

# Consider Rx metformin to prevent metabolic syndrome

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Many atypical antipsychotics, particularly clozapine and olanzapine, are associated with weight gain, insulin resistance, and metabolic syndrome. Metabolic syndrome is associated with type 2 diabetes mellitus (T2DM) and cardiovascular disease, which are among the leading causes of morbidity and mortality in persons with severe mental illness.<sup>1</sup>

Clinicians should take measures to prevent T2DM and weight gain in individuals taking antipsychotics *before* these conditions develop. Metformin re-sensitizes the body to insulin and is a first-line treatment for T2DM. Adding metformin when patients start metabolically high-risk antipsychotics or shortly after they begin gaining weight is an evidence-based strategy to prevent metabolic syndrome.

## Evaluate the evidence

In randomized controlled trials, metformin was associated with modest weight loss and improvement in metabolic parameters (eg, fasting blood glucose, serum triglycerides, and total cholesterol) in patients with schizophrenia receiving antipsychotics.<sup>1,2</sup> Metformin is effective for preventing metabolic syndrome and as a treatment intervention; therefore, it may prove most beneficial early in treatment before weight gain or insulin resistance develop.

Importantly, weight gain and metabolic syndrome are risk factors for cardiovascular disease, but the number needed to treat for metformin to prevent cardiovascular outcomes, such as myocardial infarction, is not known. Also, metformin is not FDA-approved for this indication. Clinicians should discuss with the patient

the risks and benefits of prophylactic metformin, and consider his (her) treatment preferences.

## Tolerability and adverse effects

Metformin generally is well-tolerated. Gastrointestinal (GI) symptoms, including nausea and vomiting (14%) and diarrhea (7%), are the most common adverse effects.<sup>2</sup> Lactic acidosis is rare and is associated with alcohol use disorders and impaired renal, hepatic, or cardiopulmonary function.<sup>3</sup> Because metformin is excreted renally, toxicity could occur in patients with impaired renal function.

Before initiating prophylactic metformin, confirm that the patient does not have T2DM (eg, hemoglobin A<sub>1c</sub> <6.5%). A thorough medical history, including alcohol use and kidney and liver function tests, are needed to reduce the risk of lactic acidosis.<sup>3</sup>

## Dosing

Although metformin has been studied at many dosages,<sup>2</sup> we recommend gradual titration to 1,000 mg, twice daily, taken with meals to reduce the risk of GI effects.

continued

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### Disclosures

The authors report no financial relationships with any company whose products are mentioned in this article or with manufacturers of competing products.

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**Metformin is associated with weight loss and improvement in metabolic parameters in persons with schizophrenia**

### Additional interventions

Metformin alone is not sufficient to mitigate metabolic risk. Providers should address dietary interventions, exercise, and smoking cessation at each visit, and communicate actively with other providers to create a comprehensive treatment plan.

### References

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