NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal

Methylnaltrexone bromide for treating opioid-induced constipation

Final scope

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 management 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 opioids 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 to 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 oral laxative therapy is ineffective at producing a bowel movement, a suppository or enema may be appropriate. NICE technology appraisal 345 recommends naloxegol as an option for treating opioid induced constipation in adults whose constipation has not adequately responded to laxatives.

The technology

Methylnaltrexone bromide (Relistor, Swedish Orphan Biovitrum) 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 when response to laxative therapy has not been sufficient in adult patients, aged 18 years and older. The summary of product characteristics states that methylnaltrexone bromide can be used for treating opioid-induced constipation in adult patients with chronic non-cancer

pain and also for opioid-induced constipation in adults with advanced illness (palliative care).

Intervention(s)	Methylnaltrexone bromide
Population(s)	Adults whose opioid-induced constipation has not responded sufficiently to laxative therapy
Comparators	• rectal interventions (e.g. suppositories and enemas) • naloxegol For adults who are already receiving oxycodone: • oxycodone with naloxone
Outcomes	The outcome measures to be considered include: • frequency of spontaneous bowel movements • symptoms of constipation • time to first bowel action after intervention • use of rescue medication or interventions • response rate • upper gastrointestinal symptoms including nausea • pain • adverse effects of treatment (including pain from reversal of opioid induced analgesia) • 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	If evidence allows the following subgroup will be considered: • adults for whom previous treatment with more than one oral laxative has been unsuccessful in providing adequate relief. 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.
Related NICE recommendations and NICE Pathways	Related Technology Appraisals: Technology Appraisal No. 345, July 2015 'Naloxegol for treating opioid-induced constipation'. Review Proposal Date July 2018 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'. Moved to static list 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