q-Bid LA, Q-Tussin, Respa-GF, Robafen , Robafen Congestion, Robitussin, Robitussin Mucus + Chest Congestion, Ru-Tuss, Scot-Tussin Expectorant, Siltussin DAS, Siltussin Diabetic DAS-Na , Siltussin SA, Touro EX, TUSNEL-EX, Tussin DM, Xpect

Indication Specific Dosing

For the treatment of cough associated with colds and minor upper respiratory tract infections and for loosening phlegm and thin bronchial secretions to aid in clearing bronchial passages and making coughs more productive

Oral dosage (immediate-release capsules or tablets)

Adults, Adolescents, and Children 12 years and older

200 to 400 mg PO every 4 hours as needed. Max: 6 doses/day (2400 mg/day).

Oral dosage (extended-release or biphasic capsules or tablets)

Adults, Adolescents, and Children 12 years and older

600 to 1200 mg PO every 12 hours as needed. Max: 2400 mg/day PO.

Oral dosage (oral solutions or syrups)

Adults and Adolescents

200 to 400 mg PO every 4 hours as needed. Max: 2400 mg/day PO.

Children 6 to 11 years

100 to 200 mg PO every 4 hours as needed. Max: 1200 mg/day PO.

Children 2 to 5 years

50 to 100 mg PO every 4 hours as needed. Max: 600 mg/day PO.

Oral dosage (oral granule packets with guaifenesin 100 mg per packet; e.g., Mucinex Children's Chest Congestion Expectorant Mini-Melts)

Adults, Adolescents, and Children 12 years and older

2 to 4 packets PO every 4 hours as needed. Do not exceed 6 doses/24 hours.

Children 6 to 11 years

1 to 2 packets PO every 4 hours as needed. Do not exceed 6 doses/24 hours.

Children 4 to 5 years

1 packet PO every 4 hours as needed. Do not exceed 6 doses/24 hours.

For the treatment of cervical factor infertility†, including cervical mucus thickening induced by clomiphene treatment

Oral dosage (immediate release, alcohol-free formulations)

Adult non-pregnant females

A dosage of 200 mg PO 3 times daily during the follicular phase of the menstrual cycle (i.e., until ovulation) has been reported to be effective at thinning cervical secretions for the purpose of enhancing sperm penetration. When used with clomiphene treatment, guaifenesin use typically follows the last dose of clomiphene and continues until ovulation. Although widely reported as a potential usage, no controlled clinical trials exist. Use for this purpose is limited to the prescription by a qualified fertility specialist. Alcohol-free products should be chosen.

Contraindications And Precaution

Drug Interactions

The coadministration of certain medications may lead to harm and require avoidance or therapy modification; review all drug interactions prior to concomitant use of other medications.

asthma, chronic obstructive pulmonary disease, tobacco smoking

Guaifenesin should not be used for persistent or chronic cough such as occurs with tobacco smoking, asthma, chronic obstructive pulmonary disease (i.e., emphysema or chronic bronchitis), or any other condition where cough is associated with excessive secretions, unless under the supervision of a health care professional. Individuals should discontinue use and contact their care team if the cough lasts more than 7 days, returns, or occurs with fever, rash or persistent headache since these could be signs of serious illness. Guaifenesin should not be used for a cough that is specifically associated with heart failure or ACE inhibitor therapy.

Hypersensitivity

This medication is contraindicated in patients with a history of hypersensitivity to it or any of its components.

children, infants, neonates

Due to the risk for serious adverse reactions, the FDA recommends against administration of over the counter (OTC) cough and cold products to neonates, infants and children younger than 2 years of age. When administering OTC medications to older pediatric patients, they advise caregivers to read product labels carefully, use caution when administering multiple products to avoid duplication of ingredients, and use only measuring devices specifically designed for use with medications. Care teams should thoroughly assess the use of similar products, both prescription and nonprescription, to avoid duplication of therapy and the potential for inadvertent overdose.

pregnancy

Safe use of guaifenesin in pregnancy has not been established, and it is not clear if the drug crosses the placenta. Use during pregnancy only if clearly needed. Few studies have been done to evaluate the use of expectorants during pregnancy and thus first trimester use is best avoided. A study examining the developmental toxicity of guaifenesin in pregnant rats reported decreased fetal weight and impaired skeletal

development in fetuses of exposed rats. In a large, population-based case control study of maternal use of cough medications during early pregnancy, guaifenesin use was associated with a small number of birth defects, including small intestinal atresia/stenosis and omphalocele. Non-pharmacologic methods (e.g., fluids, rest) are recommended to be tried first for symptomatic relief of cough and congestion during pregnancy and pregnant patients should get treatment recommendations from their health care provider.

breast-feeding

Guaifenesin is usually considered compatible with breast-feeding due to a lack of reported adverse effects in breastfed infants. It is not known if guaifenesin is excreted into breast milk. However, it is unlikely that with usual maternal doses, amounts in breast milk would harm the nursing infant, especially in infants over 2 months of age. Increased fluids to ease expectoration are usually recommended for first-line treatment in the lactating individual. If the use of guaifenesin is necessary during lactation, it is best to chose products that are alcohol-free.

Pregnancy And Lactation

Safe use of guaifenesin in pregnancy has not been established, and it is not clear if the drug crosses the placenta. Use during pregnancy only if clearly needed. Few studies have been done to evaluate the use of expectorants during pregnancy and thus first trimester use is best avoided. A study examining the developmental toxicity of guaifenesin in pregnant rats reported decreased fetal weight and impaired skeletal development in fetuses of exposed rats. In a large, population-based case control study of maternal use of cough medications during early pregnancy, guaifenesin use was associated with a small number of birth defects, including small intestinal atresia/stenosis and omphalocele. Non-pharmacologic methods (e.g., fluids, rest) are recommended to be tried first for symptomatic relief of cough and congestion during pregnancy and pregnant patients should get treatment recommendations from their health care provider.

Interactions

Abiraterone: (Moderate) Abiraterone inhbits CYP2D6 and dextromethorphan is a CYP2D6 substrate. Monitor for dextromethorphan-related side effects, such as drowsiness, nausea or vomiting, sweating, restlessness, or tremor. If dextromethorphan- related side effects occur, a dose reduction or discontinuation of dextromethorphan may be necessary. In an in vivo drug-drug interaction trial, the Cmax

and AUC of the CYP2D6 substrate dextromethorphan were increased 2.8- and 2.9-fold, respectively when dextromethorphan 30 mg was given with abiraterone acetate 1,000 mg daily along with prednisone 5 mg twice daily. The AUC for dextrorphan, the active metabolite of dextromethorphan, increased approximately 1.3 fold.
Acetaminophen; Codeine: (Moderate) Because of the potential risk and severity of serotonin syndrome, caution should be observed when administering codeine with dextromethorphan. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome particularly during treatment initiation and dose adjustment. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs.
ALFentanil: (Moderate) Because of the potential risk and severity of serotonin syndrome, caution should be observed when administering alfentanil with dextromethorphan. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome particularly during treatment initiation and dose adjustment. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs.
Almotriptan: (Moderate) Monitor for signs and symptoms of serotonin syndrome, particularly during treatment initiation and dosage increase, during concomitant dextromethorphan and serotonin-receptor agonists use. If serotonin syndrome occurs, discontinue therapy. Concomitant use increases the risk for serotonin syndrome.
Amitriptyline: (Moderate) Because of the potential risk and severity of serotonin syndrome, caution should be observed when administering dextromethorphan with tricyclic antidepressants. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome particularly during treatment initiation and dose adjustments. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs.
Artemether; Lumefantrine: (Moderate) Use of dextromethorphan with lumefantrine may result in increased dextromethorphan exposure. Lumefantrine inhibits CYP2D6 and dextromethorphan is a CYP2D6 substrate. Monitor for dextromethorphan-related side effects, such as drowsiness, nausea or vomiting, sweating, restlessness, or tremor.
Aspirin, ASA; Carisoprodol; Codeine: (Moderate) Because of the potential risk and severity of serotonin syndrome, caution should be observed when administering codeine with dextromethorphan. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome particularly during treatment initiation and dose adjustment. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs.
Atazanavir; Cobicistat: (Moderate) Use of dextromethorphan with cobicistat may result in increased dextromethorphan exposure. Cobicistat inhibits CYP2D6 and dextromethorphan is a CYP2D6 substrate. Monitor for dextromethorphan-related side effects, such as drowsiness, nausea or vomiting, sweating, restlessness, or tremor.

Benzoic Acid; Hyoscyamine; Methenamine; Methylene Blue; Phenyl Salicylate: (Major) Because of the potential risk and severity of serotonin syndrome, coadministration of dextromethorphan and IV methylene blue should be avoided if possible. Methylene blue has been demonstrated to be a potent monoamine oxidase inhibitor (MAOI) and may cause potentially fatal serotonin toxicity (serotonin syndrome) when combined with serotonin reuptake inhibitors (SRIs). Dextromethorphan increases central serotonin effects. If methylene blue is judged to be indicated, all SRIs, including dextromethorphan, must be ceased prior to treatment/procedure/surgery. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs.
Buprenorphine: (Moderate) If concomitant use of buprenorphine and dextromethorphan is warranted, monitor patients for the emergence of serotonin syndrome. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs. The concomitant use of opioids with other drugs that affect the serotonergic neurotransmitter system has resulted in serotonin syndrome.
Buprenorphine; Naloxone: (Moderate) If concomitant use of buprenorphine and dextromethorphan is warranted, monitor patients for the emergence of serotonin syndrome. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs. The concomitant use of opioids with other drugs that affect the serotonergic neurotransmitter system has resulted in serotonin syndrome.
buPROPion: (Moderate) Monitor for dextromethorphan-related side effects, such as dizziness or drowsiness, if concomitant use of bupropion is necessary. Concomitant use may increase dextromethorphan exposure and side effects. Dextromethorphan is a CYP2D6 substrate and bupropion is a strong CYP2D6 inhibitor. Concomitant use with another strong CYP2D6 inhibitor increased dextromethorphan overall exposure by 2.69-fold.
buPROPion; Naltrexone: (Moderate) Monitor for dextromethorphan-related side effects, such as dizziness or drowsiness, if concomitant use of bupropion is necessary. Concomitant use may increase dextromethorphan exposure and side effects. Dextromethorphan is a CYP2D6 substrate and bupropion is a strong CYP2D6 inhibitor. Concomitant use with another strong CYP2D6 inhibitor increased dextromethorphan overall exposure by 2.69-fold.
Butalbital; Acetaminophen; Caffeine; Codeine: (Moderate) Because of the potential risk and severity of serotonin syndrome, caution should be observed when administering codeine with dextromethorphan. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome particularly during treatment initiation and dose adjustment. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs.
Butalbital; Aspirin; Caffeine; Codeine: (Moderate) Because of the potential risk and severity of serotonin syndrome, caution should be observed when administering

codeine with dextromethorphan. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome particularly during treatment initiation and dose adjustment. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs.
chlordiazePOXIDE; Amitriptyline: (Moderate) Because of the potential risk and severity of serotonin syndrome, caution should be observed when administering dextromethorphan with tricyclic antidepressants. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome particularly during treatment initiation and dose adjustments. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs.
Chlorpheniramine; Codeine: (Moderate) Because of the potential risk and severity of serotonin syndrome, caution should be observed when administering codeine with dextromethorphan. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome particularly during treatment initiation and dose adjustment. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs.
Citalopram: (Moderate) Because of the potential risk and severity of serotonin syndrome, caution should be observed when administering dextromethorphan with citalopram. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome, particularly during treatment initiation and dose adjustment. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs.
cloBAZam: (Moderate) Use of dextromethorphan with clobazam may result in increased dextromethorphan exposure. Monitor for dextromethorphan-related side effects, such as drowsiness, nausea or vomiting, sweating, restlessness, or tremor. Clobazam inhibits CYP2D6 and dextromethorphan is a CYP2D6 substrate. A dosage reduction of dextromethorphan may be necessary for some patients. During one in vivo study, co-administration of dextromethorphan and clobazam resulted in increased AUC and Cmax of dextromethorphan by 90% and 59%, respectively.
clomiPRAMINE: (Moderate) Because of the potential risk and severity of serotonin syndrome, caution should be observed when administering dextromethorphan with tricyclic antidepressants. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome particularly during treatment initiation and dose adjustments. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs.
Cobicistat: (Moderate) Use of dextromethorphan with cobicistat may result in increased dextromethorphan exposure. Cobicistat inhibits CYP2D6 and dextromethorphan is a CYP2D6 substrate. Monitor for dextromethorphan-related side effects, such as drowsiness, nausea or vomiting, sweating, restlessness, or tremor.
Codeine: (Moderate) Because of the potential risk and severity of serotonin syndrome,

caution should be observed when administering codeine with dextromethorphan. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome particularly during treatment initiation and dose adjustment. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs.
Codeine; Dexbrompheniramine: (Moderate) Because of the potential risk and severity of serotonin syndrome, caution should be observed when administering codeine with dextromethorphan. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome particularly during treatment initiation and dose adjustment. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs.
Codeine; guaiFENesin: (Moderate) Because of the potential risk and severity of serotonin syndrome, caution should be observed when administering codeine with dextromethorphan. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome particularly during treatment initiation and dose adjustment. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs.
Codeine; guaiFENesin; Pseudoephedrine: (Moderate) Because of the potential risk and severity of serotonin syndrome, caution should be observed when administering codeine with dextromethorphan. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome particularly during treatment initiation and dose adjustment. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs.
Codeine; Phenylephrine; Promethazine: (Moderate) Because of the potential risk and severity of serotonin syndrome, caution should be observed when administering codeine with dextromethorphan. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome particularly during treatment initiation and dose adjustment. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs.
Codeine; Promethazine: (Moderate) Because of the potential risk and severity of serotonin syndrome, caution should be observed when administering codeine with dextromethorphan. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome particularly during treatment initiation and dose adjustment. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs.
Dacomitinib: (Moderate) Monitor for dextromethorphan-related side effects, such as dizziness or drowsiness, if concomitant use of dacomitinib is necessary. For patients receiving combination dextromethorphan; bupropion, do not exceed a maximum dose of 45 mg dextromethorphan; 105 mg bupropion once daily. Concomitant use may increase dextromethorphan exposure and side effects. Dextromethorphan is a CYP2D6

substrate and dacomitinib is a strong CYP2D6 inhibitor. Concomitant use with another strong CYP2D6 inhibitor increased dextromethorphan overall exposure by 2.69-fold.
Darifenacin: (Minor) Use of dextromethorphan with darifenacin may result in increased dextromethorphan exposure. Darifenacin is a moderate inhibitor of CYP2D6 and dextromethorphan is a CYP2D6 substrate. Monitor for dextromethorphan-related side effects, such as drowsiness, nausea or vomiting, sweating, restlessness, or tremor.
Darunavir; Cobicistat: (Moderate) Use of dextromethorphan with cobicistat may result in increased dextromethorphan exposure. Cobicistat inhibits CYP2D6 and dextromethorphan is a CYP2D6 substrate. Monitor for dextromethorphan-related side effects, such as drowsiness, nausea or vomiting, sweating, restlessness, or tremor.
Darunavir; Cobicistat; Emtricitabine; Tenofovir alafenamide: (Moderate) Use of dextromethorphan with cobicistat may result in increased dextromethorphan exposure. Cobicistat inhibits CYP2D6 and dextromethorphan is a CYP2D6 substrate. Monitor for dextromethorphan-related side effects, such as drowsiness, nausea or vomiting, sweating, restlessness, or tremor.
Desipramine: (Moderate) Because of the potential risk and severity of serotonin syndrome, caution should be observed when administering dextromethorphan with tricyclic antidepressants. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome particularly during treatment initiation and dose adjustments. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs.
Desvenlafaxine: (Moderate) Because of the potential risk and severity of serotonin syndrome, caution should be observed when administering dextromethorphan with desvenlafaxine. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome particularly during treatment initiation and dose adjustment. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs. In addition, the manufacturer of desvenlafaxine recommends that the dose of CYP2D6 substrates, such as dextromethorphan, be reduced by up to 50% if used with desvenlafaxine 400 mg/day, a CYP2D6 inhibitor.
Dextromethorphan; buPROPion: (Moderate) Monitor for dextromethorphan-related side effects, such as dizziness or drowsiness, if concomitant use of bupropion is necessary. Concomitant use may increase dextromethorphan exposure and side effects. Dextromethorphan is a CYP2D6 substrate and bupropion is a strong CYP2D6 inhibitor. Concomitant use with another strong CYP2D6 inhibitor increased dextromethorphan overall exposure by 2.69-fold.
Dextromethorphan; quiNIDine: (Moderate) Monitor for dextromethorphan-related side effects, such as dizziness or drowsiness, if concomitant use of quinidine is necessary. For patients receiving combination dextromethorphan; bupropion, do not exceed a maximum dose of 45 mg dextromethorphan; 105 mg bupropion once daily.

Concomitant use may increase dextromethorphan exposure and side effects. Dextromethorphan is a CYP2D6 substrate and quinidine is a strong CYP2D6 inhibitor. Concomitant use with another strong CYP2D6 inhibitor increased dextromethorphan overall exposure by 2.69-fold.
Donepezil; Memantine: (Moderate) Dextromethorphan is a NMDA antagonist and may lead to additive adverse effects if combined with memantine, also an NMDA antagonist. It may be prudent to avoid coadministration of dextromethorphan with memantine. If coadministration cannot be avoided, monitor for increased adverse effects such as agitation, dizziness and other CNS events.
Doxepin: (Moderate) Because of the potential risk and severity of serotonin syndrome, caution should be observed when administering dextromethorphan with tricyclic antidepressants. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome particularly during treatment initiation and dose adjustments. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs.
Dronedarone: (Moderate) Use of dextromethorphan with dronedarone may result in increased dextromethorphan exposure. Dronedarone inhibits CYP2D6 and dextromethorphan is a CYP2D6 substrate. Monitor for dextromethorphan-related side effects, such as drowsiness, nausea or vomiting, sweating, restlessness, or tremor.
DULoxetine: (Moderate) Because of the potential risk and severity of serotonin syndrome, caution should be observed when administering dextromethorphan with duloxetine. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome particularly during treatment initiation and dose adjustment. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs.
Eletriptan: (Moderate) Monitor for signs and symptoms of serotonin syndrome, particularly during treatment initiation and dosage increase, during concomitant dextromethorphan and serotonin-receptor agonists use. If serotonin syndrome occurs, discontinue therapy. Concomitant use increases the risk for serotonin syndrome.
Eliglustat: (Moderate) Use of dextromethorphan with eliglustat may result in increased dextromethorphan exposure. Eliglustat inhibits CYP2D6 and dextromethorphan is a CYP2D6 substrate. Monitor for dextromethorphan-related side effects, such as drowsiness, nausea or vomiting, sweating, restlessness, or tremor.
Elvitegravir; Cobicistat; Emtricitabine; Tenofovir Alafenamide: (Moderate) Use of dextromethorphan with cobicistat may result in increased dextromethorphan exposure. Cobicistat inhibits CYP2D6 and dextromethorphan is a CYP2D6 substrate. Monitor for dextromethorphan-related side effects, such as drowsiness, nausea or vomiting, sweating, restlessness, or tremor.
Elvitegravir; Cobicistat; Emtricitabine; Tenofovir Disoproxil Fumarate: (Moderate) Use of dextromethorphan with cobicistat may result in increased dextromethorphan exposure.

Cobicistat inhibits CYP2D6 and dextromethorphan is a CYP2D6 substrate. Monitor for dextromethorphan-related side effects, such as drowsiness, nausea or vomiting, sweating, restlessness, or tremor.
Escitalopram: (Moderate) Because of the potential risk and severity of serotonin syndrome, caution should be observed when administering dextromethorphan with escitalopram. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome, particularly during treatment initiation and dose adjustment. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs.
Fedratinib: (Moderate) Use of dextromethorphan with fedratinib may result in increased dextromethorphan exposure. Fedratinib is a moderate inhibitor of CYP2D6 and dextromethorphan is a CYP2D6 substrate. Monitor for dextromethorphan-related side effects, such as drowsiness, nausea or vomiting, sweating, restlessness, or tremor.
Fenfluramine: (Moderate) Use fenfluramine and dextromethorphan with caution due to an increased risk of serotonin syndrome. Monitor patients for the emergence of serotonin syndrome. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs.
fentaNYL: (Moderate) Because of the potential risk and severity of serotonin syndrome, caution should be observed when administering fentanyl with dextromethorphan. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome particularly during treatment initiation and dose adjustment. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs.
FLUoxetine: (Moderate) Monitor for dextromethorphan-related side effects, such as dizziness or drowsiness, if concomitant use of fluoxetine is necessary. For patients receiving combination dextromethorphan; bupropion, do not exceed a maximum dose of 45 mg dextromethorphan; 105 mg bupropion once daily. Additionally, monitor patients for signs and symptoms of serotonin syndrome. Concomitant use may increase dextromethorphan exposure and the risk for serotonin syndrome. Dextromethorphan is a CYP2D6 substrate and fluoxetine is a strong CYP2D6 inhibitor. Concomitant use with another strong CYP2D6 inhibitor increased dextromethorphan overall exposure by 2.69-fold.
fluvoxaMINE: (Moderate) Because of the potential risk and severity of serotonin syndrome, caution should be observed when administering dextromethorphan with fluvoxamine. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome, particularly during treatment initiation and dose adjustment. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs.
Frovatriptan: (Moderate) Monitor for signs and symptoms of serotonin syndrome, particularly during treatment initiation and dosage increase, during concomitant

dextromethorphan and serotonin-receptor agonists use. If serotonin syndrome occurs, discontinue therapy. Concomitant use increases the risk for serotonin syndrome.
Gepirone: (Moderate) Monitor for serotonin syndrome if concomitant use of gepirone and dextromethorphan is necessary. Both medications affect the serotonergic neurotransmitter system; concomitant use increases the risk for serotonin syndrome.
Givosiran: (Moderate) If possible, avoid concomitant use of dextromethorphan with givosiran due to the risk of increased dextromethorphan-related adverse reactions. If use is necessary, consider decreasing the dextromethorphan dose. Monitor for dextromethorphan-related side effects, such as drowsiness, nausea or vomiting, sweating, restlessness, or tremor. Dextromethorphan is a sensitive CYP2D6 substrate. Givosiran may moderately reduce hepatic CYP2D6 enzyme activity because of its pharmacological effects on the hepatic heme biosynthesis pathway.
Grapefruit juice: (Minor) Intake of grapefruit juice or seville orange juice increased dextromethorphan bioavailability in one study. Patients with increased concentrations of dextromethorphan may experience drowsiness or serotonergic side effects (dizziness, nervousness or restlessness, nausea, vomiting, stomach upset) not usually noted with prescribed or nonprescription product doses. Grapefruit juice and seville orange juice contain compounds that can inhibit P-glycoprotein in the intestinal wall, and dextromethorphan absorption may be affected by P-glycoprotein activity. Dextromethorphan is largely metabolized by CYP2D6, so this particular interaction with grapefruit juice may be more relevant in patients who are poor CYP2D6 metabolizers.
Hyoscyamine; Methenamine; Methylene Blue; Phenyl Salicylate; Sodium Biphosphate: (Major) Because of the potential risk and severity of serotonin syndrome, coadministration of dextromethorphan and IV methylene blue should be avoided if possible. Methylene blue has been demonstrated to be a potent monoamine oxidase inhibitor (MAOI) and may cause potentially fatal serotonin toxicity (serotonin syndrome) when combined with serotonin reuptake inhibitors (SRIs). Dextromethorphan increases central serotonin effects. If methylene blue is judged to be indicated, all SRIs, including dextromethorphan, must be ceased prior to treatment/procedure/surgery. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs.
Imatinib: (Moderate) Use of dextromethorphan with imatinib may result in increased dextromethorphan exposure. Imatinib inhibits CYP2D6 and dextromethorphan is a CYP2D6 substrate. Monitor for dextromethorphan-related side effects, such as drowsiness, nausea or vomiting, sweating, restlessness, or tremor.
Imipramine: (Moderate) Because of the potential risk and severity of serotonin syndrome, caution should be observed when administering dextromethorphan with tricyclic antidepressants. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome particularly during treatment initiation and dose adjustments. Discontinue all serotonergic agents and

initiate symptomatic treatment if serotonin syndrome occurs.
Isocarboxazid: (Contraindicated) Dextromethorphan products are contraindicated in patients taking a monoamine oxidase inhibitor (MAOI) or in patients who have taken an MAOI within the last 14 days, due to the risk of serious and possibly fatal drug interactions, including serotonin syndrome. A washout period of at least 14 days should elapse between the start of dextromethorphan after discontinuation of an MAOI. Patients should read nonprescription product labels carefully. Before initiating an MAOI after using other serotonergic agents, a sufficient amount of time must be allowed for clearance of the serotonergic agent and its active metabolites.
Lasmiditan: (Moderate) Serotonin syndrome may occur during coadministration of lasmiditan and dextromethorphan. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome, particularly after a dose increase or the addition of other serotonergic medications to an existing regimen. Discontinue all serotonergic agents if serotonin syndrome occurs and implement appropriate medical management.
Levomilnacipran: (Moderate) Because of the potential risk and severity of serotonin syndrome, caution should be observed when administering dextromethorphan with levomilnacipran. Dextromethorphan has serotonergic activity. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome particularly during treatment initiation and dose adjustment. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs.
Linezolid: (Moderate) Because of the potential risk and severity of serotonin syndrome, caution should be observed when administering linezolid with dextromethorphan. Linezolid is an antibiotic that is also a reversible, non-selective MAO inhibitor and has potential to interact with serotonergic agents. Dextromethorphan has serotonergic activity. However, the potential for interaction has been studied. Subjects were administered dextromethorphan (two 20-mg doses given 4 hours apart) with or without linezolid. No serotonin syndrome effects (confusion, delirium, restlessness, tremors, blushing, diaphoresis, hyperpyrexia) have been observed in normal subjects receiving linezolid and dextromethorphan.
Mavorixafor: (Moderate) Monitor for dextromethorphan-related side effects, such as dizziness or drowsiness, if concomitant use of mavorixafor is necessary. For patients receiving combination dextromethorphan; bupropion, do not exceed a maximum dose of 45 mg dextromethorphan; 105 mg bupropion once daily. Concomitant use may increase dextromethorphan exposure and side effects. Dextromethorphan is a CYP2D6 substrate and mavorixafor is a strong CYP2D6 inhibitor. Concomitant use increased dextromethorphan overall exposure by 9-fold.
Meloxicam; Rizatriptan: (Moderate) Monitor for signs and symptoms of serotonin syndrome, particularly during treatment initiation and dosage increase, during

concomitant dextromethorphan and serotonin-receptor agonists use. If serotonin syndrome occurs, discontinue therapy. Concomitant use increases the risk for serotonin syndrome.
Memantine: (Moderate) Dextromethorphan is a NMDA antagonist and may lead to additive adverse effects if combined with memantine, also an NMDA antagonist. It may be prudent to avoid coadministration of dextromethorphan with memantine. If coadministration cannot be avoided, monitor for increased adverse effects such as agitation, dizziness and other CNS events.
Methenamine; Sodium Acid Phosphate; Methylene Blue; Hyoscyamine: (Major) Because of the potential risk and severity of serotonin syndrome, coadministration of dextromethorphan and IV methylene blue should be avoided if possible. Methylene blue has been demonstrated to be a potent monoamine oxidase inhibitor (MAOI) and may cause potentially fatal serotonin toxicity (serotonin syndrome) when combined with serotonin reuptake inhibitors (SRIs). Dextromethorphan increases central serotonin effects. If methylene blue is judged to be indicated, all SRIs, including dextromethorphan, must be ceased prior to treatment/procedure/surgery. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs.
Methylene Blue: (Major) Because of the potential risk and severity of serotonin syndrome, coadministration of dextromethorphan and IV methylene blue should be avoided if possible. Methylene blue has been demonstrated to be a potent monoamine oxidase inhibitor (MAOI) and may cause potentially fatal serotonin toxicity (serotonin syndrome) when combined with serotonin reuptake inhibitors (SRIs). Dextromethorphan increases central serotonin effects. If methylene blue is judged to be indicated, all SRIs, including dextromethorphan, must be ceased prior to treatment/procedure/surgery. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs.
Milnacipran: (Moderate) Because of the potential risk and severity of serotonin syndrome, caution should be observed when administering dextromethorphan with milnacipran. Dextromethorphan has serotonergic activity. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome particularly during treatment initiation and dose adjustment. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs.
Mirabegron: (Minor) Use of dextromethorphan with mirabegron may result in increased dextromethorphan exposure. Mirabegron moderately inhibits CYP2D6 and dextromethorphan is a CYP2D6 substrate. Monitor for dextromethorphan-related side effects, such as drowsiness, nausea or vomiting, sweating, restlessness, or tremor.
Mirtazapine: (Moderate) Because of the potential risk and severity of serotonin syndrome, caution should be observed when administering dextromethorphan with mirtazapine. Inform patients taking this combination of the possible increased risk and

monitor for the emergence of serotonin syndrome particularly during treatment initiation and dose adjustment. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs.
Monoamine oxidase inhibitors: (Contraindicated) Dextromethorphan products are contraindicated in patients taking a monoamine oxidase inhibitor (MAOI) or in patients who have taken an MAOI within the last 14 days, due to the risk of serious and possibly fatal drug interactions, including serotonin syndrome. A washout period of at least 14 days should elapse between the start of dextromethorphan after discontinuation of an MAOI. Patients should read nonprescription product labels carefully. Before initiating an MAOI after using other serotonergic agents, a sufficient amount of time must be allowed for clearance of the serotonergic agent and its active metabolites.
Naratriptan: (Moderate) Monitor for signs and symptoms of serotonin syndrome, particularly during treatment initiation and dosage increase, during concomitant dextromethorphan and serotonin-receptor agonists use. If serotonin syndrome occurs, discontinue therapy. Concomitant use increases the risk for serotonin syndrome.
Nefazodone: (Moderate) Because of the potential risk and severity of serotonin syndrome, caution should be observed when administering dextromethorphan with nefazodone. Both drugs have serotonergic activity. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome particularly during treatment initiation and dose adjustment. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs.
Niraparib; Abiraterone: (Moderate) Abiraterone inhbits CYP2D6 and dextromethorphan is a CYP2D6 substrate. Monitor for dextromethorphan-related side effects, such as drowsiness, nausea or vomiting, sweating, restlessness, or tremor. If dextromethorphan- related side effects occur, a dose reduction or discontinuation of dextromethorphan may be necessary. In an in vivo drug-drug interaction trial, the Cmax and AUC of the CYP2D6 substrate dextromethorphan were increased 2.8- and 2.9-fold, respectively when dextromethorphan 30 mg was given with abiraterone acetate 1,000 mg daily along with prednisone 5 mg twice daily. The AUC for dextrorphan, the active metabolite of dextromethorphan, increased approximately 1.3 fold.
Nortriptyline: (Moderate) Because of the potential risk and severity of serotonin syndrome, caution should be observed when administering dextromethorphan with tricyclic antidepressants. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome particularly during treatment initiation and dose adjustments. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs.
OLANZapine; FLUoxetine: (Moderate) Monitor for dextromethorphan-related side effects, such as dizziness or drowsiness, if concomitant use of fluoxetine is necessary. For patients receiving combination dextromethorphan; bupropion, do not exceed a maximum dose of 45 mg dextromethorphan; 105 mg bupropion once daily. Additionally,

monitor patients for signs and symptoms of serotonin syndrome. Concomitant use may increase dextromethorphan exposure and the risk for serotonin syndrome. Dextromethorphan is a CYP2D6 substrate and fluoxetine is a strong CYP2D6 inhibitor. Concomitant use with another strong CYP2D6 inhibitor increased dextromethorphan overall exposure by 2.69-fold.
Oliceridine: (Moderate) If concomitant use of oliceridine and dextromethorphan is warranted, monitor patients for the emergence of serotonin syndrome. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs. The concomitant use of opioids with other drugs that affect the serotonergic neurotransmitter system has resulted in serotonin syndrome.
Oritavancin: (Moderate) Administration of oritavancin, a weak inducer of CYP2D6 and CYP3A4, with dextromethorphan resulted in a 31% reduction in the ratio of dextromethorphan to dextrorphan concentrations in the urine. The efficacy of dextromethorphan may be reduced if these drugs are administered concurrently.
Panobinostat: (Major) Avoid coadministrating panobinostat with sensitive CYP2D6 substrates such as dextromethorphan due to increased dextromethorphan exposure. Consider alternatives to dextromethorphan if possible. If concomitant use cannot be avoided, closely monitor for dextromethorphan-related side effects, such as drowsiness, nausea or vomiting, sweating, restlessness, or tremor. Panobinostat inhibits CYP2D6. When a single 60-mg dose of dextromethorphan (DM) was administered after 3 doses of panobinostat (20 mg on days 3, 5, and 8), the DM Cmax increased by 20% to 200% and DM exposure (AUC) increased by 20% to 130% (interquartile ranges) vs. when DM was given alone; however, the change in exposure was highly variable among the patients studied.
PARoxetine: (Moderate) Monitor for dextromethorphan-related side effects, such as dizziness or drowsiness, if concomitant use of paroxetine is necessary. For patients receiving combination dextromethorphan; bupropion, do not exceed a maximum dose of 45 mg dextromethorphan; 105 mg bupropion once daily. Additionally, monitor patients for signs and symptoms of serotonin syndrome. Concomitant use may increase dextromethorphan exposure and the risk for serotonin syndrome. Dextromethorphan is a CYP2D6 substrate and paroxetine is a strong CYP2D6 inhibitor. Concomitant use with paroxetine increased dextromethorphan overall exposure by 2.69-fold.
PAZOPanib: (Moderate) Use of dextromethorphan with pazopanib may result in increased dextromethorphan exposure. Monitor for dextromethorphan-related side effects, such as drowsiness, nausea or vomiting, sweating, restlessness, or tremor. Results from drug-drug interaction trials conducted in cancer patients suggest that pazopanib is a weak inhibitor of CYP2D6 and dextromethorphan is a CYP2D6 substrate. Coadministration of dextromethorphan and pazopanib resulted in an increase of 33% to 64% in the ratio of dextromethorphan to dextrorphan concentrations in the urine, indicating reduced CYP2D6 metabolism to the dextrorphan metabolite.

Peginterferon Alfa-2b: (Minor) Monitor for adverse effects associated with increased exposure to dextromethorphan if peginterferon alfa-2b is coadministered. Peginterferon alfa -2b is a CYP2D6 inhibitor, while dextromethorphan is a CYP2D6 substrate.
Perphenazine; Amitriptyline: (Moderate) Because of the potential risk and severity of serotonin syndrome, caution should be observed when administering dextromethorphan with tricyclic antidepressants. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome particularly during treatment initiation and dose adjustments. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs.
Phenelzine: (Contraindicated) Dextromethorphan products are contraindicated in patients taking a monoamine oxidase inhibitor (MAOI) or in patients who have taken an MAOI within the last 14 days, due to the risk of serious and possibly fatal drug interactions, including serotonin syndrome. A washout period of at least 14 days should elapse between the start of dextromethorphan after discontinuation of an MAOI. Patients should read nonprescription product labels carefully. Before initiating an MAOI after using other serotonergic agents, a sufficient amount of time must be allowed for clearance of the serotonergic agent and its active metabolites.
Procarbazine: (Moderate) Because of the potential risk and severity of serotonin syndrome, caution should be observed when administering dextromethorphan with procarbazine, an antineoplastic agent with monoamine oxidase inhibitor (MAOI) activity. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome particularly during treatment initiation and dose adjustments. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs.
Propafenone: (Minor) Use of dextromethorphan with propafenone might increase dextromethorphan exposure. Monitor for dextromethorphan-related side effects, such as drowsiness, nausea or vomiting, sweating, restlessness, or tremor. In vitro studies suggest that propafenone inhibits CYP2D6, but clinically relevant interactions have not been reported due to this potential action. Dextromethorphan is a CYP2D6 substrate.
Protriptyline: (Moderate) Because of the potential risk and severity of serotonin syndrome, caution should be observed when administering dextromethorphan with tricyclic antidepressants. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome particularly during treatment initiation and dose adjustments. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs.
quiNIDine: (Moderate) Monitor for dextromethorphan-related side effects, such as dizziness or drowsiness, if concomitant use of quinidine is necessary. For patients receiving combination dextromethorphan; bupropion, do not exceed a maximum dose of 45 mg dextromethorphan; 105 mg bupropion once daily. Concomitant use may

increase dextromethorphan exposure and side effects. Dextromethorphan is a CYP2D6 substrate and quinidine is a strong CYP2D6 inhibitor. Concomitant use with another strong CYP2D6 inhibitor increased dextromethorphan overall exposure by 2.69-fold.
quiNINE: (Moderate) Although clinical drug interaction studies have not been performed, antimalarial doses of quinine (greater than or equal to 600 mg/day in adults) may inhibit the metabolism of CYP2D6 substrates such as dextromethorphan and may result in increased dextromethorphan exposure. Monitor for dextromethorphan-related side effects, such as drowsiness, nausea or vomiting, sweating, restlessness, or tremor.
Rasagiline: (Contraindicated) Dextromethorphan prescription products are contraindicated in patients taking monoamine oxidase inhibitors (MAOIs) or in patients who have taken MAOIs within the preceding 14 days, due to the risk of serious and possibly fatal drug interactions, including serotonin syndrome. Allow at least 14 days after stopping dextromethorphan before starting an MAOI, including rasagiline. Brief episodes of psychosis or bizarre behavior have also been reported with this combination. Patients should read nonprescription product labels carefully. Before initiating an MAOI after using other serotoninergic agents, a sufficient amount of time must be allowed for clearance of the serotoninergic agent and its active metabolites.
Rizatriptan: (Moderate) Monitor for signs and symptoms of serotonin syndrome, particularly during treatment initiation and dosage increase, during concomitant dextromethorphan and serotonin-receptor agonists use. If serotonin syndrome occurs, discontinue therapy. Concomitant use increases the risk for serotonin syndrome.
Rolapitant: (Moderate) Rolapitant increases exposure to dextromethorphan. Monitor for dextromethorphan-related side effects, such as drowsiness, nausea or vomiting, sweating, restlessness, or tremor. Rolapitant is a moderate CYP2D6 inhibitor with a prolonged effect; the inhibitory effect of rolapitant is expected to persist beyond 28 days for an unknown duration. During drug interaction studies, exposure (AUC) to dextromethorphan following a single dose of rolapitant increased close to 3-fold on Days 8 and Day 22. The inhibition of CYP2D6 persisted on Day 28 with a 2.3-fold increase in dextromethorphan exposure (AUC), the last time point measured.
Safinamide: (Contraindicated) Dextromethorphan prescription products are contraindicated in patients taking monoamine oxidase inhibitors (MAOIs) or in patients who have taken MAOIs within the preceding 14 days, due to the risk of serious and possibly fatal drug interactions, including serotonin syndrome. Allow at least 14 days after stopping dextromethorphan before starting an MAOI, including safinamide. Brief episodes of psychosis or bizarre behavior have also been reported with this combination. Patients should read nonprescription product labels carefully. Before initiating an MAOI after using other serotoninergic agents, a sufficient amount of time must be allowed for clearance of the serotoninergic agent and its active metabolites.
Selegiline: (Contraindicated) Dextromethorphan products are contraindicated in patients taking selegiline, a selective monoamine oxidase type B inhibitor (MAO-B inhibitor) or in

patients who have taken an selegiline within the last 14 days, due to the risk of serious and possibly fatal drug interactions, including serotonin syndrome. A washout period of at least 14 days should elapse between the start of dextromethorphan after discontinuation of selegiline. Patients should read nonprescription product labels carefully. Before initiating selegiline after using dextromethorphan, a sufficient amount of time is advisable for clearance of dextromethorphan.
Serotonin-Receptor Agonists: (Moderate) Monitor for signs and symptoms of serotonin syndrome, particularly during treatment initiation and dosage increase, during concomitant dextromethorphan and serotonin-receptor agonists use. If serotonin syndrome occurs, discontinue therapy. Concomitant use increases the risk for serotonin syndrome.
Sertraline: (Moderate) Because of the potential risk and severity of serotonin syndrome, caution should be observed when administering dextromethorphan with sertraline. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome, particularly during treatment initiation and dose adjustment. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs. In addition, sertraline inhibits CYP2D6 and may increase systemic dextromethorphan exposure. Increased dextromethorphan concentrations may result in adverse effects consistent with the serotonin syndrome.
St. John's Wort, Hypericum perforatum: (Moderate) Because of the potential risk and severity of serotonin syndrome, caution should be observed when administering dextromethorphan with St. John's Wort. Inform patients of the possible increased risk and monitor for the emergence of serotonin syndrome, particularly during treatment initiation and dose adjustments. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs.
SUMAtriptan: (Moderate) Monitor for signs and symptoms of serotonin syndrome, particularly during treatment initiation and dosage increase, during concomitant dextromethorphan and serotonin-receptor agonists use. If serotonin syndrome occurs, discontinue therapy. Concomitant use increases the risk for serotonin syndrome.
SUMAtriptan; Naproxen: (Moderate) Monitor for signs and symptoms of serotonin syndrome, particularly during treatment initiation and dosage increase, during concomitant dextromethorphan and serotonin-receptor agonists use. If serotonin syndrome occurs, discontinue therapy. Concomitant use increases the risk for serotonin syndrome.
Terbinafine: (Moderate) Monitor for dextromethorphan-related side effects, such as dizziness or drowsiness, if concomitant use of terbinafine is necessary. For patients receiving combination dextromethorphan; bupropion, do not exceed a maximum dose of 45 mg dextromethorphan; 105 mg bupropion once daily. Concomitant use may increase dextromethorphan exposure and side effects. Dextromethorphan is a CYP2D6 substrate and terbinafine is a strong CYP2D6 inhibitor. Concomitant use with another

strong CYP2D6 inhibitor increased dextromethorphan overall exposure by 2.69-fold.
Tipranavir: (Moderate) Monitor for dextromethorphan-related side effects, such as dizziness or drowsiness, if concomitant use of tipranavir is necessary. For patients receiving combination dextromethorphan; bupropion, do not exceed a maximum dose of 45 mg dextromethorphan; 105 mg bupropion once daily. Concomitant use may increase dextromethorphan exposure and side effects. Dextromethorphan is a CYP2D6 substrate and tipranavir is a strong CYP2D6 inhibitor. Concomitant use with another strong CYP2D6 inhibitor increased dextromethorphan overall exposure by 2.69-fold.
Tocilizumab: (Minor) Concomitant use of tocilizumab and dextromethorphan may lead to a decrease in the efficacy of dextromethorphan; clinical significance of this interaction is not known or established. Inhibition of IL-6 signaling by tocilizumab may restore CYP450 activities to higher levels leading to increased metabolism of drugs that are CYP450 substrates as compared to metabolism prior to treatment. This effect on CYP450 enzyme activity may persist for several weeks after stopping tocilizumab. A 5% decrease in dextromethorphan exposure and a 29% decrease in its metabolite, dextrorphan was noted 1 week after a single tocilizumab infusion. In vitro, tocilizumab has the potential to affect expression of multiple CYP enzymes, including CYP1A2, CYP2B6, CYP2C9, CYP2C19, CYP2D6, and CYP3A4. Dextromethorphan is a CYP2D6 substrate.
Tranylcypromine: (Contraindicated) Dextromethorphan products are contraindicated in patients taking a monoamine oxidase inhibitor (MAOI) or in patients who have taken an MAOI within the last 14 days, due to the risk of serious and possibly fatal drug interactions, including serotonin syndrome. A washout period of at least 14 days should elapse between the start of dextromethorphan after discontinuation of an MAOI. Patients should read nonprescription product labels carefully. Before initiating an MAOI after using other serotonergic agents, a sufficient amount of time must be allowed for clearance of the serotonergic agent and its active metabolites.
Tricyclic antidepressants: (Moderate) Because of the potential risk and severity of serotonin syndrome, caution should be observed when administering dextromethorphan with tricyclic antidepressants. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome particularly during treatment initiation and dose adjustments. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs.
Trimipramine: (Moderate) Because of the potential risk and severity of serotonin syndrome, caution should be observed when administering dextromethorphan with tricyclic antidepressants. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome particularly during treatment initiation and dose adjustments. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs.
Vemurafenib: (Minor) Use of dextromethorphan with vemurafenib increases dextromethorphan exposure. Vemurafenib is a weak CYP2D6 inhibitor and

dextromethorphan is a CYP2D6 substrate. Monitor for dextromethorphan-related side effects, such as drowsiness, nausea or vomiting, sweating, restlessness, or tremor. Coadministration of vemurafenib and dextromethorphan increased the AUC of dextromethorphan by 47% and the dextromethorphan Cmax by 36%.
Venlafaxine: (Moderate) Because of the potential risk and severity of serotonin syndrome, caution should be observed when administering dextromethorphan with venlafaxine. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome, particularly during treatment initiation and dose increases. If serotonin syndrome occurs, serotonergic drugs should be discontinued and appropriate medical treatment should be initiated.
Vilazodone: (Moderate) Because of the potential risk and severity of serotonin syndrome, caution should be observed when administering dextromethorphan with vilazodone. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome particularly during treatment initiation and dose adjustments. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs.
Viloxazine: (Moderate) Monitor for an increase in dextromethorphan-related adverse effects if concomitant use of viloxazine is necessary. Concomitant use may increase dextromethorphan exposure; viloxazine is a weak CYP2D6 inhibitor and dextromethorphan is a CYP2D6 substrate.
Vortioxetine: (Moderate) Because of the potential risk and severity of serotonin syndrome, caution should be observed when administering dextromethorphan with vortioxetine. Inform patients taking this combination of the possible increased risk and monitor for the emergence of serotonin syndrome particularly during treatment initiation and dose adjustments. Discontinue all serotonergic agents and initiate symptomatic treatment if serotonin syndrome occurs.
ZOLMitriptan: (Moderate) Monitor for signs and symptoms of serotonin syndrome, particularly during treatment initiation and dosage increase, during concomitant dextromethorphan and serotonin-receptor agonists use. If serotonin syndrome occurs, discontinue therapy. Concomitant use increases the risk for serotonin syndrome.

Adverse Reaction

abdominal pain, diarrhea, dizziness, drowsiness, headache, nausea, rash (unspecified), vomiting

In general, adverse reactions to guaifenesin are infrequent and usually not serious. With recommended doses, adverse GI effects are rare. When given in high or excessive dosage, nausea, vomiting, diarrhea, and/or abdominal pain may occur. Drowsiness,

dizziness, and headache occur rarely at therapeutic doses of guaifenesin. Rash (unspecified) has also been reported with guaifenesin products.

nephrolithiasis

Excessive use or dosage of guaifenesin may result in nephrolithiasis; the resulting renal stones have been documented to contain guaifenesin metabolites including the active metabolite, beta-(2-methoxyphenoxy)-lactic acid. In another report, 11 of 24 patients with kidney stones containing the guaifenesin metabolite, beta-(2-methoxyphenoxy)-lactic acid, were using excessive amounts of over-the-counter stimulants and bronchodilators (stated dosages of 3 to 120 tablets/day or approximately 600 to 24,000 mg/day of guaifenesin); some patients had a history of substance abuse.

Description

Guaifenesin is an oral expectorant, which is commonly used to treat cough due to colds and minor upper respiratory infections. Despite its long history of use since the 1950s, the efficacy of guaifenesin has only recently been substantiated. Guaifenesin is used for dry, nonproductive cough when there is the presence of tenacious mucus and/or mucus plugs. The results of a few studies have favored active treatment with guaifenesin over placebo in treating productive cough due to upper respiratory illness (URI). In patients with chronic bronchitis, guaifenesin, is not recommended for aiding with cough suppression since studies have shown no benefit in reducing cough. However, the mucolytic properties of guaifenesin may be independently helpful in clearing mucus, and patients may subjectively report benefit to use. Guaifenesin is an ingredient contained in many combination non-prescription (over-the-counter or OTC) and prescription cough and cold products.

Mechanism Of Action

Guaifenesin loosens and thins phlegm and bronchial secretions to ease expectoration. By reducing the viscosity and adhesiveness of secretions, guaifenesin increases the efficacy of the mucociliary mechanism in removing accumulated secretions from the upper and lower airway. The increased flow of less viscous secretions promotes ciliary action and changes a dry, unproductive cough to one that is more productive and less frequent. Despite its long history of use since the 1950's, the efficacy of guaifenesin has only recently been substantiated. Guaifenesin is used for dry, nonproductive cough when there is the presence of tenacious mucus and/or mucus plugs. The results of a few studies have favored active treatment with guaifenesin over placebo in treating productive cough due to upper respiratory illness (URI).

Pharmacokinetics

Guaifenesin is administered orally. The plasma half-life is approximately 1 hour. Guiafenesin is rapidly hydrolyzed (60% within seven hours) and then excreted in the urine, with beta-(2-methoxyphenoxy)-lactic acid as its major urinary metabolite. No unchanged drug was detected in the urine following administration. Renal stones that developed during drug therapy have been documented to contain beta-(2-methoxyphenoxy)-lactic acid and other guaifenesin metabolites. Other pharmacokinetic parameters of guaifenesin are not known.

Route-Specific Pharmacokinetics

- **Oral Route**

Guaifenesin is rapidly and well absorbed from the gastrointestinal tract. Extended release products (e.g., Humibid LA) release drug slowly over a period of several hours, allowing for less frequent dosing. The Mucinex brand tablet, a combination immeditate-release/extended-release product, utilizes a patented bilayer delivery system which releases guaifenesin immediately from the first layer and over 12 hours from the second layer. Guaifenesin has a plasma half-life of approximately 1 hour.

Administration

For storage information, see the specific product information within the How Supplied section.

Oral Administration

To assist expectoration, patients should have an adequate intake of fluids while taking guaifenesin.

Oral Solid Formulations

Extended-release tablets: Swallow whole; do not crush, break, or chew. Take with a full glass of water. May be given with or without food.
Oral granules: Open packet, sprinkle entire contents onto tongue, and swallow. For best taste, do not chew granules. Liquid is not necessary for administration.

Oral Liquid Formulations

Oral solutions: Administer using a calibrated measuring device to ensure accurate

dosage.

Maximum Dosage Limits

- **Adults**
  2400 mg/day PO.
- **Geriatric**
  2400 mg/day PO.
- **Adolescents**
  2400 mg/day PO.
- **Children**
  12 years: 2400 mg/day PO.
  6 to 11 years: 1200 mg/day PO.
  2 to 5 years: 600 mg/day PO.
  Less than 2 years: Safety and efficacy have not been established.
- **Infants**
  Safety and efficacy have not been established.

Dosage Forms

- Adult Tussin Expectorant 200mg/10mL Solution (Original)
- Adult Tussin Mucus & Chest Congestion Sugar Free 200mg/10mL Solution
- Altarussin 100mg/5ml Solution
- Bronkaid 25mg-400mg Caplet
- Chest Congestion Relief Expectorant 100mg/5mL Solution (Cherry Menthol)
- Congestac 400mg-60mg Caplet
- CVS Chest Congestion Relief 400mg Tablet
- CVS Chest Congestion Relief D 60mg-400mg Caplet
- CVS Chest Congestion Relief PE 400mg-10mg Tablet
- CVS Children's Chest Congestion Expectorant 100mg/5ml Solution (Grape)
- CVS Mucus 12 Hour 600mg Extended-Release Tablet
- CVS Mucus 12 Hour Extended-Release Maximum Strength 1200mg Tablet
- CVS Mucus 12 Hour Maximum Strength 1200mg Extended-Release Tablet
- CVS Mucus D 1200mg-120mg Maximum Strength Extended-Release Tablet
- CVS Mucus D 600mg-60mg Extended-Release Tablet
- CVS Mucus Extended-Release 600mg Extended-Release Tablet
- CVS Sinus PE Non-Drying 200mg-5mg Tablet
- CVS Tussin Adult Chest Congestion Solution

- CVS Tussin Chest Congestion Solution
- Dextromethorphan Hydrobromide 10mg/5mL, Guaifenesin 100mg/5mL Oral syrup
- Diabetic Tussin 200mg/10mL Liquid
- Diabetic Tussin Expectorant 100mg/5ml Solution (Cherry Vanilla)
- Diabetic Tussin Mucus Relief 200mg/5ml Liquid
- Diabetic Tussin Mucus Relief 400mg Caplet
- Duravent PE 395mg-10mg Tablet
- ED Bron GP 100mg-5mg/5mL Liquid
- ElixSure EX 50mg/5ml Solution
- Equaline Adult Tussin Expectorant 200mg/10mL Solution (Original)
- Equaline Non-Drowsy Tussin Cough and Chest Congestion DM 20mg-200mg/10mL Solution
- Equate Mucus D 600mg-60mg Extended-Release Tablet
- Equate Mucus ER 600mg Extended-Release Tablet
- Equate Mucus ER 600mg Extended-Release Tablet
- Equate Mucus ER Maximum Strength 1200mg Extended-Release Tablet
- Equate Mucus Relief 12 Hour 600mg Extended-Release Tablet
- Equate Mucus Relief 600mg Extended-Release Tablet
- Equate Mucus Relief D 1200mg-120mg Maximum Strength Extended-Release Tablet
- Equate Mucus Relief ER Maximum Strength 1200mg Extended-Release Tablet
- Equate Mucus-D 12 Hour 600mg-60mg Extended-Release Tablet
- ExeFen 80mg-780mg Tablet
- ExeFen-IR 60mg-400mg Tablet
- ExeTuss 900mg-25mg Extended-Release Tablet
- Foster & Thrive Adult Tussin Expectorant 200mg/10mL Solution
- Foster & Thrive Chest Congestion Relief 400mg Caplet
- Foster & Thrive Chest Congestion Relief PE 400mg-10mg Caplet
- Foster & Thrive Mucus Relief D 600mg-60mg Extended-Release Tablet
- Foster & Thrive Mucus Relief Regular Strength 600mg Extended-Release Tablet
- Foster & Thrive Mucus Relief-D 12 Hour 600mg-60mg Extended-Release Tablet
- Foster & Thrive Mucus Relief-D Maximum Strength 1200mg-120mg Extended-Release Tablet
- GERI-TUSSIN 100mg/5mL Solution
- GERI-TUSSIN 200mg/10mL Solution
- Gilphex TR 388mg-10mg Tablet
- Gilphex TR 390mg-10mg Tablet
- Giltuss EX Children's Expectorant 200mg/5mL Solution (Assorted Fruit)
- Giltuss EX Expectorant Maximum Strength 400mg/10mL Solution (Assorted Fruit)
- Giltuss Sinus Plus 390mg-10mg Tablet

- GNP Adult Tussin Mucus & Chest Congestion Expectorant 200mg/10mL Solution (Fruit Punch)
- GNP Adult Tussin Mucus and Chest Congestion Solution
- GNP AdultTussin Mucus and Chest Congestion Solution
- GNP Mucus 600mg Extended-Release Tablet
- GNP Mucus ER 12 Hour 600mg Extended-Release Tablet
- GNP Mucus ER 600mg Extended-Release Tablet
- GNP Mucus ER Maximum Strength 1200mg Extended-Release Tablet
- GNP Mucus ER Maximum Strength 1200mg Extended-Release Tablet
- GNP Mucus Relief 400mg Tablet
- GNP Mucus Relief Chest Congestion 400mg Tablet
- GNP Mucus Relief ER Maximum Strength 1200mg Extended-Release Tablet
- GNP Mucus Relief PE Dye Free 400mg-10mg Tablet
- GNP Mucus Relief PE Tablet
- GNP Mucus-D 600mg-60mg Extended-Release Tablet
- GNP Mucus-ER Extended-Release 600mg Tablet
- GNP Tussin Tablet
- GoodSense 12-Hour Mucus ER 600mg Extended-Release Tablet
- GoodSense 12-Hour Mucus ER Maximum Strength 1200mg Extended-Release Tablet
- GoodSense Children's Mucus Relief 100mg/5mL Liquid
- GoodSense Mucus ER Maximum Strength 1200mg Extended-Release Tablet
- Guaifenesin 1,200mg Oral tablet, extended release
- Guaifenesin 1,200mg, Pseudoephedrine Hydrochloride 120mg Oral tablet, biphasic release
- Guaifenesin 100mg Oral solution
- Guaifenesin 100mg/5mL Oral solution
- Guaifenesin 200mg Oral tablet
- Guaifenesin 200mg/10mL Oral solution
- Guaifenesin 20mg/1mL, Phenylephrine Hydrochloride 1.5mg/1mL Oral drops, solution
- Guaifenesin 400mg Oral tablet
- Guaifenesin 400mg, Phenylephrine Hydrochloride 10mg Oral tablet
- Guaifenesin 600mg Oral tablet, biphasic release
- Guaifenesin 600mg Oral tablet, extended release
- Guaifenesin 600mg, Pseudoephedrine Hydrochloride 60mg Oral tablet, biphasic release
- Guaifenesin Bulk powder
- HEB Children's Mucus Relief 100mg/5mL Liquid
- Kirkland Mucus Relief Chest 400mg Tablet
- Leader Adult Tussin Chest Congestion 100mg/5mL Solution

- Leader Adult Tussin Mucus + Chest Congestion 200mg/10mL Solution (Cherry)
- Leader Adult Tussin Mucus + Chest Congestion Solution
- Leader Chest Congestion Relief 400mg Tablet
- Leader Cough Tabs 200mg Tablet
- Leader Mucus ER 600mg Extended-Release Tablet
- Leader Mucus Relief D 600mg-60mg Extended-Release Tablet
- Leader Mucus Relief Maximum Strength 1200mg Extended-Release Tablet
- Leader Mucus Relief PE Sinus Congestion 400mg-10mg Tablet
- Liquibid 400mg Tablet
- Liquibid-D 650mg-40mg Tablet
- MAXTussin 200mg/10mL Mucus & Chest Congestion Solution (Cherry)
- MAXTussin Expectorant 200mg/10mL Solution (Cherry)
- Mucinex 600mg Extended-Release Tablet
- MUCINEX 600mg Extended-Release Tablet
- Mucinex 600mg Extended-Release Tablet
- Mucinex 600mg Extended-Release Tablet
- Mucinex Children's Stuffy Nose & Chest Congestion 100mg-2.5mg/5mL Liquid (Very Berry)
- Mucinex D 1200mg-120mg Extended-Release Tablet
- Mucinex D 1200mg-120mg Extended-Release Tablet
- Mucinex D 600mg-60mg Extended-Release Tablet
- Mucinex D 600mg-60mg Extended-Release Tablet
- Mucinex Fast-Max Chest Congestion 400mg/20mL Solution (Honey & Berry)
- Mucinex Maximum Strength 1200mg Extended-Release Tablet
- Mucinex Maximum Strength 1200mg Extended-Release Tablet
- Mucolyte 100mg/5mL Liquid (Cherry)
- Mucosa 400mg Tablet
- Mucus + Chest Congestion 200mg/10mL Solution
- Mucus Relief 12 Hour 600mg Extended-Release Tablet
- Mucus Relief 12 Hour 600mg Extended-Release Tablet
- Mucus Relief 400mg Tablet
- Mucus Relief 600mg Extended-Release Tablet
- Mucus Relief 600mg Extended-Release Tablet
- Mucus Relief D 12 Hour 600mg-60mg Extended-Release Tablet
- Mucus Relief ER 600mg Extended-Release Tablet
- Mucus Relief ER Maximum Strength 1,200mg Extended-Release Tablet
- Mucus Relief Maximum Strength 1200mg Extended-Release Tablet
- Mucus Relief Maximum Strength 1200mg Extended-Release Tablet
- Mucus-D 12 Hour 600mg-60mg Extended-Release Tablet
- Mucus-D 12 Hour Maximum Strength 1200mg-120mg Extended-Release Tablet

- Mucus-D 600mg-60mg Extended-Release Tablet
- Premier Value Chest and Sinus Congestion Relief 400mg-10mg Tablet
- Premier Value Chest Congestion Relief 400mg Tablet
- Premier Value Chest Congestion Relief D 60mg-400mg Caplet
- Premier Value Children's Mucus Relief Expectorant 100mg/5ml Liquid (Grape)
- Premier Value TabTussin 400mg Tablet
- Premier Value Tussin DM Syrup
- Premier Value Tussin Expectorant 100mg/5mL Solution
- Publix Tussin Chest Congestion 100mg/5ml Solution
- Q-Tussin DM 10mg-100mg/5mL Syrup
- Quality Choice Adult Tussin Expectorant 100mg/5mL Non-Drowsy Solution (Cherry)
- Quality Choice Adult Tussin Mucus + Chest Congestion 200mg/10mL Solution
- Quality Choice Children's Mucus Relief Expectorant 100mg/5mL Solution (Grape)
- Quality Choice Mucus Relief 12 Hour 600mg Extended-Release Tablet
- Quality Choice Mucus Relief 12 Hour Maximum Strength 1200mg Extended-Release Tablet
- Quality Choice Mucus Relief 400mg Caplet
- Quality Choice Mucus Relief D Sinus Congestion 400mg-40mg Tablet
- Quality Choice Mucus Relief ER Maximum Strength 1200mg Extended-Release Tablet
- Quality Choice Mucus Relief Maximum Strength 1200mg Extended-Release Tablet
- Rescon GG 100mg-5mg/5ml Liquid
- RITE AID Adult Tussin Mucus & Chest Congestion Solution
- RITE AID Mucus + Chest Congestion 200mg/10mL Solution
- RITE AID Mucus Relief Chest Congestion 400mg Tablet
- RITE AID Mucus Relief ER 600mg Extended-Release Tablet
- RITE AID Mucus Relief Sinus Congestion PE 400mg-10mg Tablet
- Scot-Tussin Expectorant 100mg/5ml Solution
- Select Brand Mucus Relief 400mg Tablet
- Siltussin SA 100mg/5mL Liquid
- SudaTex-G 40mg-400mg Tablet
- SUPRESS-PE 50mg-2.5mg/mL Pediatric Drops (Grape)
- Today's Health Chest Congestion Relief 400mg Tablet
- Today's Health Chest Congestion Relief PE 400mg-10mg Tablet
- Today's Health Tussin Chest Congestion Formula Solution
- Top Care Children's Mucus Relief 100mg/5ml Liquid (Grape)
- Top Care Mucus Relief 12hr Maximum Strength 1200mg Extended-Release Tablet
- Top Care Tussin Chest Congestion Solution
- TopCare Chest Congestion Relief 400mg Tablet
- Topcare Tussin Mucus & Chest Congestion 200mg/10mL Solution

- Triaminic Chest & Nasal Congestion Solution
- TUSNEL 25mg-1.25mg/mL Pediatric Drops (Grape)
- TUSNEL-EX Expectorant 100mg/5mL Solution (Apple Banana)
- TUSNEL-EX Expectorant 100mg/5mL Solution (Apple Banana)
- Wal-Tussin Chest Congestion Solution
- Wal-Tussin Chest Congestion Solution (Cherry)
- Wal-Tussin Cold Severe Congestion Softgel
- Walgreens Children's Chest Congestion Alcohol Free 100mg/5mL Solution (Grape)
- Walgreens Children's Chest Congestion Relief 100mg/5mL Solution (Grape)
- Walgreens Children's Chest Congestion Relief 100mg/5mL Solution (Grape)
- Walgreens Mucus Relief 12 Hour 600mg Extended-Release Tablet
- Walgreens Mucus Relief 400mg Tablet
- Walgreens Mucus Relief 400mg Tablet
- Walgreens Mucus Relief D 12 Hour 600mg-60mg Extended-Release Tablet
- Walgreens Mucus Relief D 600mg-60mg Extended-Release Tablet
- Walgreens Mucus Relief D 600mg-60mg Extended-Release Tablets
- Walgreens Mucus Relief D Maximum Strength 1200mg-120mg Extended-Release Tablet
- Walgreens Mucus Relief D Sinus Congestion 400mg-40mg Tablet
- Walgreens Mucus Relief ER 12 Hour 600mg Extended-Release Tablet
- Walgreens Mucus Relief ER 12 Hour Maximum Strength 1200mg Extended-Release Tablet
- Walgreens Mucus Relief ER Maximum Strength 1200mg Extended-Release Tablet
- Walgreens Mucus Relief PE 400mg-10mg Tablet
- Zotex GPX 550mg-8.5mg Tablet

Dosage Adjustment Guidelines

Hepatic Impairment

No dosage adjustment is needed. Guaifenesin is primarily renally eliminated.

Renal Impairment

Specific guidelines for dosage adjustments in renal impairment are not available; it appears that no dosage adjustments are needed.