Appendix B

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Proposed Health Technology Appraisal

Methylnaltrexone bromide for treating opioid-induced constipation

Draft scope (pre-referral)

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of methylnaltrexone bromide within its marketing authorisation for treating opioid-induced constipation.

Background

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.

Opioid-induced constipation is considered to be a side effect that will affect nearly all people taking strong opioid treatment and that will persist unless treated. The prevalence of opioid-induced constipation is not known. However, in England in 2010 there were over 17 million prescriptions for opioid items. The population likely to be eligible to receive methylnaltrexone bromide could not easily be estimated from available routine published sources.

Clinical Guideline No. 140 recommends laxative treatment should be taken regularly at an effective dose for all patients initiating strong opioids. However, laxatives taken prophylactically during opioid therapy in order to maintain bowel movement are not always effective. When patients do not respond to laxatives, a suppository or enema may be appropriate.

The technology

Methylnaltrexone bromide (Relistor, TMC Pharma Services) is a selective antagonist at opioid receptors. Methylnaltrexone bromide does not cross the blood brain barrier and, therefore, the action of methylnaltrexone bromide on opioid receptors is restricted to the periphery, thereby preserving the analgesic effect of opioid drugs within the central nervous system. It is administered by subcutaneous injection.

Methylnaltrexone bromide has a UK marketing authorisation for the treatment of opioid–induced constipation in advanced illness adult patients, aged 18 years and older, who are receiving palliative care when response to usual laxative therapy has not been sufficient. Methylnaltrexone bromide is being studied in clinical trials compared to placebo for opioid-induced constipation in patients, aged 18 years and older with with chronic non-cancer pain.

Intervention(s)	Methylnaltrexone bromide
Population(s)	Adults with opioid-induced constipation
Comparators	• oral laxative therapy • opioid analgesic and opioid receptor antagonist combinations (oxycodone with naloxone) • rectal interventions (e.g. suppositories and enemas) • naloxegol (subject to ongoing NICE appraisal)
Outcomes	The outcome measures to be considered include: • frequency of spontaneous bowel movements • symptoms of constipation • upper gastrointestinal symptoms including nausea • pain • adverse effects of treatment • 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. 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. 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. Where the wording of the therapeutic indication does not include specific treatment combinations, guidance will be issued only in the context of the evidence that has underpinned the marketing authorisation granted by the regulator. If the evidence allows the following subgroup will be considered: people for whom previous treatment with laxatives has been unsuccessful in providing adequate relief.

Related NICE recommendations and NICE Pathways	Related Technology Appraisals: Technology Appraisal No. 318, Jul 2014 'Lubiprostone for treating chronic idiopathic constipation'. Review Proposal Date June 2017 Technology Appraisal No. 277, March 2013 'Methylnaltrexone for the treatment of opioid-induced bowel dysfunction in advanced illness or palliative care' (terminated appraisal). Technology Appraisal No. 211, Dec 2010 'Prucalopride for the treatment of chronic constipation in women'. Review Proposal Date October 2013 Technology Appraisal in Preparation, 'ID674: Naloxegol for treating opioid-induced constipation'. Earliest anticipated date of publication July 2015 Technology Appraisal suspended, 'ID646: Lubiprostone for treating opioid induced constipation in people with chronic, non-cancer pain' Related Guidelines: 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 June 2016. Related Pathways: NICE Pathway: 'Opioids in palliative care', Pathway last updated Sep 2014: http://pathways.nice.org.uk/pathways/opioids-in-palliative-care NICE Pathway: 'Constipation', Pathway last updated Sep 2014: http://pathways.nice.org.uk/pathways/constipation
Related National Policy	None

Questions for consultation

In UK clinical practice, where would methylnaltrexone bromide most likely be used in the treatment pathway for opioid-induced constipation?

Have all relevant comparators for methylnaltrexone bromide been included in the scope? Which treatments are considered to be established clinical practice in the NHS for opioid-induced constipation?

Is the subgroup suggested in 'other considerations' appropriate? Are there any other subgroups of people in whom methylnaltrexone bromide is expected to be more clinically effective and cost effective or other groups that should be examined separately?

Where do you consider methylnaltrexone bromide will fit into the existing NICE pathway, Constipation?

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 methylnaltrexone bromide is 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 methylnaltrexone bromide 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 methylnaltrexone bromide 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 Single Technology Appraisal (STA) 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/article/pmg19/chapter/1-Introduction)