

Dextromethorphan and Bupropion

(deks troe meth OR fan & byoo PRO pee on)

- **Auvelity ER®**

- Tablet: dextromethorphan hydrobromide 45 mg – bupropion hydrochloride 105 mg

If you or someone you know is in crisis, please call/text 988 to speak with a trained crisis counselor 24/7 and/or call 911 for emergency services. A help line and other resources are also available through the National Alliance on Mental Illness at [nami.org](https://www.nami.org).



What is dextromethorphan and what does it treat?

Dextromethorphan has historically been used as a cough medication; however it has also been approved in combination with bupropion as an antidepressant medication. The combination product is approved for the treatment of major depressive disorder (MDD).

What is bupropion and what does it treat?

Bupropion is an antidepressant medication that works in the brain. It is approved for the treatment of MDD, seasonal affective disorder (SAD), and to help people quit smoking (smoking cessation). Bupropion is given with dextromethorphan to increase the levels and effects of dextromethorphan, but it also has known benefit alone in the treatment of MDD.

Symptoms of depression include:

- Depressed mood - feeling sad, empty, or tearful
- Feeling worthless, guilty, hopeless, and helpless
- Loss of interest or pleasure in your usual activities
- Sleep and eat more or less than usual (for most people it is less)
- Low energy, trouble concentrating, or thoughts of death (suicidal thinking)
- Psychomotor agitation ('nervous energy')
- Psychomotor retardation (feeling like you are moving and thinking in slow motion)
- Suicidal thoughts or behaviors

SAD is a type of depression that occurs mainly during the autumn-winter season. Although the common term SAD is now referred to as Major Depression with Seasonal Pattern, this fact sheet will continue to use SAD as it is more commonly known.

Bupropion alone may also be helpful when prescribed "off-label" for depression due to bipolar disorder, attention deficit hyperactivity disorder (ADHD), and sexual dysfunction due to SSRI antidepressants. "Off-label" means that it hasn't been approved by the Food and Drug Administration for this condition. Your mental health provider should justify his or her thinking in recommending an "off-label" treatment. They should be clear about the limits of the research around that medication and if there are any other options.

All FDA warnings are at the end of this fact sheet. Please consult them before taking this medication.

What is the most important information I should know about dextromethorphan/bupropion?

After starting dextromethorphan/bupropion, depression symptoms gradually decrease over a period of weeks and may decrease as quickly as one week. In MDD, sleep and other physical symptoms may improve before there is noticeable improvement in mood or interest in activities. Once symptoms are under control, MDD usually requires long-term treatment to help prevent the return of depressive symptoms. Do not stop taking dextromethorphan/bupropion, even when you feel better. With input from you, your health care provider will assess how long you will need to take the medicine.

Do not stop taking dextromethorphan/bupropion or change your dose without talking with your health care provider first.

Missing doses of dextromethorphan/bupropion may increase your risk for relapse in your symptoms.

Depression is also a part of bipolar illness. People with bipolar disorder who take antidepressants may be at risk for "switching" from depression into mania. Symptoms of mania include "high" or irritable mood, very high self-esteem, decreased need for sleep, pressure to keep talking, racing thoughts, being easily distracted, frequently involved in activities with a large risk for bad consequences (for example, excessive buying sprees). Dextromethorphan/bupropion is not approved for the treatment of bipolar depression.

Medical attention should be sought if serotonin syndrome is suspected. Please refer to serious side effects section for signs/symptoms.

Are there specific concerns about dextromethorphan/bupropion and pregnancy?

Dextromethorphan/bupropion should be discontinued during pregnancy due to potential risk to the fetus.

However, if you are planning on becoming pregnant, notify your health care provider to best manage your medications. People living with MDD who wish to become pregnant face important decisions. Untreated MDD has risks to the fetus, as well as the mother. It is important to discuss the risks and benefits of treatment with your doctor and caregivers.

Breastfeeding is not recommended during treatment with dextromethorphan/bupropion and for five days following the final dose.

What should I discuss with my health care provider before taking dextromethorphan/bupropion?

- Symptoms of your condition that bother you the most
- If you have thoughts of suicide or harming yourself
- Medications you have taken in the past for your condition, whether they were effective or caused any adverse effects
- If you experience side effects from your medications, discuss them with your provider. Some side effects may pass with time, but others may require an adjustment in the medication.
- Any other psychiatric or medical problems you have, including a history of seizure, bulimia, anorexia nervosa, bipolar disorder, or kidney or liver problems.
- All other medications you are currently taking and any medication allergies you have. This will help your prescriber assess for potential drug interactions.
- Other non-medication treatment you are receiving, such as talk therapy or substance abuse treatment. Your provider can explain how these different treatments work with the medication.
- If you are pregnant, plan to become pregnant, or are breastfeeding
- If you drink alcohol or use drugs

How should I take dextromethorphan/bupropion?

Dextromethorphan hydrobromide/bupropion hydrochloride is available as an extended release, combination tablet.

Dextromethorphan/bupropion should be taken once daily in the morning for the first 3 days of therapy; thereafter, it should be taken twice daily (with each dose given at least 8 hours).

The typical dosing range is one tablet once or twice daily based on your kidney function. Only your health care provider can determine the correct dose for you.

Dextromethorphan/bupropion can be taken with or without food and should be swallowed whole – not chewed, crushed, or broken so that the medication can work correctly in your body and to reduce the risk of serious side effects.

You should not take more than one product that contains bupropion, including the products that are used to quit smoking. Do not take more than your prescribed dose since higher doses may increase your risk of having a seizure. Since quickly increasing the dose of bupropion can cause seizures in some people, your doctor will slowly increase your dose.

You should not take more than one product that contains dextromethorphan, including cough suppressants. Taking more than the prescribed dose can increase your risk of overdose.

Consider using a calendar, pillbox, alarm clock, or cell phone alert to help you remember to take your medication. You may also ask a family member or friend to remind you or check in with you to be sure you are taking your medication.

What happens if I miss a dose of dextromethorphan/bupropion?

If you miss a dose of dextromethorphan/bupropion, do not take an extra dose to make up for the dose that you missed. Wait and take your next dose at the regular time. Do not double your dose or take more than what is prescribed.

Do not take more than one dose of dextromethorphan/bupropion at a time.

Do not take more than two tablets within 24 hours.

What should I avoid while taking dextromethorphan/bupropion?

Avoid drinking alcohol or using illegal drugs while you are taking dextromethorphan/bupropion because the beneficial effects of the medication may be decreased, and the risk of seizures and mental health side effects may be increased. Dextromethorphan/bupropion can make you more sensitive to the effects of alcohol. If you are dependent on drugs or alcohol and would like to stop, consult your health care provider for help. Abruptly stopping these substances can result in a seizure, especially when taking bupropion.

Do not drive a car or use heavy machinery until you know how dextromethorphan/bupropion affects you as it can impair your ability to do these things safely.

What happens if I overdose with dextromethorphan/bupropion?

If an overdose occurs, call your doctor or 911. You may need urgent medical care. You may also contact the poison control center at 1-800-222-1222.

A specific treatment to reverse the effects of bupropion or dextromethorphan does not exist.

What are the possible side effects of dextromethorphan/bupropion?

Common side effects

Dizziness, diarrhea, dry mouth, excessive sweating, headache, feeling sleepy, and sexual function problems are possible side effects. These may improve over the first week or two as you continue to take the medication.

Rare/serious side effects

Rare side effects that some patients may experience are thought disturbances, seizure, anxiety, constipation, decreased appetite, insomnia, joint pain, fatigue, tingling of hands or feet, blurry vision, high blood pressure, serotonin syndrome (symptoms may include shivering, diarrhea, confusion, severe muscle tightness, fever, seizures, and death), or angle closure glaucoma (symptoms of angle closure glaucoma may include eye pain, changes in vision, swelling or redness in or around eye).

In general, the risk of seizures due to bupropion is low. The risk of having a seizure increases with higher than recommended doses of bupropion, a history of seizures or head injury, brain tumor, severe liver disease, an eating disorder, alcohol or drug dependence, or taking other drugs that can also increase your risk of having a seizure.

There is a low risk of cardiovascular side events associated with stimulating agents, including bupropion. However, when given with dextromethorphan, there is also a risk of elevated blood pressure. This risk increases if you have heart disease, high blood pressure at baseline, previous heart attack, irregular heartbeat, or when used with nicotine patches and certain other mental health medications. In these cases, a thorough cardiovascular evaluation is recommended before starting this medicine and blood pressure should be assessed periodically during treatment.

Are there any risks for taking dextromethorphan/bupropion for long periods of time?

To date, there are no known problems associated with long term use of dextromethorphan/bupropion. It is a safe and effective medication when used as directed.

What other medications may interact with dextromethorphan/bupropion?

Bupropion should not be taken with or within two weeks of taking monoamine oxidase inhibitors (MAOIs). These include phenelzine (Nardil®), tranylcypromine (Parnate®), isocarboxazid (Marplan®), rasagiline (Azilect®), and selegiline (Emsam®).

There are several products with the active ingredient bupropion. Do not take more than one product that contains bupropion since this may increase your risk of having a seizure and other side effects.

There are several products with the active ingredient dextromethorphan. Do not take more than one product that contains dextromethorphan since this may increase your risk of high blood pressure and other side effects.

Certain medications may increase your risk of having a seizure when combined with dextromethorphan/bupropion. These include tricyclic antidepressants, antipsychotics, theophylline, isoniazid, tramadol, stimulants, steroids, hypoglycemic agents (including insulin), certain antibiotics (e.g., Cipro®), and abrupt discontinuation of benzodiazepines (e.g., Ativan®).

There is an increased risk of central nervous system (brain and spinal cord) side effects when bupropion is taken with other medications that increase dopamine, including amantadine (Osmolex ER®, Gocovri®) and levodopa (Sinemet®, Rytary®). These side effects include feeling restless, agitation, tremor, dizziness, vertigo, abnormal walking, and poor balance and coordination.

Although rare, there is an increased risk of serotonin syndrome when dextromethorphan/bupropion is used with other medications that increase serotonin. Examples include other antidepressants, methadone, the antibiotic linezolid (Zyvox®), ondansetron (Zofran®), amphetamines, some pain medications (e.g., tramadol), and some migraine medications called “triptans” (e.g., Imitrex®).

The following medications may **increase** the levels and effects of dextromethorphan/bupropion: paroxetine (Paxil®), fluoxetine (Prozac®)

The following medications may **decrease** the effects of dextromethorphan/bupropion: carbamazepine (Tegretol®, Equetro®), phenytoin (Dilantin®), phenobarbital, ritonavir (Norvir®), lopinavir (Kaletra™), and efavirenz (Sustiva®).

Dextromethorphan/bupropion may **increase** levels and effects of aripiprazole (Abilify®), atomoxetine (Strattera®), brexpiprazole (Rexulti®), deutetrabenazine (Austedo®), doxorubicin (Adriamycin®), fenfluramine (Fintepla®), metoclopramide (Reglan®), pimoside, pitolisant (Wakix®), risperidone (Risperdal®), sofipirionium (Sofdra®), valbenazine (Ingrezza®), and vortioxetine (Trintellix®).

Dextromethorphan/bupropion may **decrease** the effects of tamoxifen and digoxin.

How long does it take for dextromethorphan/bupropion to work?

Dextromethorphan/bupropion is a rapid acting medication with improvement in symptoms seen after taking the medication for one week. This benefit is sustained with continued use.

Summary of Black Box Warnings

Suicidal Thoughts and Behaviors in Children and Young Adults

Depression and certain other psychiatric disorders are themselves associated with increases in the risk of suicide. Patients with MDD, both adult and pediatric, may experience worsening of their depression and/or the emergence of suicidal ideation and behavior (suicidality) or unusual changes in behavior, whether or not they are taking antidepressant medications. This risk may persist until significant remission occurs.

In short-term studies, antidepressants increased the risk of suicidality in children, adolescents and young adults when compared to placebo. Short-term studies did not show an increase in the risk of suicidality with antidepressants compared to placebo in adults beyond age 24. Adults ages 65 and older taking antidepressants have a decreased risk of suicidality. Patients, their families and caregivers should be alert to the emergence of anxiety, restlessness, irritability, aggressiveness and insomnia. If these symptoms emerge, they should be reported to the patient's prescriber or health care professional. All patients being treated with antidepressants for any indication should watch for and notify their health care provider for worsening symptoms, suicidality and unusual changes in behavior, especially during the first few months of treatment.

Important Disclosure: This information is being provided as a community outreach effort of the American Association of Psychiatric Pharmacists. This information is for educational and informational purposes only and is not medical advice. This information contains a summary of important points and is not an exhaustive review of information about the topic. Always seek the advice of a physician or other qualified medical professional with any questions you may have regarding medications or medical conditions. Never delay seeking professional medical advice or disregard medical professional advice as a result of any information provided herein. The American Association of Psychiatric Pharmacists disclaims any and all liability alleged as a result of the information provided herein.