NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

GUIDANCE EXECUTIVE (GE)

Technology Appraisal Review Proposal paper

Review of 325; Nalmefene for reducing alcohol consumption in people with alcohol dependence

Original publication date:	November 2014
Review date	November 2017
Existing recommendations:	Recommended To see the complete existing recommendations and the original remit for 325, see Appendix A.

1. Proposal

The guidance should be transferred to the static list.

2. Rationale

There are no new data to warrant a review of this appraisal.

3. Summary of new evidence and implications for review

Nalmefene was found to be cost effective in Technology Appraisal 325 with a most plausible ICER of £5100 per QALY gained. The price has not changed and there are no new clinical data for nalmefene. There is therefore no new data to suggest that the recommendations would change if this guidance was reviewed.

Has there been any change to the price of the technology(ies) since the guidance was published?
No
Are there any existing or proposed changes to the marketing authorisation that would affect the existing guidance?
No

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Were any uncertainties identified in the original guidance? Is there any new evidence that might address this?
The population for whom nalmefene is licensed was a subgroup of the clinical trial populations. The clinical trials were not powered for post-hoc analyses of treatment effect in this subgroup and the committee concluded that the exact magnitude of the treatment effect was uncertain because of this. The committee was also aware that the Scientific Advisory Group to the European Medicines Agency recognised the validity of the subgroup analyses in granting a marketing authorisation for nalmefene. The committee accepted that the post hoc subgroup analyses were sufficiently robust for its decision making. There have been no further published controlled trials or observational studies of nalmefene since technology appraisal 325.
Are there any related pieces of NICE guidance relevant to this appraisal? If so, what implications might this have for the existing guidance?
See Appendix C for a list of related NICE guidance.
Additional comments
Naltrexone plus psychosocial intervention was not considered a comparator in technology appraisal 325 because it was not part of established practice for the reduction of alcohol consumption. There is no new data to suggest that this off-label use of naltrexone (for reduction of, rather than abstinence from, alcohol consumption) is now established practice. There has been further criticism of the strength and robustness of the clinical evidence for nalmefene since Technology Appraisal 325 was published[1,2]. Scepticism of the clinical evidence has been identified as one factor contributing to poor uptake of nalmefene in clinical practice in a report published by the NICE implementation collaborative[3]. That report recommended monitoring the outcomes of people currently receiving nalmefene, but noted that this was not routinely done and there is no national framework for this data collection[3]. The company has stated that it is not actively promoting the sale of nalmefene in the UK, although it remains available to patients and prescribers.

The search strategy from the original ERG report was adapted and re-run on the Cochrane Library, Medline, Medline In-Process and Embase. References from September 2013 onwards were reviewed. Additional searches of clinical trials registries and other sources were also carried out. The results of the literature search are discussed in the 'Summary of evidence and implications for review'

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section above. See Appendix C for further details of ongoing and unpublished studies.

4. Equality issues

The Committee noted the equality issue raised, suggesting that there could be issues with consent of treatment in certain populations in terms of cognitive decline and learning disability. The Committee considered that healthcare professionals should be mindful of the need to ensure equality of access to treatment for patients with disabilities.

GE paper sign off: **Helen Knight, 15/03/2018**

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Appendix A – Information from existing guidance

5. Original remit

To appraise the clinical and cost effectiveness (allowing adoption of a wider perspective than the NHS and Personal and Social Services) of nalmefene within its licensed indication for reducing alcohol consumption in people with alcohol dependence.

6. Current guidance

1.1 Nalmefene is recommended within its marketing authorisation, as an option for reducing alcohol consumption, for people with alcohol dependence:

- who have a high drinking risk level (defined as alcohol consumption of more than 60 g per day for men and more than 40 g per day for women, according to the World Health Organization's drinking risk levels) without physical withdrawal symptoms and
- who do not require immediate detoxification.

The marketing authorisation states that nalmefene should:

- only be prescribed in conjunction with continuous psychosocial support focused on treatment adherence and reducing alcohol consumption and
- be initiated only in patients who continue to have a high drinking risk level 2 weeks after initial assessment.

7. Research recommendations from original guidance

Not applicable.

8. Cost information from original guidance

“Nalmefene is available as an 18 mg film-coated tablet and is priced at £42.42 for a pack of 14 tablets or £84.84 for a packet of 28 tablets (excluding VAT; 'British national formulary' [BNF], online April 2014). It is taken orally at a maximum dose of 1 tablet daily on an 'as-needed' basis. “

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Appendix B – Explanation of options

When considering whether to review one of its Technology Appraisals NICE must select one of the options in the table below:

Options	Consequence	Selected – 'Yes/No'
A review of the guidance should be planned into the appraisal work programme. The review will be conducted through the Technology Appraisals process.	A review of the appraisal will be planned into the NICE's work programme.	No
The decision to review the guidance should be deferred for a specific trail date.	NICE will reconsider whether a review is necessary at the specified date.	No
A review of the guidance should be combined with a review of a related technology appraisal. The review will be conducted through the MTA process.	A review of the appraisal(s) will be planned into NICE's work programme as a Multiple Technology Appraisal, alongside the specified related technology.	No
A review of the guidance should be combined with a new technology appraisal that has recently been referred to NICE. The review will be conducted through the MTA process.	A review of the appraisal(s) will be planned into NICE's work programme as a Multiple Technology Appraisal, alongside the newly referred technology.	No
The guidance should be incorporated into an on-going clinical guideline.	The on-going guideline will include the recommendations of the technology appraisal. The technology appraisal will remain extant alongside the guideline. Normally it will also be recommended that the technology appraisal guidance is moved to the static list until such time as the clinical guideline is considered for review. This option has the effect of preserving the funding direction associated with a positive recommendation in a NICE technology appraisal.	No

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Appendix B

Options	Consequence	Selected – 'Yes/No'
The guidance should be updated in an on-going clinical guideline[1].	Responsibility for the updating the technology appraisal passes to the NICE Clinical Guidelines programme. Once the guideline is published the technology appraisal will be withdrawn. Note that this option does not preserve the funding direction associated with a positive recommendation in a NICE Technology Appraisal. However, if the recommendations are unchanged from the technology appraisal, the technology appraisal can be left in place (effectively the same as incorporation).	No
The guidance should be transferred to the 'static guidance list'.	The guidance will remain in place, in its current form, unless NICE becomes aware of substantive information which would make it reconsider. Literature searches are carried out every 5 years to check whether any of the Appraisals on the static list should be flagged for review.	Yes
The guidance should be withdrawn	The guidance is no longer relevant and an update of the existing recommendations would not add value to the NHS. The guidance will be stood down and any funding direction associated with a positive recommendation will not be preserved.	No

[1] Information on the criteria for NICE allowing a technology appraisal in an ongoing clinical guideline can be found in section 6.20 of the guide to the processes of technology appraisal.

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Appendix C – other relevant information Relevant Institute work

Published

Alcohol-use disorders: diagnosis, assessment and management of harmful drinking and alcohol dependence (2011) NICE guideline CG115. *Next review date: 2019.*

Alcohol-use disorders: diagnosis and management of physical complications (2010, updated 2017) NICE guideline CG100. *Next review date: 2019.*

Alcohol-use disorders: prevention (2010) NICE guideline PH24. *The latest review information on the NICE website (2014) says: "…The recommendation therefore is not to update the guidance at this time but to review again in 2016.*

Alcohol: school-based interventions (2007) NICE guideline PH7. *This guidance is in the process of being updated and replaced by "Alcohol interventions in schools", and publication is expected in January 2019.*

Coexisting severe mental illness (psychosis) and substance misuse: assessment and management in healthcare settings (2011) NICE guideline CG120. *Surveillance report 2016: "After considering all the new evidence and views of topic experts, we decided that an update is not necessary for this guideline."*

In progress

No relevant information was found.

Referred - QSs and CGs

No relevant information was found.

Suspended/terminated

No relevant information was found.

1. Details of new products

No relevant information was found, including in topic selection.

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There is a 2017 review, captured by the search, which suggests *"A number of other agents are being investigated for potential use for this indication including: baclofen, topiramate and metadoxine."* None are listed on SPS for this indication. There is a Cochrane review protocol on 'baclofen for alcohol use disorder' captured by the search.

[redacted]

2. Details of changes to the indications of the technology

Indication and price considered in original appraisal	Proposed indication (for this appraisal) and current price
No changes	No changes

3. Registered and unpublished trials

Trial name and registration number	Details
NCT02382276 A Long-term Extension Study for the Phase 3 Study of Nalmefene (339-14-001) in Patients With Alcohol Dependence	Phase not given. Ongoing not recruiting. Estimated enrolment: 400. Estimated primary completion date: March 2018.
NCT02492581 Use of Selincro and Impact on Usual Practice (USE-PACT)	Phase III. Ongoing not recruiting. Estimated enrolment: 698. Estimated primary completion date: February 2018.

4. Relevant services covered by NHS England specialised commissioning

As part of their public health remit, local authorities are responsible for commissioning alcohol and drug interventions and services:

"From April 2013, local councils will have a public health grant, which will include money for alcohol services." Source: "Policy paper 2010 to 2015 government policy: harmful drinking (updated 8 May 2015)"

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5. Additional information

There has been a supply issue with Disulfiram, which appears to be still ongoing (see the Teva press release 12 July 17).

Appendix D – References

1) Palpacuer C, Laviolle B, Boussageon R, Reymann J M, Bellissant E, and Naudet F (2015) Risks and Benefits of Nalmefene in the Treatment of Adult Alcohol Dependence: A Systematic Literature Review and Meta-Analysis of Published and Unpublished Double-Blind Randomized Controlled Trials. PLoS Medicine 12(12), e1001924

2) Fitzgerald Niamh, Angus Kathryn, Elders Andrew, de Andrade , Marisa , Raistrick Duncan, Heather Nick, and McCambridge Jim (2016) Weak evidence on nalmefene creates dilemmas for clinicians and poses questions for regulators and researchers.. Addiction (Abingdon, and England) 111(8), 1477-87

3) NICE implementation collaborative (2017) Supporting local implementation of NICE technology Appraisal 325 on reducing alcohol consumption in adults with alcohol dependence, accessed 6 September 2017.

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