Agency for Healthcare Research and Quality
Advancing Excellence in Health Care

NATIONAL GUIDELINE CLEARINGHOUSE

General

Guideline Title

Naloxegol for treating opioid-induced constipation.

Bibliographic Source(s)

National Institute for Health and Care Excellence (NICE). Naloxegol for treating opioid-induced constipation. London (UK): National Institute for Health and Care Excellence (NICE); 2015 Jul. 44 p. (Technology appraisal guidance; no. 345).

Guideline Status

This is the current release of the guideline.

This guideline meets NGC's 2013 (revised) inclusion criteria.

Recommendations

Major Recommendations

Naloxegol is recommended, within its marketing authorisation, as an option for treating opioid-induced constipation (OIC) in adults whose constipation has not adequately responded to laxatives.

- An inadequate response is defined as OIC symptoms of at least moderate severity in at least 1 of the 4 stool symptom domains (that is, incomplete bowel movement, hard stools, straining or false alarms) while taking at least 1 laxative class for at least 4 days during the prior 2 weeks.

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

Opioid-induced constipation (OIC)

Guideline Category

Assessment of Therapeutic Effectiveness

Treatment

Clinical Specialty

Anesthesiology

Family Practice

Gastroenterology

Internal Medicine

Intended Users

Advanced Practice Nurses

Physician Assistants

Physicians

Guideline Objective(s)

To assess the clinical effectiveness and cost-effectiveness of naloxegol for treating opioid-induced constipation (OIC)

Target Population

Adults with opioid-induced constipation (OIC) who have had an inadequate response to laxatives

Interventions and Practices Considered

Naloxegol

Major Outcomes Considered

- Clinical effectiveness
  - Frequency of spontaneous bowel movements
  - Symptoms of constipation
  - Use of rescue medication or interventions
  - Response rate
  - Upper gastrointestinal symptoms including nausea
  - Effects on analgesic efficacy
  - Adverse effects of treatment
  - Health-related quality of life
- Cost-effectiveness

Methodology

Methods Used to Collect/Select the Evidence

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Searches of Unpublished Data

Description of Methods Used to Collect/Select the Evidence

Note from the National Guideline Clearinghouse (NGC): The National Institute for Health and Care Excellence (NICE) commissioned an independent academic centre to perform an assessment of the manufacturer's submission on the technology considered in this appraisal and prepare an Evidence Review Group (ERG) report. The ERG report for this technology appraisal was prepared by Kleijnen Systematic Reviews Ltd, in collaboration with Erasmus University Rotterdam (EUR) and Maastricht University (see the "Availability of Companion Documents" field).

Clinical Effectiveness

Critique of the Methods of Review(s)

Searches

The company stated that in order to identify randomised controlled trial (RCT) evidence, a systematic review was conducted in October 2013 in part as an update to a 2008 Cochrane review. No reference was given for the Cochrane review. In their response to clarification, the company confirmed that this was the 2008 review by McNicol et al. The ERG requested clarification regarding the search strategies reported for this section, as those provided only appeared to search for one of the comparator groups: laxatives versus placebo. The company confirmed that there had been an error and that additional strategies had not been included in the original submission, these strategies were provided in the response to clarification. The ERG noted a disparity in the reported scope of the laxative search within the response to clarification. The company stated the search reported in the original submission was intended to retrieve 'placebo-controlled trials of laxatives that were not identified as part of the original Cochrane review or the update of that review'; however, when the ERG queried the lack of an update for this search, the company responded, 'The purpose of this search was to identify studies that compared two laxatives to each other, or a laxative versus placebo.' This is contrary to the first statement and upon a second inspection the ERG can confirm that the strategy reported would only retrieve studies comparing laxative against placebo, not laxative versus laxative. Due to time constraints the ERG was unable to conduct and screen a new search for this group, so it is unclear what impact this omission may have had on results.

The additional searches, sent at clarification, provided details of an update search to the original Cochrane review conducted in September 2012 which was designed to retrieve pharmaceutical interventions of interest excluding laxatives. This search was further updated in October 2013. The company reported that relevant papers identified by the original Cochrane review were also included in the review.

According to the company a third update was conducted in August 2014 to identify any recent studies of methylnaltrexone and naloxone-oxycodone only. The company stated that the searches were identical to the Cochrane update, with the exception that only terms relevant for the interventions methylnaltrexone and naloxone-oxycodone were included. These strategies were not provided as the company reported that line-by-line search yields were not documented; however overall numbers were provided.

Searches were carried out on all databases required by NICE. The host, search dates for the original and update searches were reported for all resources. Additional searches were reported, including conference proceedings and clinical study reports provided by the company (see Appendix 1 of the ERG report and the Manufacturer's submission [see the "Availability of Companion Documents" field] for additional details on the searches, including the search strategies used).

Measurement of Health Effects/Health-related Quality-of-Life (HRQoL)

Searches were carried out on all databases required by NICE. The host, date span and search dates were reported for all resources. Additional searches of conference proceedings, previous NICE and Scottish Medicines Consortium (SMC) submissions, Research Papers in Economics (RePEc), Cost-effectiveness Analysis (CEA) Registry, European Quality of Life-5 Dimensions (EQ-5D) Web site and the checking of reference lists were also conducted.

Summary of Searching

Searches were carried out on all databases required by NICE. The searches documented were easily reproducible and the submission reported searches of several additional resources, including conference abstracts and other relevant resources including trials databases, specialist and organisational Web sites, and the checking of references lists. The searches documented in the initial company's submission (CS) contained some areas of weakness, only those relating to reproducibility or those potentially consequential to the recall of results were included in the points of clarification letter forwarded to the company by NICE. The company addressed all the points of concern raised by the ERG in their response to clarification. However, despite the additional searches provided at clarification the ERG still has concerns regarding the comprehensiveness of searches for comparator treatments. Unfortunately, the ERG does not have the time or resources to conduct and screen new searches. Therefore, the implications of these limitations are not known.

Inclusion Criteria

Both RCTs and non-RCTs were identified according to the criteria described in Table 5 (see the ERG report). Papers excluded were not documented in detail. Papers could be further excluded after this stage if they did not 'yield the final data set' or were unsuitable for mixed treatment comparison (MTC) analyses.

ERG Comment

The ERG critiqued whether the inclusion criterion of the CS deviated from that of the scope (see Table 5 of the ERG report). The ERG noted that the population criteria of the CS concentrates on the subgroup proposed in the scope of 'laxative inadequate responders' and not on the broader criteria of the scope, which is all patients with opioid-induced constipation (OIC). This was done to reflect the intended license population. Similarly, the outcomes of interest were broader in the scope than in the CS. The ERG noted that 'comparator' now includes 'best supportive care' which was neither clearly defined nor was it included in the scope for this population. The CS comparator criteria did not clearly include rectal interventions (suppositories or manual evacuation) nor was this included in the clinical effectiveness section although it was included in the scope.

The ERG found some inconsistencies in how the inclusion and exclusion criteria were defined and adhered to (see Section 4.1 of the ERG report for details).

Overall the inclusion criteria were not appropriate for a MTC analysis and this leads to a lack of clarity of how the studies were screened and selected for inclusion.

1. It is likely that including all interventions of interest to the MTC would likely result in the inclusion of more studies which could alter the overall findings.
2. Some potentially relevant studies have been missed.
3. The differences in the inclusion specification of the 'population' between the scope and the CS report is likely to have reduced the number of included studies by limiting the naloxegol studies to the subgroup of laxative inadequate response (LIR) in the CS. In addition, this alteration of the scope leads to a difference between the population of the intervention and that of the comparator which is not appropriate (intervention is for LIR+ OIC, whilst comparator is for all OIC).

See Section 4.1 and Table 5 of the ERG report for additional information.

Cost-effectiveness

ERG Comment on Company's Review of Cost-effectiveness Evidence

Searches

Searches were carried out on all databases required by NICE. The host, date span and search dates were reported for all resources. Additional searches included hand searching the reference list of included studies, searches of conference proceedings, CEA registry and both the NICE, SMC and RePEc Web sites. Previous NICE technical appraisals and guidelines and SMC advice were also reviewed for relevant economic evaluations. The ERG was concerned that the economics filter utilised in the Medline and EMBASE searches appeared overly restrictive. The ERG reran the company's EMBASE search retrieving 189 results, the same search run with an alternative recognised economics filter retrieved 917 results (see Appendix 1 of the ERG report). It is unlikely however that any economic studies for naloxegol would have been missed due to the additional searches carried out on National Health Service Economic Evaluation Database (NHS EED), Econlit and the supplementary searches detailed above. Without screening these new results the ERG is unable to say whether additional relevant information in comparator treatments would have been missed.

Inclusion/Exclusion Criteria Used in the Study Selection

The inclusion and exclusion criteria of the study selection could not be found in the CS; the study selection criteria are presented in the submission.

Included/Excluded Studies in the Cost-effectiveness Review

In total, 252 publications were identified. Upon removal of duplicate papers, 231 titles and abstracts were reviewed. Two hundred and twenty-one publications were excluded. Ten were ordered for full paper review, of which six were excluded, resulting in four relevant papers for final inclusion. In addition, one relevant SMC advice document was identified and included. The identified studies evaluated interventions and comparators relevant to the submission and reported an incremental cost-effectiveness ratio (ICER)/cost per quality-adjusted life year (QALY). The economic evaluations were conducted in the UK, Belgium and the Netherlands. Of the five studies data extracted, two were available as full paper economic evaluations, two were conference abstracts, and one was a SMC advice document obtained from the SMC Web site. A summary of all identified studies is presented in Appendix 2 of the ERG report.

Reviewing the overall evidence, no economic evaluation was identified for naloxegol for the treatment of OIC. To address the lack of any published evidence for the cost-effectiveness of naloxegol, a *de novo* analysis was carried out. Table 12 in the ERG report depicts an overview of the included studies in the cost-effectiveness review.

Number of Source Documents

Clinical Effectiveness

Nine studies were included in the review (8 randomised controlled trials [RCTs] and one non-randomised study).

Cost-effectiveness

- Five relevant papers were included.
- The manufacturer presented an economic model.

Methods Used to Assess the Quality and Strength of the Evidence

Expert Consensus

Rating Scheme for the Strength of the Evidence

Not applicable

Methods Used to Analyze the Evidence

Meta-Analysis

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Note from the National Guideline Clearinghouse (NGC): The National Institute for Health and Care Excellence (NICE) commissioned an independent academic centre to perform an assessment of the manufacturer's submission on the technology considered in this appraisal and prepare an Evidence Review Group (ERG) report. The ERG report for this technology appraisal was prepared by Kleijnen Systematic Reviews Ltd in collaboration with Erasmus University Rotterdam (EUR) and Maastricht University (see the "Availability of Companion Documents" field).

Clinical Effectiveness

Critique of the Methods of Review(s)

Critique of Data Extraction

No details were given in the company's submission (CS) for the data extraction of randomised controlled studies. Details were provided for non-

randomised studies and were as follows: "Relevant information was extracted into the single technology appraisal (STA) template by a reviewer. A second reviewer checked the data extraction and any inconsistencies were resolved through discussion."

ERG Comment

Details of extracted data were provided for KODIAC 4 and 5 studies. However, insufficient details were provided in the CS for the comparator studies. Minimal details were presented for comparator study design, quality and data. However, no details were presented for baseline characteristics (e.g., age, disease severity, pain intensity, opioid dose, previous laxative use); it is unclear if the data were extracted and its absence does not allow assessment of the similarity of the studies included in the mixed treatment comparison (MTC).

These limitations prevent further analyses based on baseline characteristics (for pain intensity, opioid dose, duration of opioid use, duration of opioid-induced constipation [OIC], previous laxative use).

Quality Assessment

Nine trials were included in the CS. The quality assessments for KODIAC 4 and 5 were summarised in the CS. The ERG made comments on these assessments. This information is summarised in Table 6, Table 7 and Table 8 of the ERG report.

ERG Comment

The ERG agrees with the company's assessment on most items. Two studies were reported as abstracts only and therefore the quality assessments were largely unclear.

Disagreements with the company assessment of study quality were as follows:

- Imbalances in drop-outs between groups: The ERG noted that in three trials the placebo group had fewer discontinued patients and fewer discontinuations due to adverse events, or the different treatment arms reported different rates of discontinuation.
- Unclear risk of bias: For certain domains the ERG disagreed with the CS assessment because the ERG could find no evidence for the assessment and deemed it to be 'unclear risk of bias'.

Evidence Synthesis

Both the direct meta-analysis and indirect meta-analysis results were obtained using the same MTC analysis. The CS states that "the direct meta-analysis examines the same comparisons as the MTC, without incorporating ancillary arms of the evidence network." This was used to compare each treatment with placebo. The direct meta-analysis was conducted in R using the metaphor package and used a random effects Bayesian model. Fixed effect models were only used if there was a strong rationale for their use. Statistical heterogeneity was assessed using the I^2 statistic and was low for most outcomes apart from discontinuation due to adverse events, and treatment-emergent adverse events.

A global assessment of statistical heterogeneity for the MTC was made by considering the size of tau (the estimate of the between studies standard deviation). As for the direct meta-analysis, random effects models formed the base case, with fixed effects models used only in cases where there was a strong rationale. Model fit was assessed using the deviance information criteria (DIC), an analysis of residual deviance was not considered necessary due to the simplicity of the network.

In addition to the MTC analyses, indirect comparisons were performed using the Bucher method to compare pairs of treatments which were linked by a common comparator.

ERG Comment

Forest plots were presented for all outcomes. No details were given of the actual method used in the indirect comparison, but given that the results are reported as credible intervals, it appears that these results were also obtained from one of the Bayesian analyses.

The actual methods used for the meta-analysis are appropriate but they do seem to be overly complicated given the simplicity of the networks (all treatments are connected via placebo) and the small number of studies available for each outcome (between three and six). It was unclear why direct meta-analysis was performed using Bayesian methods in R, when these results could also have been obtained from the Bayesian model using OpenBUGs. There was no need to use both a MTC and indirect comparisons. Given that all treatments could be connected via placebo, an indirect comparison using the Bucher method would have been acceptable as a more simple analysis without additional MTC.

See Section 4 and Appendix 3 of the ERG report (see the "Availability of Companion Documents" field) for additional information on clinical effectiveness analyses.

Cost-effectiveness

Summary and Critique of Company's Submitted Economic Evaluation by the ERG

Model Structure

The company constructed a decision-analytic model to assess the cost-effectiveness of naloxegol. The model consists of a decision-tree structure for the first four weeks of treatment, with patients being classified as responders, if they have achieved constipation relief and as non-responders if they have not. This decision tree is followed by a Markov structure, with a cycle length of four weeks, and time horizon up to a maximum of five years. Patients who have responded to treatment by week four will begin the Markov model in 'non-OIC (on treatment)' state. Non-responders at week four will start the Markov phase in the 'OIC' health state (see Figure 2 and Table 15 of the ERG report).

The Markov model consists of four health states: OIC; non-OIC (on treatment), non-OIC (untreated) and death, where OIC and non-OIC are defined as:

- OIC: less than three spontaneous bowel movements (SBMs) per week in at least two out of the last four weeks
- Non-OIC: three or more SBMs per week in at least three out of the last four weeks

The company adopted this divergence from the clinical definition as it is claimed to correspond with an internationally accepted definition of constipation and because it facilitates a simplification of the model design by allowing the estimation of utility and resource use as a function of constipation status, rather than a change in that status.

ERG Comment

The ERG agrees with the definition of response used in the economic evaluation. In general, health economic models should use absolute health states rather than health states relative to a baseline situation. However, it is likely that the health state non-OIC is too broad to be homogeneous regarding quality of life. In the current definition only nine SBMs should occur over a 28-day period to be classified as a responder (i.e., move to the non-OIC on treatment state). But patients who have 28 SBM in these 28 days are in the same health state and thus are assumed to have the same quality of life as those with only nine SBM. This appears unlikely to the ERG.

Sensitivity Analyses

The company assessed the various uncertainties in the economic evaluation through deterministic sensitivity analysis, scenario analysis and probabilistic sensitivity analysis. While the first two show which parameters and assumption have the largest impact on the model outcomes, the latter shows the overall uncertainty around the incremental cost-effectiveness ratio (ICER).

See Section 5 of the ERG report (see the "Availability of Companion Documents" field) for additional information on cost-effectiveness analysis.

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

Considerations

Technology appraisal recommendations are based on a review of clinical and economic evidence.

Technology Appraisal Process

The National Institute for Health and Care Excellence (NICE) invites 'consultee' and 'commentator' organisations to take part in the appraisal process. Consultee organisations include national groups representing patients and carers, the bodies representing health professionals, and the manufacturers of the technology under review. Consultees are invited to submit evidence during the appraisal and to comment on the appraisal documents.

Commentator organisations include manufacturers of the products with which the technology is being compared, the National Health Service (NHS) Quality Improvement Scotland and research groups working in the area. They can comment on the evidence and other documents but are not asked to submit evidence themselves.

NICE then commissions an independent academic centre to review published evidence on the technology and prepare an 'assessment report'. Consultees and commentators are invited to comment on the report. The assessment report and the comments on it are then drawn together in a

document called the evaluation report.

An independent Appraisal Committee then considers the evaluation report. It holds a meeting where it hears direct, spoken evidence from nominated clinical experts, patients and carers. The Committee uses all the evidence to make its first recommendations, in a document called the 'appraisal consultation document' (ACD). NICE sends all the consultees and commentators a copy of this document and posts it on the NICE Web site. Further comments are invited from everyone taking part.

When the Committee meets again it considers any comments submitted on the ACD; then it prepares its final recommendations in a document called the 'final appraisal determination' (FAD). This is submitted to NICE for approval.

Consultees have a chance to appeal against the final recommendations in the FAD. If there are no appeals, the final recommendations become the basis of the guidance that NICE issues.

Who Is on the Appraisal Committee?

NICE technology appraisal recommendations are prepared by an independent committee. This includes health professionals working in the NHS and people who are familiar with the issues affecting patients and carers. Although the Appraisal Committee seeks the views of organisations representing health professionals, patients, carers, manufacturers and government, its advice is independent of any vested interests.

Rating Scheme for the Strength of the Recommendations

Not applicable

Cost Analysis

Summary of Appraisal Committee's Key Conclusions

Availability and Nature of Evidence

The Committee concluded that although the company's model had some limitations, particularly because health state-specific utilities were used for these comparisons rather than treatment-specific utilities, overall it was an acceptable option for modelling treatment in this population.

The Committee stated that it would have preferred to see a fully incremental analysis as described in the guide to the methods of technology appraisals but, in its absence, concluded that the incremental cost-effectiveness ratios (ICERs) presented in the pairwise analyses were sufficient evidence on which to base its decisions.

Uncertainties Around and Plausibility of Assumptions and Inputs in the Economic Model

The Committee heard from the Evidence Review Group (ERG) that it would have been more appropriate to use health state-dependent utility values only, rather than assuming different utilities for the treatment arms. The Committee understood from the ERG that the non-opioid-induced constipation (OIC) (on treatment) state in the model was too broad; that is, the model structure included a heterogeneous group of patients with different number of spontaneous bowel movements (SBMs) during the same period, and that applying a single utility value to that health state would not accurately reflect patient experience in that state. The Committee understood from the ERG that although the model should have included more discrete health states reflective of the typical experience of a person with OIC, taking this approach may not necessarily have changed the model results.

Incorporation of Health-related Quality-of-Life Benefits and Utility Values. Have Any Potential Significant and Substantial Health-related Benefits Been Identified That Were Not Included in the Economic Model, and How Have They Been Considered?

The Committee heard from the ERG that it would have been more appropriate to use health state-dependent utility values only, rather than assuming different utilities for the treatment arms. The Committee understood from the ERG that although the model should have included more discrete health states reflective of the typical experience of a person with OIC, taking this approach may not necessarily have changed the model results.

The Committee considered whether naloxegol could be considered innovative in its potential to make a substantial effect on health-related benefits for people with OIC and whether it could be considered a step-change in the management of OIC. It is noted that naloxone has been in use for many years and that the only innovation it could discern was the attachment of a polyethylene glycol molecule to naloxone in order to prevent it from crossing the blood-brain barrier. The Committee considered that the pegylation of naloxegol provides advantages; however, there were no

additional gains in health-related quality of life over those already included in the quality-adjusted life year (QALY) calculations.

Are There Specific Groups of People for Whom the Technology Is Particularly Cost Effective?

Not applicable

What Are the Key Drivers of Cost-effectiveness?

The health-state utility was a key driver of cost effectiveness because of the way the model was structured, in that the non-OIC (on treatment) state was broad; that is, it included a heterogeneous group of patients with different number of SBMs during the same period, and that applying a single utility value to that health state would not accurately reflect patient experience in that state.

Most Likely Cost-effectiveness Estimate (Given as an ICER)

The Committee noted that the company's base-case results and most of the ERG's exploratory analyses for naloxegol compared with placebo (with bisacodyl) resulted in ICERs up to £13,000 per QALY gained. In addition, naloxegol dominated (that is, was both more effective and less costly) methylnaltrexone and naloxone-oxycodone in almost every scenario except when naloxegol was given with oxycodone compared with naloxone-oxycodone (which produced an ICER of £34,100 per QALY gained), but as naloxone-oxycodone is rarely used in England, this ICER was not central to the Committee's decision making.

The Committee concluded that in light of the robustness of the company's model, the ICERs being mostly below £20,000 per QALY gained for the comparison of naloxegol plus bisacodyl with placebo plus bisacodyl, and naloxegol mostly dominating methylnaltrexone and naloxone-oxycodone, naloxegol was considered a cost-effective use of National Health Service (NHS) resources. The Committee therefore recommended naloxegol as an option within its marketing authorisation for people with OIC that has not responded adequately to laxatives.

Method of Guideline Validation

External Peer Review

Description of Method of Guideline Validation

Consultee organisations from the following groups were invited to comment on the draft scope, Assessment Report and the appraisal consultation document (ACD) and were provided with the opportunity to appeal against the final appraisal determination (FAD).

- Manufacturer/sponsors
- Professional/specialist and patient/carer groups
- Commentator organisations (without the right of appeal)

In addition, individuals selected from clinical expert and patient advocate nominations from the professional/specialist and patient/carer groups were also invited to comment on the ACD.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of evidence supporting the recommendation is not specifically stated.

The Appraisal Committee considered clinical and cost-effectiveness evidence submitted by the manufacturer of naloxegol and a review of this submission by the Evidence Review Group (ERG). The main clinical effectiveness evidence came from 2 randomised controlled trials (RCTs). For cost-effectiveness, the Appraisal Committee considered an economic model submitted by the manufacturer.

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Potential Benefits

Appropriate use of naloxegol for treating opioid-induced constipation (OIC)

Potential Harms

The most commonly reported adverse reactions to naloxegol are abdominal pain, diarrhoea, nausea, headache and flatulence. The majority of gastrointestinal adverse reactions are graded as mild to moderate, occur early in treatment and resolve with continued treatment.

For full details of adverse reactions and contraindications, see the summary of product characteristics.

Qualifying Statements

Qualifying Statements

- This guidance represents the views of the National Institute for Health and Care Excellence (NICE) and was arrived at after careful consideration of the evidence available. Healthcare professionals are expected to take it fully into account when exercising their clinical judgement. However, the guidance does not override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.
- Implementation of this guidance is the responsibility of local commissioners and/or providers. Commissioners and providers are reminded that it is their responsibility to implement the guidance, in their local context, in light of their duties to have due regard to the need to eliminate unlawful discrimination, advance equality of opportunity and foster good relations. Nothing in this guidance should be interpreted in a way that would be inconsistent with compliance with those duties.

Implementation of the Guideline

Description of Implementation Strategy

- Section 7(6) of the National Institute for Health and Care Excellence (NICE) (Constitution and Functions) and the Health and Social Care Information Centre (Functions) Regulations 2013 requires clinical commissioning groups, National Health Service (NHS) England and, with respect to their public health functions, local authorities to comply with the recommendations in this appraisal within 3 months of its date of publication.
- When NICE recommends a treatment 'as an option', the NHS must make sure it is available within the period set out in the paragraph above. This means that, if a patient has opioid-induced constipation (OIC) and the doctor responsible for their care thinks that naloxegol is the right treatment, it should be available for use, in line with NICE's recommendations.
- The Welsh Assembly Minister for Health and Social Services has issued directions to the NHS in Wales on implementing NICE technology appraisal guidance. When a NICE technology appraisal recommends the use of a drug or treatment, or other technology, the NHS in Wales must usually provide funding and resources for it within 3 months of the guidance being published.

Implementation Tools

Mobile Device Resources

Patient Resources

Resources

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report

Categories

IOM Care Need

Getting Better

Living with Illness

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)

National Institute for Health and Care Excellence (NICE). Naloxegol for treating opioid-induced constipation. London (UK): National Institute for Health and Care Excellence (NICE); 2015 Jul. 44 p. (Technology appraisal guidance; no. 345).

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2015 Jul

Guideline Developer(s)

National Institute for Health and Care Excellence (NICE) - National Government Agency [Non-U.S.]

Source(s) of Funding

National Institute for Health and Care Excellence (NICE)

Guideline Committee

Appraisal Committee

Composition of Group That Authored the Guideline

Committee Members: Professor Eugene Milne (*Vice Chair of Appraisal Committee C*), Director of Public Health, City of Newcastle upon Tyne; Professor Kathryn Abel, Institute of Brain and Behaviour Mental Health, University of Manchester; David Chandler, Lay member; Gail Coster, Advanced Practice Sonographer, Mid Yorkshire Hospitals NHS Trust; Professor Peter Crome, Honorary Professor, Dept of Primary Care and Population Health, University College London; Professor Rachel A Elliott, Lord Trent Professor of Medicines and Health, University of

Nottingham; Dr Nigel Langford, Consultant in Clinical Pharmacology and Therapeutics and Acute Physician, Leicester Royal Infirmary; Dr Claire McKenna, Research Fellow in Health Economics, University of York; Dr Iain Miller, Founder and CEO, Health Strategies Group; Professor Stephen O'Brien, Professor of Haematology, Newcastle University; Dr Anna O'Neill, Deputy Head of Nursing & Healthcare School/Senior Clinical University Teacher, University of Glasgow; Dr John Radford, General Practitioner, NHS Sheffield; Professor Peter Selby, Consultant Physician, Central Manchester University Hospitals NHS Foundation Trust; Professor Matt Stevenson, Technical Director, School of Health and Related Research, University of Sheffield; Dr Paul Tappenden, Reader in Health Economic Modelling, School of Health and Related Research, University of Sheffield; Dr Judith Wardle, Lay member

Financial Disclosures/Conflicts of Interest

Committee members are asked to declare any interests in the technology to be appraised. If it is considered there is a conflict of interest, the member is excluded from participating further in that appraisal.

The minutes of each Appraisal Committee meeting, which include the names of the members who attended and their declarations of interests, are posted on the National Institute for Health and Care Excellence (NICE) Web site.

Guideline Status

This is the current release of the guideline.

This guideline meets NGC's 2013 (revised) inclusion criteria.

Guideline Availability

Available from the National Institute for Health and Care Excellence (NICE) Web site .

Availability of Companion Documents

The following are available:

- Naloxegol for treating opioid-induced constipation. Costing statement. London (UK): National Institute for Health and Care Excellence (NICE); 2015 Jul. 7 p. (Technology appraisal guidance; no. 345). Available from the National Institute for Health and Care Excellence (NICE) Web site .
- Wolff R, Al M, Zaim R, Lang S, Leunis A, Noake C, Ryder S, Worthy G, Stirk L, Armstrong N, Riemsma R, Severens JL, Kleijnen J. Naloxegol for treating opioid-induced constipation: a single technology appraisal. York (UK): Kleijnen Systematic Reviews Ltd.; 2015. 122 p. Available from the NICE Web site .
- Naloxegol for treating opioid-induced constipation. Single technology appraisal. Manufacturer's submission. AstraZeneca; 2014 Nov 7. 460 p. Available from the NICE Web site .

Patient Resources

The following is available:

- Naloxegol for treating opioid-induced constipation. Information for the public. London (UK): National Institute for Health and Care Excellence (NICE); 2015 Jul. 2 p. (Technology appraisal guidance; no. 345). Available from the National Institute for Health and Care Excellence (NICE) Web site . Also available for download in eBook or ePub formats from the NICE Web site .

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

NGC Status

This NGC summary was completed by ECRI Institute on September 10, 2015.

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