

Prescribing information and adverse event reporting can be found on the back page.

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QUICK GUIDE

Why opioid-induced constipation should be managed differently

Opioid analgesics are dispensed to approximately 13% of the population each year.¹ While national and local initiatives aim to reduce opioid prescribing, many patients continue to require opioids for pain that is not adequately controlled with non-opioid analgesics.¹ This includes not only acute pain but also chronic pain associated with conditions such as cancer, neurodegenerative diseases, and musculoskeletal disorders, among other causes.² Opioid-induced constipation (OIC) is a common but under-treated complication,³ with factors such as challenges in patient-healthcare professional (HCP) communication and a lack of standardised protocols hindering diagnosis and treatment.³ However, OIC is treatable: it does not have to be accepted by patients as an inevitable side effect of opioids. This article provides key information on the assessment and treatment of OIC in primary care.

Pathophysiology of OIC

Opioids alleviate pain by binding to opioid receptors throughout the central nervous system and peripheral nervous system.² However, opioids also act on μ -opioid receptors in the gastrointestinal (GI) tract, reducing motility and increasing

water absorption from the GI tract, therefore causing drier, harder stools.^{2,4} This leads to constipation in approximately 58–83% of patients on opioids, depending on the underlying disease.⁵

Symptoms of OIC

Key symptoms of OIC include fewer spontaneous bowel movements, straining during defaecation, lumpy or hard stools, sensations of incomplete evacuation, and sensations of anorectal blockage/obstruction.³ Other non-specific GI symptoms such as abdominal pain, heartburn, nausea and bloating are common and reflect the pan-enteric effects of opioids.³ Complications if not treated include faecal loading and impaction, progressive faecal retention, distension of the rectum, loss of sensory and motor function, haemorrhoids and anal fissure.⁶

Impacts of OIC

OIC has profound impacts on quality of life and daily functioning.⁷ Some patients reduce or stop opioid therapy due to these impacts. In a large multinational survey including the

Continued overleaf →

UK (N=951), 40% of patients reported reducing their opioid medication to relieve their constipation.⁷

Although opioid therapy should always be optimised to the lowest effective dose,⁸ effective management of OIC can support adherence to prescribed treatments, helping ensure pain management is guided by pain control needs rather than avoidable adverse effects.⁹

Conversations at opioid initiation

A panel of European experts recommends that patients should be informed about the risk of constipation when opioid therapy is started, increased or switched.⁴ However, a multinational survey found only 41% of patients with OIC recalled their HCP warning them about the constipation side effects of opioids, highlighting these conversations are often missed or forgotten.⁷

Experts also recommend that HCPs educate patients on the diverse of symptoms of OIC to enable them to recognise and report constipation.⁴ Information about the risks and symptoms of OIC should be accompanied by advice on diet and lifestyle measures to prevent constipation, such as adequate fibre, fluid intake and physical activity.⁴ However, these are generally not effective in OIC.⁵

Laxatives can be co-prescribed or recommended at the point of opioid initiation.³ However, this is often not successful in preventing OIC. Approximately 40–94% of patients taking laxatives for OIC still experience inadequate symptoms control, with variation reported across studies due to differences in patient populations, study design, laxative use and reporting bias.¹⁰

Evaluating OIC

Effective patient-clinician communication is key to managing OIC.⁴ However, conversations with patients can be challenging, as highlighted in the list of barriers to diagnosing OIC identified by a panel of European experts (Box 1).³

HCPs should ask patients on opioids about constipation and

Box 1 Barriers to diagnosing OIC³

- 1 Patients might feel ashamed to disclose symptoms
- 2 Awareness of OIC varies among HCPs
- 3 Constipation may rarely be discussed during consultations
- 4 Clinical assessment often focuses on bowel movement frequency while other burdensome symptoms may be under-explored (e.g. bloating, straining, hard stools, incomplete bowel movements and abdominal discomfort)
- 5 Assessment tools may not cover the whole spectrum of OIC symptoms
- 6 There is a lack of standardised treatment protocols to support treatment decision-making

other problematic side effects at every consultation.³ This enables pro-active identification of OIC and assessment of whether prophylactic measures, including laxatives if prescribed, are actually working. Importantly, assessing OIC needs to be more than just asking patients about their bowel movements: HCPs should ask about more wide-ranging symptoms and impacts of OIC too.^{3,4}

OIC is differentiated from other forms of constipation by the symptoms appearing or worsening when initiating, changing, or increasing opioid therapy.³ Evaluation of OIC therefore requires a comprehensive history with particular focus on baseline bowel habits and changes that have occurred since initiating, changing, or increasing opioid treatment.³

Multiple factors may contribute to a patient's constipation. Alongside treating OIC, other contributing factors to constipation should be evaluated and managed, such as functional constipation, pre-existing conditions (e.g. diabetes), or constipating medications (e.g. antidepressants or iron).³



Pharmacological treatment – laxatives

The first-line treatments for OIC are traditional laxatives. These may be osmotic (e.g. macrogol), stimulant (e.g. senna, biscaodyl) or stool-softening laxatives (e.g. docusate sodium).^{2,4} Bulk-forming laxatives and non-absorbable sugars such as lactulose are not recommended in patients with OIC.^{4,11} Osmotic laxatives work by retaining water in the GI tract whereas stimulants work by increasing GI contractility and inducing fluid secretion.²

The most common adverse effects observed with osmotic laxatives are abdominal pain, bloating, flatulence, nausea, vomiting and dehydration. Stimulant laxatives are associated with abdominal cramps, diarrhoea, nausea, vomiting, and, in the case of senna, yellowish-brown urine.¹²

Laxatives should not be prescribed in suspected intestinal obstruction, perforation, ileus, Crohn's disease, ulcerative colitis, or toxic megacolon. Prolonged use may lead to electrolyte disturbances. Caution is advised in patients with fluid or electrolyte imbalance, and laxatives should be discontinued if symptoms occur. Macrogol may reduce absorption of other oral medicines, necessitating separate dosing, and its sodium content should be considered in patients on a low-salt diet.¹³

Crucially, laxatives do not address the underlying cause and have limited efficacy in specifically treating OIC.²

Pharmacological treatment – PAMORAs

If OIC does not respond to laxatives, peripherally acting μ -opioid receptor antagonists (PAMORAs) should be considered.⁴ PAMORAs selectively block μ -opioid receptors in the GI tract, thereby targeting the underlying cause of OIC.⁴

There are three PAMORAs on the market: two oral (naldemedine [Rizmoic®], naloxegol [Moxventig®]) and one injectable (methylnaltrexone [Relistor®]). The two oral products are recommended by NICE and the SMC, while the injectable is accepted by the SMC for restricted use in patients with advanced illness receiving palliative care.^{14–18}

PAMORAs have been shown to be effective in treating OIC and well-tolerated in clinical trials, resulting in increased frequency of bowel movements, reductions in gastrointestinal symptoms, and improvements in quality of life.^{15,18–22}

The most common adverse reactions with PAMORAs are abdominal pain, nausea, vomiting, diarrhoea, headache and flatulence, which are generally mild-moderate and resolve without treatment.^{19–21}

PAMORAs are contraindicated in patients with known or suspected GI obstruction, or at increased risk of recurrent obstruction, due to the potential for GI perforation, or in patients with severe hepatic impairment.^{19–21} Relevant interactions with other medications must be considered.⁴ For example, concomitant use of naldemedine or naloxegol with strong CYP3A inhibitors or inducers should be avoided.^{19,20} The product SmPCs provide further product-specific guidance and safety information.

Pharmacy roles

When dispensing opioids, pharmacists can advise patients about constipation, reinforce education on OIC symptoms, and advise on diet, fluids, and lifestyle.⁴ As the first point of contact for many seeking constipation relief, pharmacists can ask patients about their symptoms, identify OIC, evaluate additional contributing factors to constipation, and initiate first-line treatment.^{3,23} If OIC persists or worsens, pharmacists can reassure patients that they do not have to learn to live with

constipation because other effective treatment options are available, referring them to a GP for further evaluation and consideration of a PAMORA.^{3,23}

Monitoring

Patients should be reassessed shortly after starting OIC treatment.³ Patient-reported outcome measures can support assessment of response to treatment. For example, the Bristol Stool Form Scale measures stool consistency and the Bowel Function Index assesses ease of defecation, incomplete evacuation, and overall constipation severity.⁴

Box 2 Key points

- OIC is a common but under-treated complication of opioid analgesics.³
- HCPs should proactively manage OIC with laxatives and review patient response.³
- Laxatives do not target the underlying mechanism of OIC and have limited efficacy in OIC.^{2,4}
- PAMORAs are an effective and well-tolerated treatment option for patients who do not respond to first-line treatment.^{3,4}

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Rizmoic® must not be used in patients with known or suspected GI obstruction or in patients at increased risk of recurrent obstruction, due to the potential for GI perforation. In patients with chronic non-cancer pain and OIC the most commonly reported side effects are diarrhoea, abdominal pain, nausea and vomiting. In patients with cancer and OIC, diarrhoea is very common and abdominal pain is common.

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