**NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE**

**Health Technology Evaluation**

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

**Draft scope**

## Draft 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

Obesity is a chronic condition characterised by increased body fat. People who are 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, obesity is typically defined by a BMI of 30 kg/m2 or more. In childhood, obesity is usually defined as a BMI at or above the 95th percentile for individuals of the same age and sex.

Acquired hypothalamic obesity is a rare subtype of obesity characterized by rapid weight gain due to reduced metabolic rate and feelings of excessive or insatiable hunger (hyperphagia). It may follow from an injury to the hypothalamus, a brain region with many important functions including energy balance, temperature and autonomic nervous system regulation, modulation of sleep and daily (circadian) rhythm, and controlling pituitary hormones. This damage may occur due to the growth of brain tumours, or as a complication of brain tumor surgery. Other possible causes include traumatic brain injury, infections, inflammatory conditions, radiation therapy, or bleeding in the brain.[1]

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 acquired hypothalamic obesity. For the management of overweight and obesity, 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.

Pharmacological treatments for the management of overweight and obesity are usually considered only after dietary, exercise and behavioural approaches have been started and evaluated.

- 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/m$^2$, non-diabetic hyperglycaemia and a high risk of cardiovascular disease.


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- 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/m$^2$ or, a BMI of 30 kg/m$^2$ to 34 kg/m$^2$ 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/m$^2$ and at least 1 weight-related comorbidity. In the NICE recommendations above, BMI thresholds are reduced by 2.5 kg/m$^2$ 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 may be used in children over the age of 12 where co-morbidities are present. They are not generally recommended for children younger than 12 years and are typically only used in exceptional circumstances, if severe comorbidities are present. 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 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.

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| **Intervention** | Setmelanotide |
| **Population** | People aged 4 years and above with acquired hypothalamic obesity |
| **Comparators** | Children and young people, age 4 years and above:<br>• Established clinical management without setmelanotide (including a reduced-calorie diet and increased physical activity)<br>• Orlistat (off-label)<br>Adults, age 18 and above:<br>• Established clinical management without setmelanotide (including a reduced-calorie diet and increased physical activity)<br>• Tirzepatide (for the population for whom tirzepatide is recommended in TA1026) |


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| | • Semaglutide (for the population for whom semaglutide is recommended in TA875)<br>• Liraglutide (for the population for whom liraglutide is recommended in TA664)<br>• Orforglipron (subject to NICE appraisal, ID6516)<br>• Orlistat<br>• Bariatric surgery |
| **Outcomes** | The outcome measures to be considered include:<br>• BMI<br>• BMI-Z<br>• weight loss<br>• percentage body fat<br>• waist circumference<br>• hunger<br>• incidence of type 2 diabetes<br>• clinical measure of diabetic control<br>• cardiovascular events<br>• mortality adverse effects of treatment<br>• health-related quality of life. |
| **Economic analysis** | The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year.<br>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.<br>Costs will be considered from an NHS and Personal Social Services perspective.<br>The availability of any commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account.<br>The availability and cost of biosimilar and generic products should be taken into account. |
| **Other considerations** | 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. |
| **Related NICE recommendations** | **Related technology appraisals:** |


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| | Tirzepatide for managing overweight and obesity (2024) NICE technology appraisal guidance 1026.<br><br>Semaglutide for managing overweight and obesity (2023). NICE technology appraisal guidance 875.<br><br>Liraglutide for managing overweight and obesity (2020) NICE technology appraisal guidance 664<br><br>**Related technology appraisals in development**<br><br>Orforglipron for managing overweight and obesity. NICE technology appraisal guidance [ID6516]. Publication date to be confirmed<br><br>**Related NICE guidelines:**<br><br>Overweight and obesity management (2025) NICE guideline NG246<br><br>**Related quality standards:**<br><br>Overweight and obesity management (2025) NICE quality standard QS212 |

**Questions for consultation**

Where do you consider setmelanotide will fit into the existing care pathway for treating acquired hypothalamic obesity in people 6 years and over?

Are medicines used off-label to treat obesity in children and young people under 18 years of age in the NHS? If so, which medicines are used and in what circumstances?

Please select from the following, will setmelanotide be:
A. Prescribed in primary care with routine follow-up in primary care
B. Prescribed in secondary care with routine follow-up in primary care
C. Prescribed in secondary care with routine follow-up in secondary care
D. Other (please give details):
For comparators and subsequent treatments, please detail if the setting for prescribing and routine follow-up differs from the intervention.

Would setmelanotide be a candidate for managed access?

Do you consider that the use of setmelanotide can result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation?

Please identify the nature of the data which you understand to be available to enable the committee to take account of these benefits.

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which setmelanotide will be licensed;


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- could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;

- could have any adverse impact on people with a particular disability or disabilities.

Please tell us what evidence should be obtained to enable the committee to identify and consider such impacts.

NICE intends to evaluate this technology through its Single Technology Appraisal process. (Information on NICE's health technology evaluation processes is available at https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/nice-technology-appraisal-guidance/changes-to-health-technology-evaluation).

**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


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