

OLANZAPINE (Lybalvi, Symbyax, Zyprexa) Fact Sheet [G]

Bottom Line:

Many consider olanzapine to be more effective than other antipsychotics and just below clozapine in effectiveness. Its high efficacy along with its once-daily dosing and low risk of QT interval prolongation are appealing. However, olanzapine's high risk for weight gain and metabolic complications make it a second-line choice for many. The newly approved Lybalvi combines olanzapine with samidorphan to minimize weight gain—but it's only moderately successful.

FDA Indications:

Schizophrenia (adults and children ≥ 13 years); **acute or mixed bipolar I manic episodes**, as monotherapy or adjunct (adults and children ≥ 13 years); **maintenance treatment of bipolar disorder; bipolar I depression** (with fluoxetine, sold as Symbyax, adults and children ≥ 10 years); **treatment-resistant unipolar depression** (with fluoxetine); **acute agitation** in schizophrenia and bipolar mania (injectable form).

Off-Label Uses:

Behavioral disturbances; impulse control disorders; reduced weight gain in patients on olanzapine (as Lybalvi).

Dosage Forms:

- **Tablets (G):** 2.5 mg, 5 mg, 7.5 mg, 10 mg, 15 mg, 20 mg.
- **Orally disintegrating tablets (Zyprexa Zydis, [G]):** 5 mg, 10 mg, 15 mg, 20 mg.
- **IM injection (G):** 10 mg.
- **Long-acting injection (Zyprexa Relprevv):** 210 mg, 300 mg, 405 mg (see LAI fact sheet and table).
- **Fixed-combination capsules with fluoxetine (Symbyax, [G]):** 3/25 mg, 6/25 mg, 12/25 mg, 6/50 mg, 12/50 mg olanzapine/fluoxetine.
- **Fixed-combination tablets with samidorphan (Lybalvi):** 5/10 mg, 10/10 mg, 15/10 mg, 20/10 mg olanzapine/samidorphan.

Dosage Guidance:

- Schizophrenia, bipolar disorder, depression (adults): Start most patients at 5–10 mg QD; may \uparrow by 5 mg QD, in weekly increments, to target dose 10–20 mg QD.
- Acute mania (adults): Start 10–15 mg QD; may \uparrow by 5 mg daily, in 24-hour increments, to target dose 10–20 mg QD.
- Max approved dose: 20 mg/day, although doses 30–50 mg/day have been used.
- For Lybalvi: Dose as above, using Lybalvi dose with equivalent olanzapine component. Do not divide or combine Lybalvi strengths.
- Bipolar depression (Symbyax, adults): Start 6/25 mg QPM, \uparrow as indicated to target dose 6–12/25–50 mg olanzapine/fluoxetine.
- IM for agitation: Usual dose of 2.5–10 mg IM; maximum dose of 30 mg/day. Avoid concomitant use with IM benzodiazepines because of potential for excessive sedation and cardiorespiratory depression.
- Long-acting injection: See LAI fact sheet and table.

Monitoring: Fasting glucose, lipids.

Cost: \$; combination with fluoxetine: \$\$; Lybalvi: \$\$\$\$

Side Effects:

- Most common: Somnolence (dose related), dry mouth (dose related), constipation, weight gain (up to 40% incidence; may be substantial), increased appetite, EPS (dose related).
- Serious but rare: Rare but potentially fatal drug reaction with eosinophilia and systemic symptoms (DRESS) possible; often starts as rash that may spread, fever, swollen lymph nodes, and elevated eosinophils.
- Pregnancy/breastfeeding: Considered relatively safe.

Mechanism, Pharmacokinetics, and Drug Interactions:

- Dopamine D2 and serotonin 5-HT_{2A} receptor antagonist.
- Metabolized primarily by CYP1A2, also CYP2D6 (minor), and direct glucuronidation; $t_{1/2}$: 1–2 days.
- CYP1A2 inducers (eg, carbamazepine, ritonavir, smoking) may reduce olanzapine levels by 50%; CYP1A2 inhibitors (eg, fluvoxamine) may increase olanzapine bioavailability by 50%–100%. Adjust olanzapine dosing in presence of 1A2 inducers or inhibitors.

Clinical Pearls:

- Use in children and adolescents may result in increased weight gain and sedation, as well as greater increases in LDL cholesterol, total cholesterol, triglycerides, prolactin, and liver transaminase levels when compared to adults.
- Newly approved combination with opioid antagonist samidorphan reduces risk of weight gain, but patients are still at moderate risk. In a 24-week study, 17.8% experienced $\geq 10\%$ weight gain (vs 29.8% on olanzapine alone) and 27.5% experienced $\geq 7\%$ weight gain (vs 42.7% on olanzapine alone).
- Avoid using samidorphan combination product in patients taking opioids who may experience withdrawal effects or inadvertently take a high dose of opioid in order to overcome samidorphan's opioid receptor blockade, leading to increased risk for overdose.

Fun Fact:

Olanzapine has been studied and is used for chemotherapy-induced nausea and vomiting.