**National Institute for Health and Care Excellence**

**Health Technology Evaluation**

# Setmelanotide for treating obesity and hyperphagia in Bardet-Biedl syndrome (review of HST31)
# ID6598
# Response to stakeholder organisation comments on the draft remit and draft scope

**Please note:** Comments received in the course of consultations carried out by NICE are published in the interests of openness and transparency, and to promote understanding of how recommendations are developed. The comments are published as a record of the submissions that NICE has received, and are not endorsed by NICE, its officers or advisory committees.

## Comment 1: the draft remit and proposed process

| Section | Stakeholder | Comments [sic] | Action |
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| Appropriateness of an evaluation and proposed evaluation route | Bardet-Biedl Syndrome | We fully support the decision to evaluate setmelanotide for adults with BBS. This is an area of significant unmet need; there are currently no licensed treatments addressing the underlying biological cause of hyperphagia and obesity in adults with BBS. A highly specialised technology (HST) evaluation continues to be the most appropriate route given the rarity, complexity and lifelong nature of the condition. | Thank you for your comment. |
| | Rhythm Pharmaceuticals UK Ltd | Rhythm Pharmaceuticals agrees with NICE's decision to route the review of setmelanotide for Bardet Biedl Syndrome (BBS) via the Highly Specialised Technologies (HST) programme.<br><br>HST31 resulted in optimised guidance for pediatric-initiated patients only, with continuation into adulthood permitted for those who initiated in childhood. | Thank you for your comment. |

| Section | Stakeholder | Comments [sic] | Action |
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| | | Accordingly, an urgent review of HST31 within the licensed indication is needed to expand access to the full licensed population. | |
| | Genetic Alliance UK | Genetic Alliance UK welcomes the opportunity to comment on this draft scope evaluation of setmelanotide for treating obesity and hyperphagia in Bardet-Biedl syndrome (BBS).<br>We agree with the committee's assessment that this is best routed via the Highly Specialised Technology (HST) appraisal as to our knowledge it meets all four criteria. | Thank you for your comment. |
| | Association for the Study of Obesity | This is appropriate | Thank you for your comment. |
| Wording | Bardet-Biedl Syndrome | NA | Thank you for your comment. |
| | Rhythm Pharmaceuticals UK Ltd | Rhythm Pharmaceuticals recommends that the remit wording should consistently refer to *"genetically confirmed Bardet Biedl Syndrome (BBS)"* to reflect the SmPC, current UK clinical practice and international standards. | Thank you for your comment. The scope is updated in light of the comment. |
| | Genetic Alliance UK | No comments | No action required. |
| | Association for the Study of Obesity | yes | Thank you for your comment. |
| Timing Issues | Bardet-Biedl Syndrome | This evaluation is extremely important and very timely. Adults with BBS currently have no access to a treatment that targets the underlying biological | Thank you for your comment. NICE has |

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| | | cause of hyperphagia, and many experience significant challenges with weight management, weight-related health complications, and reduced quality of life. Earlier access to an effective therapy could help to address an area of long-standing unmet medical need. | scheduled this topic into its work programme. No action required. |
| | Rhythm Pharmaceuticals UK Ltd | This review is urgent because adult patients with Bardet Biedl Syndrome (BBS) are waiting for access to this treatment. | Thank you for your comment. NICE has scheduled this topic into its work programme. No action required. |
| | Genetic Alliance UK | No comments | No action required. |
| | Association for the Study of Obesity | Medium urgency | Thank you for your comment. |
| Additional comments on the draft remit | Bardet-Biedl Syndrome | NA | No action required. |
| | Rhythm Pharmaceuticals UK Ltd | NA | No action required. |
| | Genetic Alliance UK | NA | No action required. |

| Section | Stakeholder | Comments [sic] | Action |
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| | Association for the Study of Obesity | NA | No action required. |

Comment 2: the draft scope

| Section | Consultee/ Commentator | Comments [sic] | Action |
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| Background information | Bardet-Biedl Syndrome | The background is generally accurate and reflects the key features of Bardet–Biedl syndrome. However, we note that the scope states that BBS affects “approximately 560 people in the UK” and cites the BBS UK website as the source. Our current data (and website) shows that BBS UK now supports over 700 individuals with a diagnosis of BBS in the UK.<br>We also suggest acknowledging the significant psychosocial and functional impact of hyperphagia on individuals and families, which is not captured by BMI alone. | Thank you for your comment. The scope has been updated with some suggested changes. The aim of the background is to provide a very brief summary of the disease area. Further details can be included in all submissions for this evaluation. |
| | Rhythm Pharmaceuticals UK Ltd | The draft background is concise and broadly accurate, but Rhythm recommends adding further detail around the following key features to help further the understanding of this complex condition.<br><br>Hyperphagia in Bardet Biedl Syndrome (BBS) is a pathological, insatiable hunger driven by impaired MC4R signalling, leading to persistent food preoccupation, abnormal food-seeking behaviours, and lack of satiety. It significantly impacts quality of life through stigma and psychosocial burden | Thank you for your comment. The aim of the background is to provide a very brief summary of the disease area. Further details can be included in all |

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| | | (Beales et al., 2024). Hyperphagia is strongly linked to early-onset severe obesity, which increases risks of metabolic syndrome, type 2 diabetes, cardiovascular disease, and ultimately contributes to higher morbidity and mortality (Pomeroy et al., 2022)<br><br>Bardet Biedl Syndrome (BBS) leads to significant multisystem complications: renal anomalies (including CKD and ESKD) affect up to 25% of adults and are a major cause of morbidity and mortality (Cetiner et al., 2024); metabolic dysfunction (insulin resistance, dyslipidemia) and obesity drive cardiovascular risks such as hypertension and cardiomyopathy (Haqq et al., 2025; Hassan et al., 2025); and these comorbidities severely impair health-related quality of life for patients and carers (Forsythe et al., 2023). Emerging therapies like setmelanotide show promise in improving metabolic markers and quality of life (Haqq et al., 2025; Forsythe et al., 2023).<br><br>To improve clarity and consistency, Rhythm Pharmaceuticals suggests adding explicit BMI references for adults and children:<br><br>Adults: obesity = BMI ≥ 30 kg/m² (WHO; CDC).<br>Children/young people: obesity = BMI-for-age ≥ 95th percentile (NICE NG246, Jan 2025; WHO 5–19 years thresholds).<br><br>These references ensure the scope reflects current UK and global guidance. | submissions for this evaluation. |
| | Genetic Alliance UK | Yes, to our knowledge this is accurate although brief, and there is a sentence that appears to have been cut off at the bottom of page 1 (under ‘the technology’).<br>Ahead of the next stage of the evaluation process, we would like to draw the Committee’s attention to the most recent version of the medical information | Thank you for your comment. |

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| | | booklet on Bardet-Biedl Syndrome UK's website, which was updated in 2025. This includes a more in-depth overview of the condition (e.g. primary and secondary features, inheritance), and we that note that BBS UK has received PIF-TIK certification the quality and accuracy of health information available on its website. https://bbsuk.org.uk/bbs-uk-publications/paged-5/2/<br>As made clear in this handbook, it is also important to note that many treatments for obesity, such as weight-loss surgeries, are not recommended for people living with BBS as they do not address the underlying cause of hyperphagia. A non-surgical treatment for hyperphagia and obesity, such as injection of setmelanotide, could therefore be transformative for individuals managing this condition and would present a potentially lower risk and less disruptive intervention that maximises the quality of life for people living with this life-long condition. | |
| | Association for the Study of Obesity | Complete, but please use people first language, i.e. people living with obesity instead of obese | Thank you for your comment. The scope has been updated with the suggested changes. |
| Population | Bardet-Biedl Syndrome | The defined population ("Adults with obesity and hyperphagia in BBS") is appropriate and captures the group excluded from treatment eligibility under HST31 | Thank you for your comment. No action required. |
| | Rhythm Pharmaceuticals UK Ltd | While the current review focuses on adults, it is important for decision making to consider the entire population included in HST31, ensuring that outcomes are inclusive and representative of the license. | Thank you for your comment. No action required. |
| | Genetic Alliance UK | To our understanding, yes. However, it is our view that sufficient flexibility should be built into the review process to minimise the risk of any further sub-groups of adults living with BBS being excluded, which could otherwise | Thank you for your comment. No action required. |

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| | | necessitate a subsequent review. We note that setmelanotide for the treatment of obesity and hyperphagia in BBS was first appraised in 2021 via STA ID3947 and subsequently via HST31 in 2024, where initial use was restricted to children and young people. Ensuring appropriate flexibility at this stage would help avoid further delays in access to a potentially transformative treatment for a condition associated with serious and progressive complications. | |
| | Association for the Study of Obesity | yes | Thank you for your comment. No action required. |
| Subgroups | Bardet-Biedl Syndrome | No. | Thank you for your comment. No action required. |
| | Rhythm Pharmaceuticals UK Ltd | There are no specific clinical subgroups to be considered. | Thank you for your comment. No action required. |
| | Genetic Alliance UK | No comments | No action required. |
| | Association for the Study of Obesity | People with Type 2 diabetes | Thank you for your comment. The scope has been updated to reflect the suggested changes. Where evidence allows and appropriate, adults with |

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| | | | type 2 diabetes may be considered. Stakeholders are welcomed to submit any evidence or information relating to the clinical- and cost-effectiveness of setmelanotide in adults with BBS and type 2 diabetes. |
| Comparators | Bardet-Biedl Syndrome | We agree with the list of comparators. | Thank you for your comment. |
| | Rhythm Pharmaceuticals UK Ltd | The comparators listed in the final scope, which include established clinical management without setmelanotide, such as a reduced-calorie diet and increased physical activity, are appropriate and reflect the current standard of care for Bardet-Biedl syndrome (BBS) in the NHS | Thank you for your comment. |
| | Genetic Alliance UK | No comments. | No action required. |
| | Association for the Study of Obesity | Yes. | Thank you for your comment. |
| Outcomes | Bardet-Biedl Syndrome | The outcomes listed are appropriate. We particularly welcome the inclusion of hunger, health-related quality of life and carer quality of life, which reflect the lived experience of adults with BBS. | Thank you for your comment. |

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| | Rhythm Pharmaceuticals UK Ltd | The outcomes listed are appropriate, but Rhythm recommends adding the following outcomes<br>- Renal function,<br>- Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD) and<br>- Metabolic markers: MetS-Z-BMI Scores, systolic blood pressure (SBP), high-density lipoprotein (HSL) cholesterol, Triglyceride, Fasting glucose | Thank you for your comment. The scope has been updated in light of the comment. Please note that the list of outcomes in the scope are not intended to be exhaustive and the committee may consider these further. |
| | Genetic Alliance UK | No comments. | No action required. |
| | Association for the Study of Obesity | Yes. Another outcome to consider is growth and development if data are available | Thank you for your comment. Please note that the list of outcomes in the scope are not intended to be exhaustive, where appropriate and evidence allows, the committee may consider these further |
| Equality | Bardet-Biedl Syndrome | Adults with BBS experience multiple overlapping inequalities, including learning difficulties, visual impairment, disability and significant stigma related to obesity. | Thank you for your comment. Where relevant and appropriate, the committee will consider |

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| | | Poor mental health, including low mood, depression and emotional dysregulation, is also common and can further affect quality of life and access to support.<br><br>Access to specialist care varies geographically, which may widen inequalities. We encourage NICE to consider these factors, as they may influence both access to treatment and the potential benefits experienced by adults with BBS. | equality issues raised during the course of the evaluation including scoping stage. No action required. |
| | Rhythm Pharmaceuticals UK Ltd | There are no equality issues. | Thank you for your comment. |
| | Association for the Study of Obesity | No changes needed | Thank you for your comment. |
| Other considerations | Bardet-Biedl Syndrome | No comments. | No action required. |
| | Rhythm Pharmaceuticals UK Ltd | No comments. | No action required. |
| Questions for consultation | Bardet-Biedl Syndrome | NA | No action required. |

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| | Rhythm Pharmaceuticals UK Ltd | NA | No action required. |
| Additional comments on the draft scope | Bardet-Biedl Syndrome | NA | No action required. |
| | Rhythm Pharmaceuticals UK Ltd | NA | No action required. |

**The following stakeholders indicated that they had no comments on the draft remit and/or the draft scope**

Neonatal and Paediatric Pharmacists Group