
DEXTROMETHORPHAN/BUPROPION (Auvelity) Fact Sheet

Bottom Line:

May provide faster onset of response and may be helpful in treatment-resistant patients; however, the evidence is too limited to endorse these preliminary findings. Risk of misuse and very high cost further limit its use.

FDA Indications:

Major depression.

Off-Label Uses:

None.

Dosage Forms:

ER tablets: 45/105 mg.

Dosage Guidance:

Start one tablet QAM, may ↑ to one tablet BID after three days; max two tablets per day with doses separated by at least eight hours.

Monitoring: No routine monitoring recommended unless clinical picture warrants.

Cost: \$\$\$\$

Side Effects:

- Most common: Dizziness, headache, diarrhea, somnolence, dry mouth, sexual dysfunction, nausea, excessive sweating.
- Serious but rare: Seizures; risk higher with rapid and large dose increases and in patients at risk for seizures, including those with a seizure history and patients with eating disorders (mainly those with purging-type bulimia). Do not chew, divide, or crush ER tablets as risk of seizures may be increased.
- Pregnancy/breastfeeding: Data for each medication used individually support safety; no data on combination.

Mechanism, Pharmacokinetics, and Drug Interactions:

- Dextromethorphan (DXM) is an NMDA receptor antagonist and sigma-1 receptor agonist; bupropion is a dopamine and norepinephrine receptor uptake inhibitor. Bupropion increases DXM levels via CYP2D6 inhibition.
- Metabolized primarily through CYP2D6 (DXM) and CYP2B6 (bupropion); bupropion inhibits CYP2D6; $t_{1/2}$: 22 hours.
- Avoid use with MAOIs and other products containing DXM or bupropion.

Clinical Pearls:

- Combines two older medications: DXM (approved 1958) and bupropion (approved 1985). By adding a CYP2D6 inhibitor (bupropion), DXM's half-life is increased from four hours to 22 hours.
- DXM provides a glutamatergic mechanism of action (via NMDA antagonism), similar to ketamine and esketamine.
- Onset of response separated from placebo at week one compared to the usual two to four weeks in other antidepressant studies.
- Before prescribing, ask patients if they've ever had a seizure or if they've had bulimia—both of which are relative contraindications.
- Bupropion can cause false-positive urine test results for amphetamines.

Fun Fact:

Another FDA-approved DXM combination medication is Nuedexta, which uses quinidine to similarly increase DXM levels; it is used to treat pseudobulbar affect.