
LOXAPINE (Adasuve, Loxitane) Fact Sheet [G]

Bottom Line:

Loxapine is being rediscovered as a well-tolerated first-generation antipsychotic—it is of medium potency, and causes minimal EPS or weight gain. An oldy-but-goody alternative to second-generation antipsychotics.

FDA Indications:

Schizophrenia; acute agitation associated with schizophrenia or acute bipolar mania.

Off-Label Uses:

Bipolar disorder; behavioral disturbances; impulse control disorders.

Dosage Forms:

- **Capsules (G):** 5 mg, 10 mg, 25 mg, 50 mg.
- **Single-use disposable inhaler (Adasuve),** for acute agitation: 10 mg as inhalation powder.

Dosage Guidance:

- Schizophrenia: Start 10 mg BID; ↑ by 10 mg/day increments weekly and adjust to lowest effective dose. Dose range 60–100 mg divided BID–TID; max FDA-approved dose is 250 mg/day, but doses >100 mg/day rarely used.
- Acute agitation (oral inhalation): Give one puff every 24 hours as needed (must be given by health care professional).

Monitoring: No routine monitoring recommended unless clinical picture warrants.

Cost: Capsule: \$; inhalation: \$\$\$

Side Effects:

- Most common: EPS, headache, drowsiness, dry mouth, prolactin elevation (sexual side effects, amenorrhea, galactorrhea), throat irritation (Adasuve).
- Serious but rare: See class warnings in chapter introduction.
- Pregnancy/breastfeeding: Not enough data to recommend.

Mechanism, Pharmacokinetics, and Drug Interactions:

- Dopamine D2 and serotonin 5-HT2A receptor antagonist.
- Metabolized primarily by CYP2D6 and CYP3A4; $t_{1/2}$: 4–8 hours.
- Caution with inhibitors of CYP2D6 and CYP3A4 and inducers of CYP3A4; adjust dose.

Clinical Pearls:

- Loxapine is an intermediate-potency first-generation antipsychotic; this leads to less EPS compared to high-potency agents (eg, fluphenazine, haloperidol) and to less sedation, less orthostasis, and fewer anticholinergic side effects compared to low-potency agents (eg, chlorpromazine).
- Loxapine belongs to the dibenzoxazepine class of antipsychotics and is structurally related to clozapine (which belongs to the chemically akin class of dibenzodiazepines). Some have argued that loxapine may behave as a second-generation antipsychotic.
- The relatively newer Adasuve oral inhalation version has the advantage of treating agitation quickly without the need for swallowing or a shot. But the risks of bronchospasm and respiratory arrest, along with the contraindication in patients with asthma, COPD, or other lung disease, make this formulation rather unappealing overall.

Fun Fact:

Loxapine is metabolized to the tetracyclic antidepressant amoxapine.