NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

GUIDANCE EXECUTIVE (GE)

Technology Appraisal Review Proposal paper

Review of 494; Naltrexone-bupropion (prolonged release) for managing overweight and obesity

Original Publication date

1. 12 December 2017

Review date

2. 2020

Existing recommendations

3. Not recommended. To see the complete existing recommendations and the original remit for TA494, see Appendix A.

Proposal

4. The guidance should be cross referenced to in an on-going guideline (CG189). TA494 will be added to the static guidance list.

Rationale

5. There is no new evidence to address the uncertainties in original guidance. The clinical guidelines for “Obesity: identification, assessment and management”, CG189, are being updated, and guidance for this appraisal should be cross referred in this, due to its relevance to the condition. TA494 will be added to the static guidance list and will remain extant alongside the guideline. Because the technology is not recommended, there are no implications for the funding direction.

Summary of new evidence and implications for review

6. In the original guidance, the committee believed there to be several areas of uncertainty regarding naltrexone-bupropion as a treatment for managing overweight and obesity. Searches have identified that no new evidence has been published since the guidance publication that could be expected to address these uncertainties or lead to a change in the recommendations.

Has there been any change to the price of the technology since the guidance was published?
No
Are there any existing or proposed changes to the marketing authorisation that would affect the existing guidance?
No
Were any uncertainties identified in the original guidance? Is there any new evidence that might address this?
The committee believed there to be a number of uncertainties surrounding the clinical and cost-effectiveness of naltrexone-bupropion for managing overweight and obesity in adults alongside a reduced-calorie diet and increased physical activity. These included the short duration of pivotal clinical trials, inability of the model used to capture episodes of retreatment and uncertainty regarding weight gain once treatment had stopped. Further to this, the committee had concerns regarding the small QALY benefit and noted that the cost-effectiveness of naltrexone-bupropion was highly sensitive to changes in the QALYs. There is no new identified evidence that might address these issues. A limited extension of clinical efficacy data was published, extending the original trial data from 56 weeks to 78 weeks (Halseth et al 2017), but this is not expected to cause a change in the recommendation of the committee, or address the other areas of uncertainty within the appraisal. The company filed an appeal against the negative recommendation, which was heard in October 2017. During the appeal hearing, NICE stated that it did not expect that it would be likely that new data would emerge to address uncertainties that appeared during the appraisal process.
Are there any related pieces of NICE guidance relevant to this appraisal? If so, what implications might this have for the existing guidance?
The cross reference to TA494 will be included in the scope of the CG189 guideline. The commissioning date for the CG189 guideline is February 19. *See Appendix C for a list of related NICE guidance.*
Additional comments
A trial with 40 expected participants is due to complete in March 2020, which could be relevant for the next review of TA494, see appendix C section 3.

The search strategy from the original ERG report was adapted for the Cochrane Library, Medline, Medline In-Process and Embase. References from June 2016 to October 2018 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’ section above. See Appendix C for further details of ongoing and unpublished studies.

Equality issues

No equality issues were raised in relation to the original guidance.

Proposal paper sign-off:

Janet Robertson, Associate Director – Technology Appraisals, 14 January 2020

Contributors to this paper:

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Appendix A – Information from existing guidance

1. Original remit

To appraise the clinical and cost effectiveness of naltrexone-bupropion prolonged release within its licensed indication, in addition to diet and physical activity, for the management of people with obesity or overweight with risk factors.

2. Current guidance

1.1 Naltrexone–bupropion is not recommended within its marketing authorisation for managing overweight and obesity in adults alongside a reduced-calorie diet and increased physical activity.

1.2 This recommendation is not intended to affect treatment with naltrexone–bupropion that was started in the NHS before this guidance was published. Adults having treatment outside this recommendation may continue without change to the funding arrangements in place for them before this guidance was published, until they and their NHS clinician consider it appropriate to stop.

3. Research recommendations from original guidance

N/A

4. Cost information from original guidance

Acquisition cost (excluding VAT) £73.00 per pack of 112 tablets (source: company's submission). Costs may vary in different settings because of negotiated procurement discounts.

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 to December 2020.	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 cross-referenced in an on-going 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 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.	**Yes**

Appendix B

Options	Consequence	Selected – 'Yes/No'
The guidance should be updated in an on-going guideline[1].	Responsibility for the updating the technology appraisal passes to the NICE 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 guideline can be found in section 6.20 of the guide to the processes of technology appraisal.

Appendix C – other relevant information

1. Relevant Institute work

Published

Obese, overweight with risk factors: liraglutide (Saxenda) (2017) NICE evidence summary 14

Obesity: clinical assessment and management (2016) NICE quality standard 127

Obesity in adults: prevention and lifestyle weight management programmes (2016) NICE quality standard 111

Preventing excess weight gain (2015) NICE guideline NG7

Obesity: identification, assessment and management (2014) NICE guideline CG189

Weight management: lifestyle services for overweight or obese adults (2014) NICE guideline PH53

Weight management: lifestyle services for overweight or obese children and young people (2013) NICE guideline PH47

BMI: preventing ill health and premature death in black, Asian and other minority ethnic groups (2013) NICE guideline PH46

In progress

Liraglutide for managing overweight and obesity [ID740] NICE technology appraisal guidance. Publication date to be confirmed

Suspended/terminated

Lorcaserin hydrochloride for the treatment of obesity and overweight [ID337] NICE technology appraisal guidance. Publication date to be confirmed.
Status: suspended (May 2013) – licensing application withdrawn

Phentermine with topiramate for the treatment of obesity and overweight [ID543] NICE technology appraisal guidance. Publication date to be confirmed.
Status: suspended (April 2013) – received CHMP negative opinion

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
Adjunct to a reduced-calorie diet and increased physical activity, for the management of weight in adult	No change Source: current SPC (November 2018)

Indication and price considered in original appraisal	Proposed indication (for this appraisal) and current price
patients (aged 18 and over) with an initial BMI of • 30 kg/m2 or more (obese) or • from 27 kg/m2 to 30 kg/m2 (overweight) in the presence of one or more weight-related co-morbidities (such as type 2 diabetes, dyslipidaemia, or controlled hypertension). Treatment should be stopped after 16 weeks if the patient has not lost at least 5% of their initial body weight. Acquisition cost (excluding VAT) £73.00 per pack of 112 tablets (source: company's submission). Costs may vary in different settings because of negotiated procurement discounts.	No change Source: current BNF (6 November 2018)

3. Registered and unpublished trials

Trial name and registration number	Details
A Multicenter, Randomized, Open-Label, Controlled, Method-of-Use Study Assessing the Effect of Naltrexone Sustained Release (SR)/Bupropion SR on Body Weight and Cardiovascular Risk Factors in Overweight and Obese Subjects NCT01764386 IGNITE	Phase: 3 Status: completed Completion date: September 2014 Primary outcome: Percent Change in Body Weight From Baseline (Day 1) to Week 26 Enrolment: 242 Results: available

Appendix C

Trial name and registration number	Details
A Multicenter, Randomized, Double-Blind, Placebo-Controlled, Phase 4 Study to Assess the Effect of Naltrexone Hydrochloride and Bupropion Hydrochloride Extended Release Combination on the Occurrence of Major Adverse Cardiovascular Events in Overweight and Obese Subjects With Cardiovascular Disease NCT02638129	Phase: 4 Status: terminated Primary outcome: 1.Time From Treatment Period Randomization to the First Confirmed Occurrence of Major Adverse Cardiovascular Events (MACE) Enrolment: 67 Results: available
A Pilot Trial of Naltrexone-Bupropion Combination Versus Placebo Combined With Bupropion for Weight Loss in Comorbid Schizophrenia and Diabetes NCT03132571	Phase: 4 Status: recruiting Expected completion date: March 2020 Primary outcome: Change in BMI from baseline Enrolment: 40

Appendix D – References

Halseth A et al. (2017) Method-of-use study of naltrexone sustained release (SR)/bupropion SR on body weight in individuals with obesity. Obesity, 25(2): 338-345.