NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE
Health Technology Evaluation

Setmelanotide for treating obesity and hyperphagia in Bardet-Biedl syndrome (review of HST31)

Final scope

Remit/evaluation objective

To appraise the clinical and cost effectiveness of setmelanotide within its marketing authorisation for treating obesity and hyperphagia caused by Bardet-Biedl Syndrome (BBS).

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.

BBS is a rare, recessively inherited condition caused by genetic mutations. Symptoms experienced vary but obesity is a key symptom due to the patient's increased appetite (hyperphagia), caused by impairment of an area of the brain that controls appetite, the melanocortin-4 receptor (MC4R) pathway. Diabetes mellitus (specifically, type II diabetes, non-insulin dependent) may affect up to 45% of patients.[1] Problems with weight management may further complicate issues with heart and blood vessels common in patients with BBS. Other symptoms may include cognitive impairment, polydactyly, renal anomalies, hypogonadism and visual impairment.

It is estimated that BBS affects approximately 560 people in the UK.[2] Many people with BBS experience excessive weight gain during the first year of life, and around 72 to 86 % develop obesity.[3]

NICE HST31 recommends setmelanotide as an option for treating obesity and hyperphagia in genetically confirmed BBS in people aged 6 years and over, only if they are aged between 6 and 17 years when treatment starts. These people can carry on having setmelanotide as adults until they need to stop. The focus of this review is on the adult population for which setmelanotide was not recommended in HST31.

The technology

Setmelanotide (IMCIVREE, Rhythm Pharmaceuticals) 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-

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opiomelanocortin (POMC), including PCSK1, deficiency or biallelic leptin receptor (LEPR) deficiency in adults and children 2 years of age and above."

Intervention(s)	Setmelanotide
Population(s)	Adults with obesity and hyperphagia in Bardet-Biedl Syndrome
Comparators	• Established clinical management without setmelanotide (including a reduced-calorie diet and increased physical activity)
Outcomes	The outcome measures to be considered include: • BMI • BMI-Z • weight loss • percentage body fat • waist circumference • hunger • incidence of type 2 diabetes • clinical measure of diabetic control • cardiovascular events • mortality • co-morbidities associated with early onset severe obesity including cancer • adverse effects of treatment • health-related quality of life (for patients and carers)
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. 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. Costs will be considered from an NHS and Personal Social Services perspective. The availability of any commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account. The availability and cost of biosimilar and generic products should be taken into account.

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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:** Setmelanotide for treating obesity and hyperphagia in Bardet-Biedl syndrome (2024). NICE highly specialised technologies guidance HST31

References

1. NORD. Bardet-Biedl Syndrome. Accessed October 2025
2. bbsUK. About bbsUK. Accessed October 2025
3. Forsythe E, Beales PL. Bardet-Biedl syndrome. Eur J Hum Genet. 2013;21:8–13. PubMed PMID: 22713813.

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