NHS
Wakefield
Clinical Commissioning Group

Commissioning Statement

Treatment	**Linaclotide▼** *Constella*® (Allergan) 290 microgram capsule
For the treatment of	The symptomatic treatment of moderate-to-severe irritable bowel syndrome with constipation (IBS-C) in adults
Commissioning position	**Wakefield CCG commissions the use of linaclotide for the treatment of irritable bowel syndrome with constipation only if the following conditions apply:** • The condition has been diagnosed based on the Rome criteria for IBS[1] • The patient has had constipation for at least 12 months and • optimal or maximum tolerated doses of previous laxatives from different classes have not helped[2] i.e*: ○ laxatives or antispasmodics (1st line) ○ antidepressants (2nd line) Patients receiving linaclotide should be reviewed after the first four weeks then at regular 12-week intervals. Treatment should be reconsidered if there is no initial improvement in symptoms and if improvement is not sustained[3]. **this includes common laxatives, antispasmodics (such as alverine, mebeverine, hyoscine butylbromide, peppermint oil) and SSRI antidepressants.*
Date effective from	13th July 2017
Policy to be reviewed by	21st November 2019 (to be reviewed earlier if NICE issues relevant guidance at an earlier date)
Background information	The Scottish Medicines Consortium (SMC) has accepted (June 2013) linaclotide for restricted use in Scotland for patients with moderate to severe IBS-C who have not responded adequately to or cannot tolerate all other suitable treatment options. NICE CG61 (2008, last updated February 2015)

	identifies self-help as a key component of the management of IBS, and advises that people should receive information on general lifestyle, physical activity and diet. Based on the nature and severity of symptoms, pharmacological management may be considered, with the choice of agent(s) depending on the predominant symptom(s). Treatments include antispasmodic agents for abdominal pain, and laxatives or antimotility agents, depending on the presence of constipation or diarrhoea. Off-label use of a SSRI may be considered for people whose condition does not respond to first-line treatments[2]. The Midlands Therapeutics Review and Advisory Committee (MTRAC) recommends linaclotide only in those patients for whom all other treatment options have been ineffective or are contraindicated. NICE ESNM16 evaluates the evidence for linaclotide and concludes that the publication of head-to-head studies against existing treatments would facilitate a better understanding of its place in the management of IBS-C.
Summary of evidence/rationale	Linaclotide is thought to act within the lumen of the intestine through the activation of the guanylate cyclase subtype C receptor. The subsequent increase in cyclic guanosine monophosphate results in increased intestinal fluid secretion and accelerated transit. In addition, in animal models, visceral pain is reduced[3]. Efficacy of linaclotide has been established in trials lasting up to 6 months[3]. Linaclotide has been evaluated in 2 double-blind, randomised, placebo-controlled trials of patients with IBS-C (Rao et al. 2012 and Chey et al. 2012). An analysis of both trials, based on the primary efficacy end points was published in 2013 (Quigley et al. 2013). In both trials, a statistically greater proportion of linaclotide-treated patients, compared with placebo-treated patients, met the two co-primary efficacy end points: '12-week abdominal pain/discomfort responders' and 'IBS degree-of-relief responders'[4]. Different outcomes were required by the US Food and Drug Administration (FDA). A significantly greater percentage of patients treated with linaclotide met the composite primary end point of 'improvement of ≥30% in average daily worst abdominal pain score' and 'increase by ≥1 complete spontaneous bowel movement from baseline for ≥50% of the weeks assessed'[5].

	However, around half of the patients in the main European studies did not sufficiently respond to linaclotide, leading to the recommendation that prescribers should assess patients regularly and reconsider treatment if there is no improvement in symptoms after four weeks[4].
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References

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