DORSET MEDICINES ADVISORY GROUP

COMMISSIONING STATEMENT ON LUBIPROSTONE (AMITIZA® 24mcg SOFT CAPSULES®) FOR THE TREATMENT OF CHRONIC IDIOPATHIC CONSTIPATION IN ADULTS

SUMMARY

NHS Dorset Clinical Commissioning Group recommends the use of lubiprostone (Amitiza®) for the treatment of chronic idiopathic constipation and associated symptoms in adults in accordance with NICE TA 318, and the locally agreed pathway for the management of constipation. A licensed course of treatment with lubiprostone is 2 weeks. The prescribing clinician should consider the efficacy of the treatment at the end of the two week course and advise a treatment break before recommencing a further course or advise the patient that further continuous treatment is off-label.

BACKGROUND	Lubiprostone is a prostone that activates chloride channels in gastrointestinal epithelial cells, relieving symptoms of chronic constipation by improving intestinal secretion. Amitiza® is licensed for the treatment of chronic constipation in adults when response to diet and other non-pharmacological measures (e.g. educational measures, physical activity) are inappropriate. Lubiprostone is recommended as a possible treatment for people with chronic idiopathic constipation: • who have previously been treated with 2 different types of laxatives at the highest possible recommended dose, for at least 6 months, but these haven't worked well enough, and • when invasive treatment is being considered. Amtiza® is not recommended for use within Scotland. The Scottish Medicines Consortium (SMC) stated that the submitting company did not present a sufficiently robust clinical and economic analysis to gain acceptance by SMC. The license holder has indicated their intention to resubmit.
RELEVANT NICE GUIDANCE	Lubiprostone for the treatment of chronic idiopathic constipation https://www.nice.org.uk/guidance/ta318 published 23rd July 2014
FORMULARY STATUS	Green
PBR STATUS	Drug cost included in PbR Tariff
COMMISSIONING IMPLICATIONS	Lubiprostone is recommended as an option for treating chronic idiopathic constipation; for adults in whom treatment with at least 2 laxatives from different classes, at the highest tolerated recommended doses for at least 6 months, has failed to provide adequate relief and for whom invasive treatment for constipation is being considered. A local pathway for the management of constipation defines its place in therapy. NICE recommends that although lubiprostone works through a novel mechanism of action, it is not a step change in the treatment pathway, and provides an alternative to prucalopride (see NICE TA 211). NICE considered the characteristics of chronic idiopathic constipation, noting that it cannot be explained by any anatomical, physiological, radiological or histological abnormalities, and is defined as 2 or more of the following symptoms at least a quarter of the time for at least 6 months: straining, lumpy or hard

	stools, a sensation of incomplete evacuation, a sensation of anorectal obstruction or blockage, and/or less than 3 spontaneous bowel movements per week.
RELEVANT CLINICAL COMMISSIONING PROGRAMME	General Medical and Surgical
PATIENT PATHWAY IMPLICATIONS	The CKS topic on Constipation in Adults advises that if lifestyle measures are insufficient (increasing dietary fibre (including the importance of regular meals), drinking an adequate fluid intake, and exercise), laxatives are recommended as follows: • Start treatment with a bulk-forming laxative, maintaining good hydration. • If stools remain hard, add or switch to an osmotic laxative. • If stools are soft but the person still finds them difficult to pass or complains of inadequate emptying, add a stimulant laxative. • If at least two laxatives (including in combination and from different classes) have been tried at the highest tolerated recommended doses for at least 6 months, consider the use of prucalopride in women only. NICE recommends that the position of lubiprostone in a care pathway is the same as prucalopride. At this stage of a pathway, lubiprostone can be substituted for prucalopride and is licensed for use in both men and women. The agreed local pathway for the management of constipation includes both these agents as NICE approved options at this stage. There is no comparative evidence between the two agents.
PRESCRIBING INFORMATION	Lubiprostone should only be prescribed by a clinician with experience of treating chronic idiopathic constipation, who has carefully reviewed the person's previous courses of laxative treatments specified The recommended dose is 24 mcg twice daily. A course of treatment for constipation with Lubiprostone is 2 to 4 weeks. Lubiprostone soft capsules are for oral use, taken with food. The capsules should be swallowed whole with a sufficient amount of water. NICE suggests that if treatment is not effective after 2 weeks, the benefit of continuing treatment should be reconsidered. Elderly: No dosage changes are required based on age. Paediatric Population: The safety and efficacy of Lubiprostone in children and adolescents aged under 18 have not yet been established. Hepatic Impairment: No dosage adjustment is required for patients with mild hepatic impairment. For patients with moderate or severe hepatic impairment (Child-Pugh classification B or C), the initial dosage should be decreased to 24 micrograms (1 capsule once a day after breakfast or supper). If this initial dose is tolerated and an adequate response has not been obtained after an appropriate interval, the dose can be increased to full dosing (one 24-microgram capsule, twice daily) with appropriate monitoring of patient response. The safety and efficacy of Lubiprostone in children and adolescents aged under 18 have not yet been established. In its approved formulation, the lubiprostone soft capsule contains gelatine of

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<tr><td></td><td>bovine origin, which may represent a potential equality issue for those with particular religious beliefs, vegetarians and vegans

The summary of product characteristics (SPC) lists the following adverse reactions for lubiprostone: nausea, palpitations, diarrhoea, abdominal distension, flatulence, abdominal discomfort, abdominal pain, indigestion, oedema (including peripheral), chest discomfort, headache, dizziness, dyspnoea, hyperhidrosis and hot flushes. For full details of adverse reactions and contraindications, see the SPC.</td></tr>
<tr><td>SUMMARY OF EVIDENCE TO SUPPORT FORMULARY STATUS</td><td>NICE considered evidence on the clinical effectiveness from 3 phase III randomised controlled trials, 2 phase II dosing studies and 4 open-label studies. The 3 phase III randomised controlled trials were parallel-group, double-blind, placebo-controlled, multicentre studies conducted in the US and Japan.

Overall baseline characteristics were similar across all phase III studies and treatment groups.

Lubiprostone was associated with statistically significantly higher mean spontaneous bowel movement frequencies compared with placebo at week 1 across all phase III trials.

During the 4 weeks there was a statistically significant (p<0.0001) difference in mean spontaneous bowel movement frequency per week and response to treatment between the lubiprostone and placebo arms.

Lubiprostone statistically significantly improved all outcomes compared with placebo except for abdominal bloating.

NICE concluded that lubiprostone is likely to be at least as effective as prucalopride.

There are differences in the adverse reaction profiles of lubiprostone and prucalopride. Lubiprostone may be better tolerated by some individuals. NICE concluded that the adverse reaction profile of lubiprostone was manageable.

Conclusion: NICE concludes that lubiprostone is clinically effective compared with placebo, and that it and prucalopride are similarly effective.</td></tr>
<tr><td>ASSESSMENT OF COST IMPLICATIONS</td><td>Amitiza soft capsules 24mg x 28 £29.68 (Takeda UK)
<table><tr><td>2 weeks’ supply – 1 BD</td><td>£29.68</td></tr><tr><td>4 weeks’ supply – 1BD</td><td>£59.36</td></tr></table>Drug price from dm+d accessed March 2018</td></tr>
<tr><td>REFERENCES</td><td>Scottish Medicines Consortium (SMC). Statement of advice. lubiprostone, 24 micrograms soft capsules (Amitiza®) SMC No. (977/14) Sucampo Pharma Europe Ltd. 11 August 2014 http://www.scottishmedicines.org.uk/SMC_Advice/Advice/977_14_lubiprostone_Amitiza/lubiprostone_Amitiza on 1st September 2014

Lubiprostone for treating chronic idiopathic constipation. Issued: July 2014. Accessed via http://www.nice.org.uk/guidance/TA318 published July 2014, last</td></tr>
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	accessed July 2017 NICE Clinical Knowledge Summaries. Constipation. Last revised October 2015, accessed July 2017 NICE CKS Scenario: Adults Summary of Product Characteristics. AMITIZA 24 microgram soft capsules. Last updated April 2016, accessed July 2017
DATE	Second edition, 30th December 2014
REVIEW DATE	December 2017
REVIEWED BY	Gastroenterology Working Group
REVIEW DATE	July 2017
DATE OF NEXT REVIEW	March 2020 or before, in light of new evidence
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