Wellbutrin XL

(bupropion hydrochloride)

Wellbutrin XL (bupropion hydrochloride); not controlled

Full Prescribing Information	DailyMed Drug Information

Summary

Wellbutrin XL is an aminoketone antidepressant supplied as a once-daily extended-release tablet, approved for major depressive disorder and for prevention of seasonal affective disorder in adults. It has no pediatric indication at any age, so every use in a child or adolescent is off-label. Among antidepressants it is distinctive for no serotonergic action and no sexual dysfunction or weight gain, at the cost of a dose-related seizure risk. Not controlled; brand and generic.

Forms & Strengths

- **Extended-release (XL) tablets:** 150 mg, 300 mg, the only two XL strengths
- **Sustained-release (SR) tablets:** 100 mg, 150 mg, 200 mg, dosed twice daily
- **Immediate-release tablets:** 75 mg, 100 mg, dosed three times daily
- **Separate NDAs:** Forfivo XL 450 mg; Aplenzin (hydrobromide) 174 mg, 348 mg, 522 mg
- **Combination products:** dextromethorphan-bupropion (Auvelity); naltrexone-bupropion (Contrave)

Dosing

- **Age:** adults only. No pediatric indication at any age and no pediatric ADHD indication at any age; any use in a young person is off-label.
- **Onset:** 1 to 2 weeks for early effect; 4 to 6 weeks for full response
- **Duration:** continuous with once-daily dosing; bupropion half-life 21 hours, hydroxybupropion about 20 hours

- **Release Profile:** once-daily matrix tablet, bioequivalent over 24 hours to immediate-release 100 mg three times daily
- **Initial Dose:** 150 mg once daily, for both approved indications
- **Titration:**
  - Major depressive disorder: may increase to 300 mg once daily after 4 days
  - Seasonal affective disorder: may increase to 300 mg once daily after 1 week
  - Increase gradually; abrupt escalation raises the seizure risk
- **Max Dose:** 300 mg/day. The 450 mg ceiling belongs to Forfivo XL, a different product
- **Considerations:** Moderate to severe hepatic impairment caps the dose at 150 mg every other day; mild impairment or GFR under 90 mL/min needs a reduced dose or frequency.

Pharmacology

- **Mechanism:** norepinephrine-dopamine reuptake inhibitor; no serotonin reuptake or monoamine oxidase inhibition
- **Metabolism:** CYP2B6 to hydroxybupropion, the principal active metabolite. Renal excretion of metabolites means impairment causes accumulation
- **Class Positioning:** chosen for the absent serotonergic action: no sexual dysfunction, appetite suppression rather than weight gain. Approved non-stimulant alternatives are Strattera and Qelbree

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Indications

- **Major Depressive Disorder** (ICD-10: F32.x, F33.x): adults only
- **Seasonal Affective Disorder, prevention** (ICD-10: F33.x seasonal pattern): adults only. Start in autumn, continue through winter
- **No pediatric indication at any age,** and specifically no pediatric ADHD indication

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Off-Label Uses

- **ADHD in children and adolescents** (ICD-10: F90.x): limited data. Second-line where a stimulant is not tolerated and depression coexists.
  - The label carries no ADHD indication and no ADHD trial.
  - AHRQ found medication improves ADHD symptoms overall but graded no bupropion-specific pediatric evidence. (AHRQ 2024)
  - Weigh the seizure risk against the two approved non-stimulants first.
- **Pediatric major depressive disorder** (ICD-10: F32.x, F33.x): insufficient; the adult indication does not extend downward.

- **Adolescent smoking or vaping cessation** (ICD-10: F17.2x): insufficient. The label's neuropsychiatric warning applies at any age.
- **Any use in a patient with an eating disorder** (ICD-10: F50.x): contraindicated, not merely unsupported.

Contraindications & Warnings

- **Boxed Warning:** SUICIDAL THOUGHTS AND BEHAVIORS. Antidepressants increased suicidal thinking and behaviour in children, adolescents and young adults. Monitor for worsening and emergent suicidality, including in off-label pediatric use.
- **Contraindicated:**
  - Seizure disorder.
  - Current or prior bulimia or anorexia nervosa; absolute, and easily missed in an adolescent.
  - Abrupt discontinuation of alcohol, benzodiazepines, barbiturates or antiepileptics; withdrawal lowers the seizure threshold.
  - Concomitant MAOI, or use within 14 days of stopping one; initiation on linezolid or intravenous methylene blue.
  - Known hypersensitivity to bupropion or any other ingredient.
- **Use with caution:**
  - Conditions lowering the seizure threshold: severe head injury, arteriovenous malformation, CNS tumour or infection, stroke, hypoglycemia, hyponatremia, hypoxia.
  - Never co-prescribe two bupropion products, and see Drug Interactions for other threshold-lowering drugs.
  - Insulin- or oral-hypoglycemic-treated diabetes, and anorectic drugs; both predispose to seizure.
  - Pre-existing hypertension, because bupropion raises blood pressure.
  - Bipolar disorder or risk factors: activation of mania or hypomania.
  - Untreated anatomically narrow angles: angle-closure glaucoma.
  - Renal impairment below GFR 90 mL/min; active metabolites accumulate.
- **Screen before starting:**
  - Seizure and head injury history, and any eating disorder. Ask the adolescent alone; bulimia is rarely volunteered.
  - Current alcohol, benzodiazepine or antiepileptic use, and any plan to stop.
  - Personal and family history of bipolar disorder or mania.
  - Blood pressure, measured before initiation.
  - Medication list for MAOIs, other bupropion products, seizure-threshold drugs.
  - Hepatic and renal function where impairment is plausible; both change the dose.

Drug Interactions

- **MAOIs** (phenelzine, tranylcypromine, linezolid, intravenous methylene blue): hypertensive reactions. Contraindicated; allow 14 days in either direction.
- **CYP2D6 substrates** (venlafaxine, nortriptyline, paroxetine, fluoxetine, risperidone, metoprolol, flecainide, atomoxetine): bupropion raises exposure. Reduce the substrate dose.
- **CYP2B6 inducers** (ritonavir, efavirenz, carbamazepine, phenytoin): exposure falls. An increase may be needed, never above 300 mg/day.
- **CYP2B6 inhibitors** (ticlopidine, clopidogrel): bupropion exposure rises 38% to 85%. Adjust on clinical response.
- **Seizure-threshold drugs** (other bupropion products, antipsychotics, tricyclics, theophylline, corticosteroids, tramadol): additive risk. Avoid, or hold at 150 mg/day.
- **Levodopa and amantadine:** CNS toxicity. Use lower doses.
- **Urine drug screens:** false-positive for amphetamines. Confirm before treating a positive as diversion of a prescribed amphetamine (Adderall).

Administration

- Give once daily in the morning to limit early insomnia.
- Swallow whole; breaking the matrix converts a daily dose into an immediate-release bolus.
- An intact tablet shell in the stool is expected, not a missed dose.
- Never escalate faster than the label allows: 4 days to 300 mg for depression, 1 week for SAD.
- Switching from immediate-release or SR: same total daily dose as one XL dose; confirm the product.
- For seasonal affective disorder, start in autumn, continue through winter, taper in early spring.
- Do not stop abruptly from 300 mg. See Discontinuation & Taper.

Side Effects

- **Common** (at least 5% and twice placebo): dry mouth, nausea, insomnia, dizziness, abdominal pain, agitation, anxiety, tremor, palpitation, sweating, anorexia, rash
- **Serious:**
  - Suicidal thoughts and behaviour: the boxed warning.
  - Seizure, dose-related: about 0.1% up to 300 mg/day sustained-release, about 0.4% at 300 to 450 mg/day immediate-release. Discontinue permanently.
  - Serious neuropsychiatric events during smoking cessation: depression, mania, psychosis, hallucinations, aggression, agitation, panic.
  - Hypertension.
  - Activation of mania or hypomania: stop and reassess the diagnosis.

    - Angle-closure glaucoma: sudden eye pain, redness or visual change needs same-day ophthalmology.
    - Hypersensitivity, including serum-sickness-like reactions.

Monitoring & Labs

- **Suicidality:** weekly for 4 weeks, every visit through 3 months, every dose change, then each routine visit.
- **Blood pressure:** baseline, 4 weeks, every dose change, then every 3 months.
- **Seizure risk review:** at every dose increase and at least every 6 months. Re-ask about threshold-lowering drugs, alcohol or benzodiazepine use, and disordered eating.
- **Weight and appetite:** baseline and every 3 months. Unexplained loss prompts a direct question about disordered eating.
- **Psychiatric:** ask about mania, agitation, anxiety and insomnia each visit during titration, then every 3 months.
- **Renal and hepatic function:** no routine schedule; recheck when circumstances change.
- **Urine drug screens:** confirm any positive amphetamine result rather than acting on the immunoassay.

Discontinuation & Taper

- Taper before stopping: from 300 mg once daily, decrease to 150 mg once daily before discontinuation.
- Discontinue permanently and never restart if a seizure occurs.
- Stop and seek review for serious neuropsychiatric symptoms.
- Drug holidays are not appropriate; the effect depends on continuous exposure.
- For seasonal affective disorder, taper in early spring rather than continuing year-round.

Pregnancy & Lactation

- **Pregnancy:** first-trimester studies show no increased risk of congenital malformations overall.
    - Registry cardiovascular malformation rate 1.3% against a roughly 1% background; cardiac findings are inconsistent.
    - Background risk is 2 to 4% for birth defects, 15 to 20% for miscarriage; weigh continuation against relapse.
- **Lactation:** maternal doses up to 300 mg daily give low milk levels. Case reports describe possible seizure in partially breastfed 6-month-olds; prefer another agent for a newborn. (LactMed 2026)

- **Exposure Registry:** National Pregnancy Registry for Antidepressants, 1-844-405-6185, womensmentalhealth.org

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Counseling Points

- **Counsel the family on:**
  - This being an adult medication used off-label, with no pediatric dose ladder.
  - Never taking two bupropion products; the drug is sold under several brands.
  - Swallowing the tablet whole; an empty shell in the stool is normal.
  - Insomnia and jitteriness in the first weeks, fixed by morning dosing.
  - Telling any clinician ordering a urine drug test, because it reads as amphetamine.
  - Stepping the dose down before stopping rather than stopping outright.
- **Advise them to call for:**
  - Any seizure, including a staring spell or single whole-body jerk; stop and call the same day.
  - New or worsening talk of self-harm, or a sudden mood change.
  - A burst of high energy, reduced need for sleep, or racing speech.
  - Hearing or seeing things that are not there, or new suspiciousness.
  - Sudden eye pain, redness or blurred vision.
  - Rash, hives, facial or tongue swelling, or joint pains with fever.
  - Any plan to stop alcohol, a benzodiazepine, or a seizure medicine abruptly.

References

1. DailyMed. Wellbutrin XL (bupropion hydrochloride extended-release tablets) prescribing information. 2025. https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=a435da9d-f6e8-4ddc-897d-8cd2bf777b21
2. LactMed. Bupropion. Drugs and Lactation Database, National Institute of Child Health and Human Development. 2026. https://www.ncbi.nlm.nih.gov/books/NBK501184/
3. AHRQ. ADHD diagnosis and treatment in children and adolescents. Comparative Effectiveness Review No. 267. 2024. https://www.ncbi.nlm.nih.gov/books/NBK603001/
4. FDA. National Drug Code Directory, openFDA. Queried by generic name bupropion. 2026. https://api.fda.gov/drug/ndc.json?search=generic_name:%22bupropion%22&limit=1000

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