

## NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

## Single Technology Appraisal

## Naltrexone-bupropion (prolonged release) for managing overweight and obesity

## Final Scope

**Remit/appraisal objective**

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.

**Background**

Overweight and obesity is a chronic condition characterised by increased body fat. People who are overweight or obese are at an increased risk of developing cardiovascular disease, type 2 diabetes, atherosclerosis (the presence of fatty deposits in the arteries), hypertension and dyslipidaemia (abnormal levels of fats in the blood). The most common method for measuring obesity is body mass index (BMI) which is calculated as the ratio of weight to height squared. In adults of European family origin, overweight is typically defined by a BMI of 25 kg/m<sup>2</sup> to <30 kg/m<sup>2</sup> and obesity by a BMI of 30 kg/m<sup>2</sup> or more (an appropriate adjustment of BMI for other ethnic groups is necessary).

In England, 24% of adults are obese and a further 36% are overweight. Of obese adults, seven in ten are Class I obese, with a BMI between 30 and 35. Around one in ten obese adults are morbidly obese, with a BMI above 40<sup>1</sup>. The prevalence of obesity has seen a sharp increase from the 1990s<sup>2</sup>. By 2050 the prevalence of obesity is predicted to affect 60% of adult men, 50% of adult women<sup>2</sup>. Drug items dispensed for managing obesity rose 44 per cent from 2012 to 563,000 in 2013<sup>3</sup>.

Current management of overweight and obesity includes dietary and lifestyle advice, behaviour modification, pharmacological treatments and surgical intervention. Specialist multi-disciplinary weight management interventions (known as tier 3 interventions) are also used in current practice. Tier 3 interventions include dietary, lifestyle and behaviour modification with or without drug therapy. NICE clinical guideline 189 'Obesity: identification, assessment and management' recommends that drug therapy with orlistat should only be considered after dietary, physical activity and behavioural approaches have been started and evaluated. It recommends orlistat for the management of obesity in people with a BMI of 30 kg/m<sup>2</sup> or more, and in people with a BMI of 28 kg/m<sup>2</sup> or more and significant comorbidities. If dietary and lifestyle advice, behaviour modification and drug treatments are unsuccessful, the NICE clinical guideline recommends bariatric surgery for people with: a BMI of 40 kg/m<sup>2</sup> or more; a BMI of between 35 kg/m<sup>2</sup> and

40 kg/m<sup>2</sup> with significant comorbidities, a BMI between 30 kg/m<sup>2</sup> and < 35 kg/m<sup>2</sup> and with recent-onset of type 2 diabetes (surgery can be considered for people of Asian family origin who have recent-onset type 2 diabetes at a lower BMI than other populations).

### The technology

Naltrexone-bupropion (Mysimba, Orexigen Therapeutics) is a fixed dose combination of naltrexone and bupropion administered orally in a prolonged-release tablet. Naltrexone is an opioid receptor antagonist and bupropion is a dopamine and noradrenaline reuptake inhibitor. The exact neurochemical appetite suppressant effect of naltrexone-bupropion is not fully understood. It is thought to stimulate pro-opiomelanocortin neuronal firing and modulates food cravings through an effect on the reward pathways of the brain.

Naltrexone-bupropion has marketing authorisation in Europe 'as an adjunct to a reduced-calorie diet and increased physical activity for the management of weight in adults with a BMI of  $\geq 30$  kg/m<sup>2</sup> (obese) or  $\geq 27$  kg/m<sup>2</sup> to < 30 kg/m<sup>2</sup> (overweight) in the presence of one or more weight-related co-morbidities'.

<b>Intervention(s)</b>	Naltrexone-bupropion prolonged-release
<b>Population(s)</b>	Adults who have a BMI of; <ul style="list-style-type: none"> <li>• <math>\geq 30</math> kg/m<sup>2</sup> (obese) or</li> <li>• <math>\geq 27</math> kg/m<sup>2</sup> to &lt; 30 kg/m<sup>2</sup> (overweight) in the presence of one or more weight-related co-morbidities</li> </ul>
<b>Comparators</b>	<ul style="list-style-type: none"> <li>• Standard management without naltrexone-bupropion</li> <li>• Orlistat (prescription dose)</li> </ul>
<b>Outcomes</b>	<p>The outcome measures to be considered include:</p> <ul style="list-style-type: none"> <li>• BMI</li> <li>• weight loss</li> <li>• percentage body fat</li> <li>• waist circumference</li> <li>• incidence of type 2 diabetes</li> <li>• cardiovascular events</li> <li>• mortality</li> <li>• adverse effects of treatment</li> <li>• health-related quality of life</li> </ul> <p>Where information on clinical endpoints is unavailable, consideration may be given to surrogate end-points such</p>

	<p>as:</p> <ul style="list-style-type: none"> <li>• glycated haemoglobin (HbA1c)</li> <li>• cholesterol levels and lipid profiles (including LDL and HDL)</li> <li>• blood pressure</li> </ul>
<b>Economic analysis</b>	<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>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>
<b>Other considerations</b>	<p>If the evidence allows, the following subgroup should be considered: people with type 2 diabetes.</p> <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 in the context of the evidence that has underpinned the marketing authorisation granted by the regulator.</p>
<b>Related NICE recommendations and NICE Pathways</b>	<p><b>Related Guidelines:</b></p> <p>Guideline in development 'Obesity: guidance on the prevention, identification, assessment and management of overweight and obesity in adults and children (update)'. Date of publication November 2014.</p> <p>Clinical Guideline No. 189, 'Obesity: guidance on the identification, assessment and management obesity in adults and children' Date of publication November 2014</p> <p>Clinical guideline No. 43. 'Obesity prevention in adults and children' Guidance updated March 2015</p> <p><b>Related Interventional Procedures:</b></p> <p>Interventional Procedure Guideline No. 432, November 2013, 'Laparoscopic gastric plication for the treatment of severe obesity'.</p> <p>Interventional Procedure Guidance No. 471, November 2012, 'Implantation of a duodenal-jejunal bypass sleeve for managing obesity'.</p> <p><b>Related Public Health Guidance/Guidelines:</b></p>

	<p>Public Health Guideline No. 53. 'Weight management: lifestyle services for overweight or obese adults'. Publication date May 2014.</p> <p>Public Health Guideline No. 47, October 2013, 'Managing overweight and obesity among children and young people'. Review proposal date 2017.</p> <p>Public Health Guideline No. 42, November 2012, 'Obesity – working with local communities'. Review proposal date 2017.</p> <p><b>Related Quality Standards:</b></p> <p>Obesity: clinical assessment and management [QS127] (adults). Published August 2017.</p> <p>Obesity in adults: prevention and lifestyle weight management programmes [QS111]. Published January 2016</p> <p>Obesity in children and young people: prevention and lifestyle weight management programmes [QS94]. Published July 2015</p> <p><b>Related NICE Pathways:</b></p> <p>NICE Pathway: Obesity, Pathway updated August 2016  <a href="http://pathways.nice.org.uk/pathways/obesity">http://pathways.nice.org.uk/pathways/obesity</a></p> <p>NICE Pathway: Obesity: working with local communities, Pathway updated: March 2016.  <a href="http://pathways.nice.org.uk/pathways/obesity-working-with-local-communities">http://pathways.nice.org.uk/pathways/obesity-working-with-local-communities</a></p>
<b>Related National Policy</b>	<p>NHS England (2013) '<a href="#">2013/14 NHS Standard contract for severe and complex obesity (all ages)</a>'. A05/S/a.</p> <p>NHS England (2013) '<a href="#">Clinical commissioning policy and specialised obesity surgery</a>'. NHS England/A05/P/a.</p>

## References

1. [Obesity statistics; House of Commons Library](#). Accessed September 2016.
2. [Adult Obesity; Public health England](#). Accessed September 2016
3. [HSCIC Statistics on obesity, physical activity and diet; England 2015](#). Accessed September 2016