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IBS

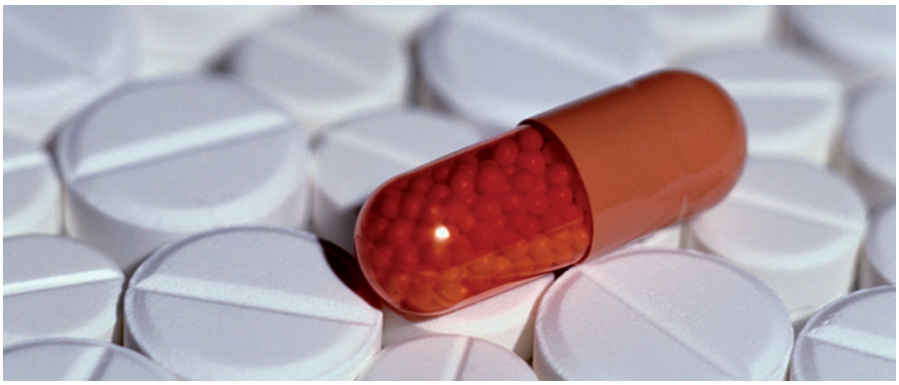
# Linaclotide approved for constipation-predominant IBS

The efficacy and safety of linaclotide for the treatment of constipation-predominant IBS (IBS-C) has been confirmed (up to 6 months) by two new phase III trials reported in the *American Journal of Gastroenterology*. The results of these trials support the recent FDA approval of linaclotide for the treatment of chronic idiopathic constipation and IBS-C.

Few effective therapies are available for the multiple symptoms associated with IBS-C (including, among others, abdominal pain, straining and hard stools), and linaclotide now appears to be a new treatment option available to clinicians. The drug is a peptide agonist of guanylate cyclase C and acts locally in the gut to activate CFTR in intestinal cells to increase luminal fluid secretion and accelerate intestinal transit.

The first study by Chey *et al.* was designed to assess the long-term (for 26 weeks) efficacy and safety of a 290 μg daily oral dose of linaclotide ($n = 402$) versus placebo ($n = 403$) in patients with IBS-C. Participants were monitored for improvements in abdominal symptoms and bowel function, as well as adverse events.

In comparison to controls, notable and sustained improvements in abdominal pain and stool frequency were observed in the linaclotide group. Moreover, linaclotide also improved other IBS-C symptoms such as bloating and stool consistency.



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In the second study, Rao *et al.* assessed the efficacy of linaclotide and the potential for 'rebound' effects—that is, whether symptoms worsened upon withdrawal from medication. Patients received either placebo ($n = 397$) or 290 μg oral linaclotide ($n = 406$) once daily over 12 weeks, followed by a 4-week withdrawal period (in which patients on linaclotide were randomly assigned to either continue the treatment or switch to placebo).

Again, marked improvements were observed in a number of abdominal symptoms (such as pain or cramping) and bowel functions (frequency and consistency of stool) over 12 weeks. For those who continued on linaclotide for a further 4 weeks, sustained improvements in IBS-C were observed. For those patients randomly re-assigned to placebo, IBS-C symptoms did return once they stopped taking linaclotide, but patients did not experience worsening of symptoms beyond their baseline levels.

"Linaclotide appears to be effective for up to 6 months in adults with IBS-C," says Anthony Lembo (Harvard Medical School, USA) who was involved in both trials. However, the authors do warn of adverse effects with linaclotide use, in particular diarrhoea (possibly as an extension of the pharmacological properties of the drug itself); 4.5–5.7% of patients discontinued linaclotide during the two trials owing to diarrhoea.

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**Original articles** Chey, W. *et al.* Linaclotide for irritable bowel syndrome with constipation: a 26-week, randomized, double-blind, placebo-controlled trial to evaluate efficacy and safety. *Am. J. Gastroenterol.* doi:10.1038/ajg.2012.254 | Rao, S. *et al.* A 12-week, randomized, controlled trial with a 4-week randomized withdrawal period to evaluate the efficacy and safety of linaclotide in irritable bowel syndrome with constipation. *Am. J. Gastroenterol.* doi:10.1038/ajg.2012.255