
METFORMIN (Glucophage, Glumetza, Riomet) Fact Sheet [G]

Bottom Line:

Metformin is a medication for type 2 diabetes that increases insulin sensitivity and decreases appetite. It's somewhat effective for antipsychotic-induced weight gain (average of 3 kg weight loss) and might work better if started prophylactically as a way to prevent excessive weight gain in the first place. It's quite safe and well tolerated (with some GI side effects) and is becoming a standard add-on treatment in patients taking clozapine or olanzapine.

FDA Indications:

Diabetes mellitus, type 2.

Off-Label Uses:

Antipsychotic-induced weight gain; polycystic ovary syndrome; prediabetes; female infertility.

Dosage Forms:

- **Tablets (G):** 500 mg, 850 mg, 1000 mg.
- **ER tablets (Glucophage XR, Glumetza, [G]):** 500 mg, 750 mg, 1000 mg.
- **Oral solution (Riomet, [G]):** 500 mg/5 mL.

Dosage Guidance:

- IR: Start 500 mg BID, ↑ by 500 mg/day increments weekly; max 2250 mg/day.
- ER: Start 500 mg QPM, ↑ by 500 mg/day increments weekly; max 2000 mg/day.
- ER formulation is preferred because it minimizes GI side effects. Better tolerated with taken with meals.

Monitoring: No routine monitoring recommended unless clinical picture warrants.

Cost: \$; liquid: \$\$\$

Side Effects:

- Most common: Diarrhea; nausea; abdominal bloating, flatulence, and discomfort.
- Serious but rare: Rare cases of lactic acidosis reported.

Mechanism, Pharmacokinetics, and Drug Interactions:

- Decreases glucose production by liver and increases insulin sensitivity.
- Not metabolized; excreted primarily through kidneys; t_{1/2}: 4–9 hours.
- Minimal clinically significant drug interactions.

Clinical Pearls:

- In psychiatry, metformin is used primarily to prevent or reverse weight gain in patients taking certain antipsychotic medications. The best-studied and most widely used dose is 500–1000 mg BID, which typically produces an average of 3 kg of weight loss in patients.
- A meta-analysis of 12 studies, representing a total of 743 patients, found metformin use resulted in more weight loss (an average of about 7 lbs) and BMI reduction than placebo in patients taking antipsychotics (de Silva VA et al, *BMC Psychiatry* 2016;16:341).
- Another review of patients with schizophrenia who were treated with antipsychotics found metformin also improved insulin resistance and decreased lipids (Mizuno Y et al, *Schiz Bull* 2014;40(6):1385–1403).
- Taking with food or using XR formulation helps to minimize the nausea and diarrhea that occurs in up to 50% of patients.
- Adjust dose in patients with eGFR less than 60 mL/minute (see Appendix H for guidance).

Fun Fact:

Metformin was introduced in the US in 1995, but it's been used in France since 1957.