

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Setmelanotide for treating acquired hypothalamic obesity in people 4 years and over ID6542

Final scope

Remit/evaluation objective

To appraise the clinical and cost effectiveness of setmelanotide within its marketing authorisation for treating acquired hypothalamic obesity in people 4 years and over.

Background

Acquired hypothalamic obesity (aHO) is a rare subtype of obesity. Unlike general obesity, aHO typically results from physical damage to the hypothalamus. This damage may occur due to brain tumours or as a complication of brain tumour surgery. Other possible causes include traumatic brain injury, infections, inflammatory conditions, radiation therapy, or bleeding in the brain.¹

aHO is characterized by rapid weight gain due to reduced metabolic rate and feelings of excessive or insatiable hunger (hyperphagia). This increases the risk of developing cardiovascular disease, kidney disease, type 2 diabetes, atherosclerosis (the presence of fatty deposits in the arteries), hypertension and dyslipidaemia (abnormal levels of fats in the blood). Also, hyperphagia can have a substantial impact on the quality of life of people with aHO and their caregivers. People with aHO also commonly experience other symptoms associated with hypothalamic dysfunction, including hypopituitarism, behavioural difficulties, temperature dysregulation and autonomic dysfunction (collectively known as hypothalamic syndrome). This is because the hypothalamus is a region of the brain that has many important functions including energy balance, temperature and autonomic nervous system regulation, modulation of sleep and daily (circadian) rhythm, and controlling pituitary hormones.

The number of people affected by acquired hypothalamic obesity in England is unknown, but estimates suggest the prevalence in Europe is approximately 0.4 per 10,000 people.²

There are currently no licensed targeted treatments for aHO. For the management of overweight and obesity more generally, [NICE guideline \(NG\) 246](#) recommends multicomponent interventions which are tailored to individual needs. Weight management programmes include behaviour change strategies to increase people's physical activity levels or decrease inactivity, improve eating behaviour and the quality of the person's diet, and reduce energy intake. But, due to the pathophysiology and multiple complex morbidities associated with aHO, lifestyle changes typically do not lead to a reduction in weight or BMI for people with this condition.

Several pharmacological treatments are available for the management of overweight and obesity:

- [NICE technology appraisal \(TA\) 664](#) recommends liraglutide alongside a reduced-calorie diet and increased activity in adults with a BMI of at least

35 kg/m², non-diabetic hyperglycaemia and a high risk of cardiovascular disease.

- [NICE technology appraisal \(TA\) 875](#) recommends semaglutide alongside a reduced-calorie diet and increased activity in adults with one weight-related comorbidity and a BMI of at least 35 kg/m² or, a BMI of 30 kg/m² to 34 kg/m² and meet the criteria or referral to specialist weight management services.
- [NICE technology appraisal \(TA\) 1026](#) recommends tirzepatide alongside a reduced-calorie diet and increased physical activity in adults with a BMI of at least 35 kg/m² and at least 1 weight-related comorbidity. In the NICE recommendations above, BMI thresholds are reduced by 2.5 kg/m² for people from some ethnic minority backgrounds.
- Additionally, [NICE NG246](#) recommends orlistat for managing obesity in adults with a BMI of 30 kg/m² or more, and in people with a BMI of 28 kg/m² or more with associated risk factors. It also recommends bariatric surgery as an option for adults who have a BMI of 40 kg/m² or more, or between 35 kg/m² and 39.9 kg/m² and with a significant health condition that could be improved if they lost weight.

Weight management medicines are sometimes taken by children over the age of 12 where co-morbidities are present. [NICE guideline \(NG\) 246](#) states that, in children younger than 12 years, medicines may only be used in exceptional circumstances, if severe comorbidities are present. The use of these treatments in children may be outside of their marketing authorisations. Surgery for obesity may be considered for older children in exceptional circumstances.

The technology

Setmelanotide (Imcivree, Rhythm Pharmaceuticals) does not currently have a marketing authorisation in the UK for treating acquired hypothalamic obesity in people 4 years and above. It has been studied in clinical trials compared with placebo with best supportive care in adults and children 4 years of age and above.

Setmelanotide has a marketing authorisation for the treatment of obesity and the control of hunger associated with genetically confirmed Bardet-Biedl syndrome (BBS), loss-of-function biallelic pro-opiomelanocortin (POMC), including PCSK1, deficiency or biallelic leptin receptor (LEPR) deficiency in adults and children 2 years of age and above.

Intervention	Setmelanotide
Population	People aged 4 years and above with acquired hypothalamic obesity
Subgroups	<p>If evidence allows, consideration may be given to subgroups, based on:</p> <ul style="list-style-type: none"> • Age • Suitability of existing medical treatments (within and outside their marketing authorisations) • Previous treatments

	<p>If consideration is given to these subgroups, the committee will consider any equalities implications of its considerations.</p>
<p>Comparators</p>	<p>Established clinical management without setmelanotide, including but not limited to:</p> <ul style="list-style-type: none"> ○ Tirzepatide ○ Semaglutide ○ Liraglutide ○ Orforglipron (subject to NICE appraisal, ID6516) ○ Orlistat ○ Bariatric surgery ○ Best supportive care
<p>Outcomes</p>	<p>The outcome measures to be considered include:</p> <ul style="list-style-type: none"> ● BMI ● BMI-Z (for children and adolescents) ● weight loss ● percentage body fat ● waist circumference ● hunger ● liver function ● incidence of type 2 diabetes ● clinical measure of diabetic control ● cardiovascular events ● other obesity-related complications (e.g. sleep apnoea) ● mortality ● adverse effects of treatment ● health-related quality of life.

<p>Economic analysis</p>	<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> <p>The availability of any commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account.</p> <p>The availability and cost of biosimilar and generic products should be taken into account.</p>
<p>Other considerations</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 only in the context of the evidence that has underpinned the marketing authorisation granted by the regulator.</p>
<p>Related NICE recommendations</p>	<p>Related technology appraisals:</p> <p>Tirzepatide for managing overweight and obesity (2024) NICE technology appraisal guidance 1026.</p> <p>Semaglutide for managing overweight and obesity (2023). NICE technology appraisal guidance 875.</p> <p>Liraglutide for managing overweight and obesity (2020) NICE technology appraisal guidance 664</p> <p>Related technology appraisals in development</p> <p>Orforglipron for managing overweight and obesity. NICE technology appraisal guidance [ID6516]. Publication date to be confirmed</p> <p>Related NICE guidelines:</p> <p>Overweight and obesity management (2025) NICE guideline NG246</p> <p>Related quality standards:</p> <p>Overweight and obesity management (2025) NICE quality standard QS212</p>

References

1. National Organization for Rare Disorders, [Hypothalamic Obesity, Acquired](#), accessed November 2025
2. EMA, Committee for Orphan Medical Products (COMP), [Minutes for the meeting on 05-07 September 2023](#), accessed November 2025