

Bardet-Biedl Syndrome

What is BBS?

Bardet-Biedl syndrome (BBS) is a rare ciliopathy, resulting from genetic variants within the BBS family of genes. This heterogeneous genetic disease presents with a variety of symptoms that evolve over time, including.¹⁻³



Solomon, living with BBS



Visual impairments



Early-onset, severe obesity
Hyperphagia



Renal disease



Cognitive impairment



Polydactyly



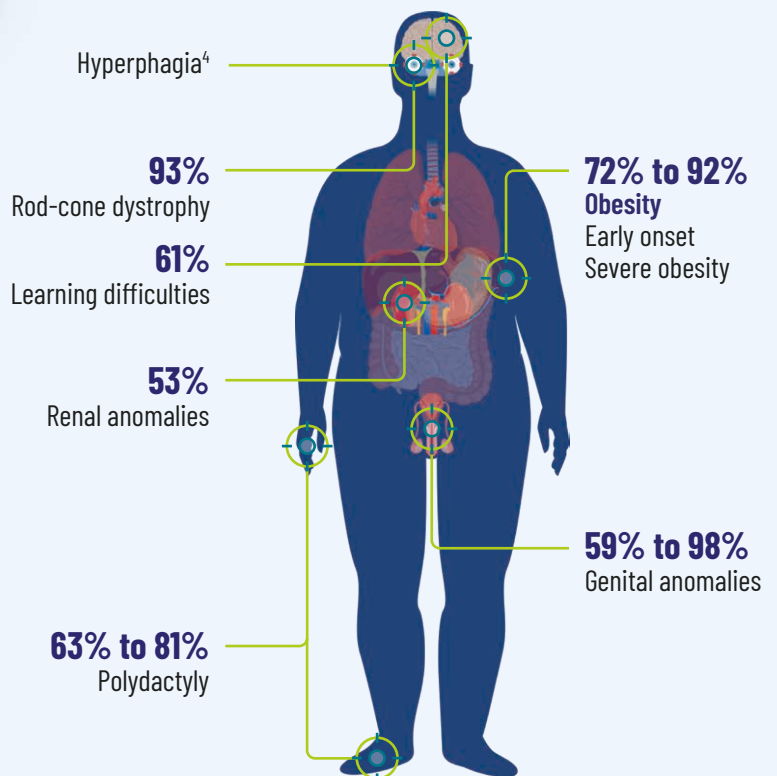
Genital anomalies

Common Clinical Features of BBS⁴

Prevalence:



Prevalence estimates may increase as more healthcare providers become aware of the clinical features of BBS and genetically test to aid in clinical diagnosis^{6,7}



Percentages represent frequency of feature appearance among individuals diagnosed with BBS.

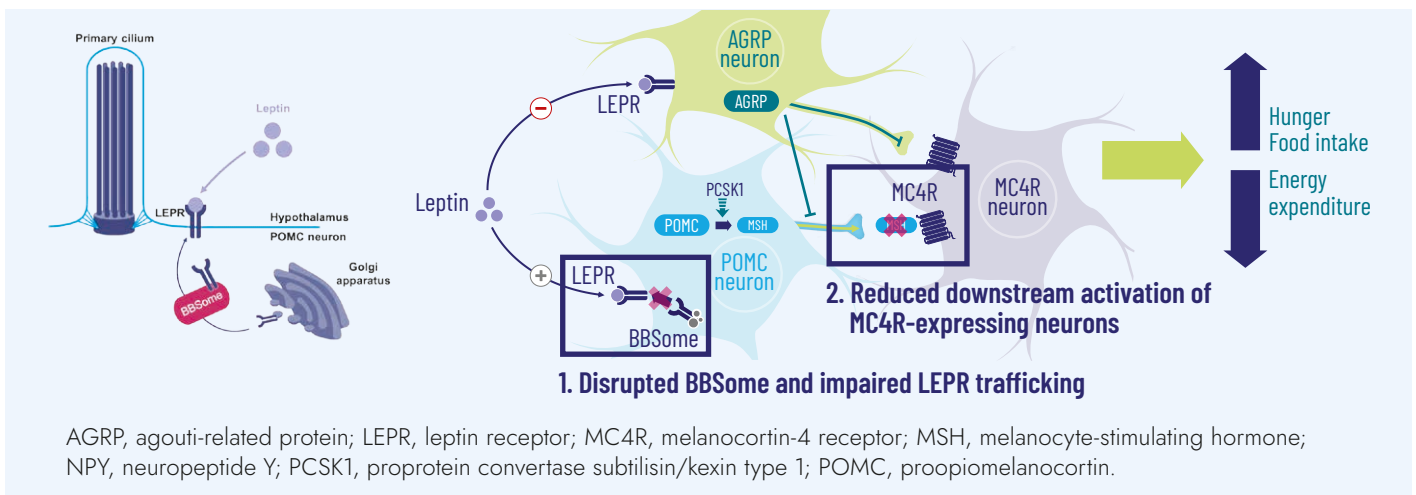
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More than 20 genes associated with BBS are involved in the melanocortin-4 receptor (MC4R) pathway.^{1,2,8-11}

Eight BBS proteins form a stable complex, the BBSome, which contributes to cilia development and function by trafficking intracellular proteins to ciliary membranes and potentially to other membrane compartments.¹¹

Variants in BBS genes disrupt the BBSome, resulting in ciliary defects and impaired signaling of receptors that regulate body weight, such as LEPR.^{8,10,12,13}

This disrupts LEPR signaling, reducing activation of MC4R-expressing neurons, and can lead to hyperphagia and obesity.^{8,10,12,13}



How is BBS diagnosed?

Diagnosis of BBS is based on clinical findings; diagnosis confirmed by genetic testing⁴

The following criteria have been used to help diagnose BBS. According to these criteria, diagnosis is based on the presence of a combination of features.^{1,14}



Primary features

- Rod-cone dystrophy
- Polydactyly
- Obesity
- Genital anomalies
- Renal anomalies
- Learning difficulties



Secondary features

- Speech delay or speech impairments
- Developmental delay
- Diabetes mellitus
- Dental anomalies
- Left ventricular hypertrophy or congenital heart disease
- Mild spasticity (especially lower limbs)
- Brachydactyly or syndactyly
- Strabismus, cataracts, or astigmatism
- Ataxia or poor coordination
- Anosmia or hyposmia
- Polyuria or polydipsia
- Hepatic fibrosis

There is no specific therapy for BBS, and patients are treated and monitored based on individual symptoms¹

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Obesity in BBS

- Obesity can begin in childhood and can increase in severity with age⁴
- Obesity may have a detrimental impact on long-term health, due to its association with increased morbidity, social stigma, and reduced quality of life¹⁵
- Hyperphagia may contribute to obesity in patients with BBS^{16,17}
- Hyperphagia is generally characterized by the following:^{16,18}



Insatiable hunger

Heightened and prolonged hunger
Longer time to reach satiation
Shorter duration of satiety



Excessive drive to eat

Severe preoccupation with food
Persistent food-seeking behaviors (eg, stealing food, night eating, eating food from the bin)



Distress and functional impairment due to denial of food

Mean Body Mass Index (BMI) of Patients With BBS by Age¹⁹

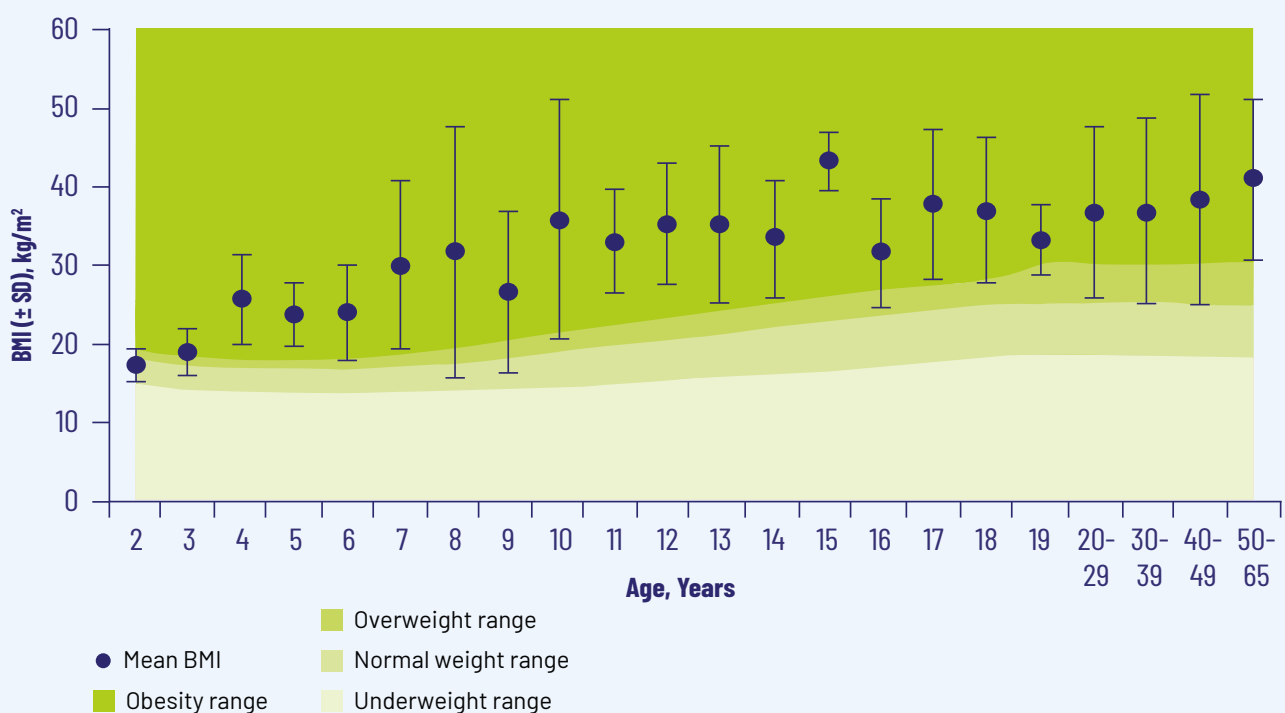


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Prescribing information and adverse event reporting information can be found on page 5

Rhythm
PHARMACEUTICALS

Prescribing Information

▼ **IMCIVREE® (setmelanotide)** 10mg/ml solution for injection. **Active ingredient:** Setmelanotide. **Presentation:** Each vial contains 10mg setmelanotide in 1ml solution for subcutaneous injection.

Indications: 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 6 years of age and above. **Dosage and method of administration:** IMCIVREE should be prescribed and supervised by a physician with expertise in obesity with underlying genetic aetiology. **POMC, including PCSK1, deficiency and LEPR deficiency:** *Adults and children 12 to 17 years of age:* 1mg daily for 2 weeks. If well-tolerated, dose can be increased to 2mg daily. If dose escalation is not tolerated, dose can be maintained at 1mg daily. If additional weight loss is desired in adults, and if weight remains above the 90th percentile in children 12 to 17 years of age, dose can be increased to 2.5mg with a maximum dose of 3mg daily. *Children aged 6 to <12 years:* 0.5mg daily for 2 weeks. If tolerated after 2 weeks, dose can be increased to 1mg daily. If dose escalation is not tolerated, dose can be maintained at 0.5mg daily. If 1mg is tolerated after 2 weeks, dose can be increased to 2mg daily. If weight remains above the 90th percentile and additional weight loss is desired, dose may be increased to 2.5mg daily. **BBS:** *Adults and children more than 16 years of age:* 2mg daily for 2 weeks. If well-tolerated, dose can be increased to 3mg daily. If 2mg starting dose is not tolerated, reduce to 1mg daily. If 1mg daily is tolerated, continue dose titration. Following starting dose, if a subsequent dose is not tolerated, reduce to previous level dose. If reduced dose is tolerated, continue dose titration. *Children aged 6 to <16 years:* 1mg daily for 1 week. If well-tolerated, dose can be increased to 2mg daily. If well-tolerated, dose can be increased to 3mg daily. If 1mg starting dose is not tolerated, reduce to 0.5mg daily. If 0.5mg dose is tolerated, continue dose titration. Following starting dose, if a subsequent dose is not tolerated, reduce to previous level dose. If reduced dose is tolerated, continue dose titration. **Renal impairment:** *Mild-to-moderate:* no dose adjustments are necessary. *Severe: POMC, including PCSK1, deficiency and LEPR deficiency (adults and children 12 to 17 years of age) and BBS (adults and children 16 to 17 years of age):* 0.5mg daily for 2 weeks. If well-tolerated, dose can be increased to 1mg daily. If well-tolerated and clinical response is insufficient, increase to 2mg daily. If well-tolerated and clinical response is insufficient, increase to 2.5mg daily. If well-tolerated and clinical response is insufficient, increase to 3mg daily. If 0.5mg dose is not tolerated, reduce to 0.25mg daily. If 0.25mg dose is tolerated, continue dose titration. Following starting dose, if a subsequent dose is not tolerated, reduce to previous level dose. If reduced dose is tolerated, continue dose titration. *POMC, including PCSK1, deficiency and LEPR deficiency (children aged 6 to <12 years) and BBS (children 6 to <16 years of age):* 0.25mg daily for 2 weeks. If not tolerated, discontinue treatment. If well-tolerated, dose can be increased to 0.5mg daily for 3 weeks. If well-tolerated, increase to 1mg daily. If well-tolerated and clinical response is insufficient, increase to 2mg daily. Following the starting dose, if a subsequent dose is not tolerated, reduce

to previous level dose. If reduced dose is tolerated, continue dose titration. **End-stage renal disease:** Setmelanotide should not be administered to patients with end-stage renal disease. **Hepatic impairment:** Setmelanotide should not be administered to patients with hepatic impairment. **Method of administration:** For subcutaneous use. **Contraindications:** Hypersensitivity to the active ingredient or any excipients. **Special warnings and precautions: Skin monitoring** – full body skin examinations should be conducted annually to monitor pre-existing and new skin pigmented lesions before and during treatment with setmelanotide. **Heart rate and blood pressure monitoring** – monitor as part of standard clinical practice at each medical visit (at least every 6 months). **Prolonged penile erection** – patients experiencing penile erection lasting longer than 4 hours should be instructed to seek emergency medical attention for potential treatment for priapism. **Depression** – patients with depression should be monitored at each medical visit during treatment and consideration should be given to discontinuing treatment if patients experience suicidal thoughts or behaviours. **Paediatric population** – prescribing physician should periodically assess response to setmelanotide therapy. Growing children should be monitored for height and weight using age- and sex-appropriate growth curves. **Excipients** – medicine contains benzyl alcohol and may cause allergic reactions. This medicine contains less than 1mmol sodium (23mg) per dose, that is to say essentially “sodium-free”. **Adverse reactions:** Based on observation from clinical studies: **Very common:** skin hyperpigmentation, injection site reactions, nausea, vomiting, headache, spontaneous penile erection. **Common:** pruritus, dry skin, hyperhidrosis, skin discolouration, skin lesion, alopecia, fatigue, asthenia, pain, diarrhoea, abdominal pain, dry mouth, dyspepsia, constipation, abdominal discomfort, dizziness, erection increased, disturbance in sexual arousal, libido increased, depression, insomnia, melanocytic naevus, back pain, myalgia, muscle spasms, pain in extremity, hot flush, vertigo. For more information on other adverse reactions, see Summary of Product Characteristics. **Legal category:** POM (subject to restricted medical prescription). **Marketing Authorisation Holder:** Rhythm Pharmaceuticals Netherlands B.V., Radarweg 29, 1043NX Amsterdam, Netherlands. Tel: +31 20 8546071. For any enquiries, contact EU_Medinfo@Rhythmtx.com or use the following Toll-Free phone numbers: **In United Kingdom: +44 (0) 80 005 413 01.** **Marketing authorisation number: GB:** PLGB 55587/0001 **NI / EU:** EU/1/21/1564/0001. **Cost: GB / NI £2,376** per one 1ml vial. **Ireland, price on application. Additional information is available on request. Last revised:** February 2024.

Adverse events should be reported.

Reporting forms and information can be found at:
UK: yellowcard.mhra.gov.uk
Ireland: **HPR**A Pharmacovigilance, www.hpra.ie
Adverse events should also be reported to Rhythm Pharmaceuticals Netherlands B.V., Radarweg 29, 1043NX Amsterdam, Netherlands.
Tel: +31 20 8546071.