

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Naldemedine for treating opioid-induced constipation

Final scope

Remit/appraisal objective

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

Background

Opioid analgesics are widely used for managing pain. Opioid receptors are present in the gastrointestinal tract, and when opioids bind to these receptors they can disrupt normal gastrointestinal function, resulting in opioid-induced 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 (used to treatment moderate to severe chronic pain)^{1,2}, and will persist unless treated. The prevalence of opioid-induced constipation is not known. However, in England in 2017 there were almost 24 million prescriptions for opioid analgesics³. Estimates on the prevalence of opioid-induced constipation among people taking opioids may be around 45–57% for non-cancer pain patients and 90% for cancer-related pain patients^{4,5}.

[NICE clinical guideline 140](#) recommends that laxative treatment is taken regularly at an effective dose for people initiating strong opioids. When oral laxative therapy is ineffective at producing a bowel movement, a suppository or enema may be appropriate. [NICE technology appraisal guidance 345](#) recommends naloxegol as an option for treating opioid-induced constipation in adults whose constipation has not adequately responded to laxatives. Methylnaltrexone is also licenced and used in clinical practice for treating opioid-induced constipation. The opioid-antagonist naloxone may also be used in people who are treated with oxycodone.

The technology

Naldemedine (Rizmoic, Shionogi) is a peripherally-active opioid receptor antagonist intended for the treatment of opioid-induced constipation. It is administered orally.

Naldemedine does not currently have a marketing authorisation in the UK for treating opioid-induced constipation. It has been studied in four randomised placebo-controlled trials in adults who have either non-malignant chronic pain or cancer pain with opioid-induced constipation.

Intervention	Naldemedine
Population	Adults with opioid-induced constipation who have had previous laxative treatment
Comparators	<ul style="list-style-type: none"> oral laxative treatment without naldemedine <p>For adults in whom oral laxatives have provided inadequate relief:</p> <ul style="list-style-type: none"> naloxegol peripheral mu-opioid receptor antagonists (methylnaltrexone) rectal interventions (e.g. suppositories and enemas) <p>For adults who are already receiving oxycodone:</p> <ul style="list-style-type: none"> oxycodone with naloxone
Outcomes	<p>The outcome measures to be considered include:</p> <ul style="list-style-type: none"> frequency of bowel movements (including 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 effects on analgesic efficacy adverse effects of treatment health-related quality of life
Economic analysis	<p>The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year.</p> <p>If the technology is likely to provide similar or greater health benefits at similar or lower cost than technologies recommended in published NICE technology appraisal guidance for the same indication, a cost-comparison may be carried out.</p>

	<p>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.</p> <p>Costs will be considered from an NHS and Personal Social Services perspective.</p>
<p>Other considerations</p>	<p>If the evidence allows the following subgroup will be considered:</p> <ul style="list-style-type: none"> • reason for taking opioids (cancer pain or non-cancer pain) <p>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.</p>
<p>Related NICE recommendations and NICE Pathways</p>	<p>Related Technology Appraisals</p> <p>Naloxegol for treating opioid-induced constipation (2015) NICE technology appraisal 345. Moved to the static list in July 2018.</p> <p>Terminated appraisals</p> <p>Methylnaltrexone for treating opioid-induced bowel dysfunction in people with advanced illness receiving palliative care (terminated appraisal) (2013). NICE technology appraisal 277.</p> <p>Methylnaltrexone bromide for treating opioid-induced constipation (terminated appraisal) (2017). NICE technology appraisal 468.</p> <p>Appraisals in development (including suspended appraisals)</p> <p>Constipation (opioid induced) – lubiprostone NICE technology appraisal guidance [ID646]. Suspended May 2014.</p> <p>Related Guidelines</p> <p>Constipation in children and young people: diagnosis and management (2010) NICE clinical guideline 99. Review date 2018.</p> <p>Palliative care for adults: strong opioids for pain relief (updated 2016) NICE clinical guideline 140 Next review 2021.</p> <p>Related Quality Standards:</p> <p>http://www.nice.org.uk/guidance/qualitystandards/quality</p>

	<p>standards.jsp</p> <p>Constipation in children and young people (2014) NICE quality standard 62</p> <p>Related NICE Pathways:</p> <p>Constipation (last updated July 2015) NICE pathway</p> <p>http://pathways.nice.org.uk/</p>
Related National Policy	<p>Department of Health (2016) NHS outcomes framework 2016 to 2017</p>

References

1. NICE (2012). Palliative care for adults: strong opioids for pain relief. (CG140).
2. World Health Organization “Pain Relief Ladder”. Accessed February 2019.
3. NHS Digital (2018). Prescription Cost Analysis England 2017. Accessed February 2019
4. National Institute for Health and Care Excellence. Lubiprostone for treating chronic idiopathic Constipation final scope. London: NICE; November 2013. Accessed March 2017
5. NICE (2015). Costing statement: Naloxegol for treating opioid-induced constipation (TA345).