# NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

## Proposed Health Technology Appraisal

## Lubiprostone for the treatment of chronic idiopathic and opioid induced constipation

## Draft scope (pre-referral)

### Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of lubiprostone within its licensed indications for the treatment of chronic idiopathic and opioid-induced constipation.

### Background

Chronic constipation has been defined as two or more of the following symptoms at least a quarter of the time for at least six months: straining, lumpy or hard stools, a sensation of incomplete evacuation, a sensation of anorectal obstruction or blockage, and/or less than three defecations per week. Constipation may also be the consequence of an underlying condition. However, when constipation cannot be explained by any anatomical, physiological, radiological or histological abnormalities, it is referred to as idiopathic constipation.

Opioid analgesics, such as morphine, are widely used for the treatment of pain. Opioid receptors are present in the gastrointestinal tract and when opioids bind to these receptors, they can disrupt normal gastrointestinal function, resulting in bowel dysfunction. Constipation is one of the most common and debilitating symptoms of opioid-induced bowel dysfunction.

Reported prevalence rates of constipation in the UK vary widely between studies, with figures ranging from 4% to 20%. Constipation affects twice as many women as men, and older people are five times more likely than younger adults to suffer from constipation. Opioid-induced constipation is considered to be a side effect that will affect nearly all patients taking strong opioid treatment and that will persist unless treated. Approximately 32,000 people receive strong opioids (for cancer and non-cancer pain) in England. In 2010-11, there were 57,506 hospital admissions due to constipation in England. In 2010, there were 103 deaths registered in England and Wales due to constipation.

If dietary and lifestyle changes are ineffective or impractical, a short course of laxatives may relieve symptoms and restore normal bowel function. NICE clinical guideline No. 140 recommends laxative treatment to be taken regularly at an effective dose for all patients initiating strong opioids. Long-term laxative use should be avoided where possible. When oral laxative therapy is ineffective at producing a bowel movement, a suppository or enema may be appropriate. For people for whom laxatives have failed to provide

adequate relief, other treatments such as prokinetic medication (i.e. prucalopride, methylnaltrexone); rectal irrigation; and surgical treatments (pelvic floor surgery, neuromodulation or resectional) are considered.

NICE technology appraisal No. 211 recommends prucalopride as an option for the treatment of chronic constipation in women for whom treatment with at least two laxatives from different classes, at the highest tolerated recommended doses for at least 6 months, has failed to provide adequate relief and invasive treatment for constipation is being considered.

## The technology

Lubiprostone (Amitiza, Sucampo Pharma Europe) is a prostone that specifically activates a chloride ion channel located in the apical intestinal membrane enhancing the intestinal fluid secretion. It is administered orally.

Lubiprostone has a UK marketing authorisation for the treatment of chronic idiopathic constipation and associated symptoms in adults when response to diet and non-pharmacological treatments are inappropriate.

Lubiprostone does not have a UK marketing authorisation for the treatment of opioid-induced constipation. It has been studied in clinical trials, compared with placebo, in adults with opioid bowel dysfunction who have been treated with opioids for chronic non-cancer pain.

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| **Intervention** | Lubiprostone |
| **Populations** | • Adults with chronic idiopathic constipation and associated symptoms when response to diet and other non-pharmacological treatments are inappropriate.<br>• Adults treated for chronic non-cancer pain with opioid-induced constipation |
| **Comparators** | For people with chronic idiopathic constipation:<br>• prucalopride<br>For people with opioid induced constipation:<br>• methylnaltrexone (subject to NICE appraisal)<br>• prucalopride<br>• rectal interventions e.g. suppositories and enemas |

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| **Outcomes** | The outcome measures to be considered include:<br>• frequency of bowel movements<br>• time to bowel movement<br>• response rate<br>• symptoms of constipation<br>• pain<br>• use of rescue medication<br>• adverse effects of treatment<br>• health-related quality of life. |
| **Economic analysis** | The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year.<br>The reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared.<br>Costs will be considered from an NHS and Personal Social Services perspective. |
| **Other considerations** | Guidance will only be issued in accordance with the marketing authorisation. |

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| **Related NICE recommendations** | Related Technology Appraisals:<br>Technology Appraisal No. 211. December 2010, 'Prucalopride for the treatment of chronic constipation in women'. Review proposal date October 2013<br>Technology Appraisal in Preparation, 'Methylnaltrexone for the treatment of opioid-induced bowel dysfunction in advanced illness or palliative care'. Earliest anticipated date of publication November 2013<br>Related Guidelines:<br>Clinical Guideline No. 99, May 2010, 'Diagnosis and management of idiopathic childhood constipation in primary and secondary care'. Review proposal date May 2013<br>Clinical Guideline No. 140, May 2012, 'Opioids in palliative care: safe and effective prescribing of strong opioids for pain in palliative care of adults'. Review proposal date TBC<br>Related Pathways:<br>NICE Pathway: 'Opioids in palliative care', Pathway created: Jun 2012. http://pathways.nice.org.uk/pathways/opioids-in-palliative-care#content=view-node%3Anodes-communication-and-review |

## Questions for consultation

Have the most appropriate comparators for lubiprostone for the treatment of chronic idiopathic constipation been included in the scope? Should invasive procedures such as rectal interventions (including enemas, suppositories and manual evacuation) be considered a comparator in this population?

Have the most appropriate comparators for lubiprostone for the treatment of opioid-induced constipation been included in the scope?

Should the following be considered comparators for lubiprostone for the treatment of chronic idiopathic or opioid-induced constipation?

- laxatives
- bowel surgery

Are the outcome measures in the scope appropriate for measuring chronic idiopathic and opioid induced constipation?

Are there any subgroups of people in whom the technology is expected to be more clinically effective and cost effective or other groups that should be examined separately?

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which lubiprostone is and will be licensed;

- could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;

- could have any adverse impact on people with a particular disability or disabilities.

Please tell us what evidence should be obtained to enable the Committee to identify and consider such impacts.

Do you consider the technology to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)?

Do you consider that the use of the technology can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation?

Please identify the nature of the data which you understand to be available to enable the Appraisal Committee to take account of these benefits.

NICE intends to appraise this technology through its Multiple Technology Appraisal (MTA) Process. We welcome comments on the appropriateness of appraising this topic through this process. (Information on the Institute's Technology Appraisal processes is available at http://www.nice.org.uk/aboutnice/howwework/devnicetech/technologyappraisalprocessguides/technology_appraisal_process_guides.jsp)