



Clozapine: Managing Constipation and GI Hypomotility Updated June 2025 (supersedes May 2015 version)

Clozapine is the preferred medication choice for treatment-resistant schizophrenia.

We know from growing experience that **constipation** is an under-recognized potential side effect of clozapine that occurs in about 30% of treated patients. Untreated constipation can be associated with **serious medical complications**, including fecal impaction, bowel obstruction and perforation, paralytic ileus, megacolon, gastrointestinal ischemia, acute abdomen, and even death. **Patients at elevated risk** for constipation include patients on opiates or medications with anticholinergic activity, including clozapine; patients with poor hydration; and those who are sedentary and on low-fiber diets.

Clozapine is responsible for the highest rate of mortality stemming from constipation complications among patients treated with antipsychotics. This rate is more than three times the rate of mortality from medication-induced agranulocytosis. Thus, all clinical staff should be aware of this association and actively screen, monitor and provide early intervention for constipation.

Approaches for preventing, monitoring and treating constipation and gastrointestinal (GI) hypomotility associated with clozapine include:

- **Screen** patients regularly for constipation and monitor GI hypomotility, not only during initial treatment but also during the continuation treatment.
- Employ **Prevention**, which includes asking patients about and encouraging adequate hydration, a high-fiber diet, and increasing levels of physical activity. Discontinue unnecessary anticholinergic medications.
- **Treat** assertively and start routinely with docusate for most patients. The next agent will be an osmotic laxative, such as polyethylene glycol 3350 (Miralax). If these agents are not successful, add a stimulant laxative, such as bisacodyl or senna. Importantly, avoid bulk forming agents.
- Develop and implement a plan for **ongoing individualized monitoring** of patients with a known history of constipation.