South East London Area Prescribing Committee
Formulary recommendation

Reference	**007**
Intervention:	**Linaclotide (Constella®) for the treatment of moderate-to- severe irritable bowel syndrome with constipation (IBS-C) in adults.** Linaclotide is a first-in-class, oral, once-daily, guanylate cyclase-C receptor agonist - The increase in cyclic guanosine monophosphate caused by linaclotide results in increased intestinal fluid secretion and accelerated transit.
Date of Decision	**December 2013, updated November 2017**
Date of Issue:	**January 2014, then April 2015. Recommendation revised and re-issued December 2017 to align with updated SEL IBS pathway**
Recommendation:	**Green – 2nd line option. Can be prescribed within agreed criteria for use in primary or secondary care.** Patients with red flag symptoms should be referred and investigated by specialists – see NICE IBS pathway
Further Information	Linaclotide is recommended for the treatment of moderate to severe irritable bowel syndrome (IBS) with constipation in adults as a **2rd line option** if therapies recommended by NICE[3] (CG 61) have been ineffective or not tolerated: • 1st line: antispasmodics/anti-motility agents/laxatives (not lactulose) • 2nd line: ▪ If pain and diarrhoea predominant IBS (IBS-D) consider a tricyclic antidepressant ▪ If pain and constipation predominant IBS (IBS-C) consider a selective serotonin reuptake inhibitor (SSRI) antidepressant. ▪ If IBS-C more than 12 months and not responding to maximum dose of different laxatives, consider linaclotide For initiation, a single 28 day supply is recommended initially and clear treatment review plan should be in place. In trials approximately 45% of patients had no improvement in abdominal pain with linaclotide treatment, therefore patients should have a scheduled review after **4 weeks** treatment and regularly thereafter to assess improvement in symptoms before continuation. These medicines should form part of a multifaceted approach to management of IBS to include the importance of self-help, general lifestyle, physical activity and diet. Refer to the SEL Irritable Bowel Syndrome Pathway for further detail.
Shared Care/Transfer of care document required:	No Linaclotide appears safe, with little chance of interaction with other medications. The main adverse effect appears to be diarrhoea due to excessive pharmacological effect.

Cost Impact for agreed patient group	• Based on assumptions in the evidence review, a reasonable estimate would be to assume that introduction of linaclotide to the healthcare economy might cost between £60,000 to £100,000 per 100,0000 population. **NOTE:** This recommendation was originally issued in December 2013 and updated in November 2017, therefore some of this spend is already likely to be occurring. • There may be savings from reduced referrals to secondary care.
Usage Monitoring & Impact Assessment	**Trusts** Usage data to be provided upon request to the APC and follow up of exception reports as required.
	CCGs Epact data monitoring and exception reporting as needed of inappropriate use to Trust via medicines teams.
Evidence reviewed	1. Evidence Summary: New Medicine 16. The National Institute of Health and Care Excellence. April 2013. 2. Quigley E, Tack J, Chey D, Rao S et al. Randomised clinical trials:linaclotide phase 3 studies in IBS-C – a prespecified further analysis based on European Medicines Agency-specified endpoints. Alimentary Pharmacology and Therapeutics 2012 37 p49-61. 3. Iritable Bowel Syndrome in Adults. Diagnosis and management of irritable bowel syndrome in primary care. The National Institute of Care and Clinical Excellence Clinical Guideline 61, Updated 2012. 4. Constella CHMP assessment report. The European Medicines Agency, September 2012. 5. Constella 290 micrograms hard capsules. Summary of Product Characteristics. Available online at: http://www.medicines.org.uk/emc/medicine/27499/SPC/Constella+290+micrograms+hard+capsules/ (accessed on 29/10/2013) 6. Rao S, Lembo A, Shiff S, Lavins B et al. A 12-Week, randomised, controlled trial with a 4-week randomized withdrawal period to evaluate the efficacy and safety of linaclotide in irritable bowel syndrome with constipation. The American Journal of Gastroenterology 2012 **107** p1714-1724. 7. Chey W, Lembo, Lavins B, Shiff S et al. Linaclotide for irritable bowel syndrome with constipation: A 26-week, randomized, double-blind, placebo-controlled trial to evaluate efficacy and safety. The American Journal of Gastroenterology 2012 **107** p1702-1712. 8. Linaclotide hard capsules, Constella®. The Scottish Medicines Consortium June 2013, 869/13 9. Wilson S, Roberts L, Roalfe A, Bridge P. Prevalence of irritable bowel syndrome: a community survey. British Journal of General Practice 2004 **54** (504) p495-504. 10. Hugin A, Whorwell P, Tack J, Mearin F. The prevalence, patterns and impact of irritable bowel syndrome: an international survey of 40 000 subjects. Ailmentary Pharmacological Therapy 2003 **17**, p643-650

NOTES:

a) Area Prescribing Committee recommendations and minutes are available publicly on the APC website.

b) This Area Prescribing Committee recommendation has been made on the cost effectiveness, patient outcome and safety data available at the time. The recommendation will be subject to review if new data becomes available, costs are higher than expected or new NICE guidelines or technology appraisals are issued.

c) **Not to be used for commercial or marketing purposes. Strictly for use within the NHS.**