

# Specialty Guideline Management

## Imcivree

### Products Referenced by this Document

Drugs that are listed in the following table include both brand and generic and all dosage forms and strengths unless otherwise stated. Over-the-counter (OTC) products are not included unless otherwise stated.

Brand Name	Generic Name
Imcivree	setmelanotide

### Indications

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

#### FDA-approved Indications<sup>1</sup>

Imcivree is indicated to reduce excess body weight and maintain reduction long term in adults and pediatric patients aged:

- 4 years and older with acquired hypothalamic obesity (HO)
- 2 years and older with Bardet-Biedl syndrome (BBS)
- 2 years and older with pro-opiomelanocortin (POMC), proprotein convertase subtilisin/kexin type 1 (PCSK1), or leptin receptor (LEPR) deficiency confirmed by genetic testing demonstrating variants in POMC, PCSK1, or LEPR genes that are interpreted as pathogenic, likely pathogenic, or of uncertain significance (VUS).

#### Limitations of Use:

Imcivree is not indicated for the treatment of patients with the following conditions as Imcivree would not be expected to be effective:

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4378-A

- Obesity due to suspected POMC, PCSK1, or LEPR deficiency with POMC, PCSK1, or LEPR variants classified as benign or likely benign.
- Other types of obesity not related to acquired HO, BBS, or POMC, PCSK1, or LEPR deficiency, including obesity associated with other genetic syndromes and general (polygenic) obesity.

All other indications are considered experimental/investigational and not medically necessary.

## Documentation

Submission of the following information is necessary to initiate the prior authorization review:

- Acquired Hypothalamic Obesity
  - Initial requests:
    - MRI or CT scan records documenting structural damage, lesions, or tumors in the hypothalamus
    - Medical record (e.g., chart notes) and growth chart (in members less than 18 years of age) documentation of pretreatment BMI and weight
  - Continuation requests (where applicable): Medical record (e.g., chart notes) and growth chart documentation of current BMI and current weight
- Obesity due to POMC, PCSK1, or LEPR deficiency
  - Initial requests:
    - Genetic test results documenting homozygous or compound heterozygous variants in POMC, PCSK1, or LEPR genes
    - Medical record (e.g., chart notes) and growth chart (in members less than 18 years of age) documentation of pretreatment BMI and weight
  - Continuation requests (where applicable): Medical record (e.g., chart notes) and growth chart documentation of current BMI and current weight
- Obesity due to Bardet-Biedl Syndrome (BBS)
  - Initial requests:
    - Chart notes, medical record documentation, or genetic testing confirming a variant in both alleles of one of the core genes associated with Bardet-Biedl syndrome (if applicable)
    - Chart notes or medical record documentation supporting clinical diagnosis
    - Medical record (e.g., chart notes) and growth chart (in members less than 18 years of age) documentation of pretreatment BMI and weight
  - Continuation requests (where applicable): Medical record (e.g., chart notes) and growth chart documentation of current BMI and current weight

## Prescriber Specialties

This medication must be prescribed by or in consultation with one of the following:

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- Obesity due to POMC, PCSK1, or LEPR deficiency and BBS: an endocrinologist, a geneticist or a prescriber specialized in the treatment of metabolic disorders
- Acquired Hypothalamic Obesity: an endocrinologist or a prescriber specialized in the treatment of metabolic disorders

## Exclusion Criteria

### Acquired Hypothalamic Obesity<sup>1</sup>

- Diagnosis of Prader-Willi syndrome (PWS) or Rapid-onset obesity with hypoventilation, hypothalamic, autonomic dysregulation, neuroendocrine tumor syndrome (ROHHADNET).

## Coverage Criteria

### Acquired Hypothalamic Obesity<sup>1,7</sup>

Authorization of 12 months may be granted to reduce excess body weight and maintain weight reduction long term for members 4 years of age or older with acquired hypothalamic obesity (HO) when all of the following criteria are met:

- Member has documented diagnosis of acquired HO defined as both of the following:
  - The member has experienced a traumatic or disease-related (e.g., oncological) injury to the hypothalamus detectable on MRI or CT scan.
  - Member has had a rapid, clinically significant increase in BMI (more than or equal to 5% BMI increase in adults and more than or equal to 1.0 BMI standard deviation [SDS] increase in pediatric patients) that began within the first 12 months after the onset of hypothalamic damage.
- The member has obesity defined as one of the following:
  - BMI greater than or equal to 30 kg/m<sup>2</sup> in members 18 years of age or older
  - BMI greater than or equal to equal to 95<sup>th</sup> percentile for age on growth chart assessment in members less than 18 years of age

### Obesity due to POMC, PCSK1, or LEPR Deficiency<sup>1,2,4,6</sup>

Authorization of 6 months may be granted to reduce excess body weight and maintain weight reduction long term for members with obesity due to proopiomelanocortin (POMC), proprotein convertase subtilisin/kexin type 1 (PCSK1), or leptin receptor (LEPR) deficiency when all of the following criteria are met:

- Diagnosis is confirmed by genetic testing demonstrating homozygous or compound heterozygous variants in POMC, PCSK1, or LEPR genes

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- POMC, PCSK1, or LEPR gene variants are interpreted as pathogenic, likely pathogenic, or of uncertain significance (VUS)
- The member is 2 years of age or older
- The member has obesity defined as one of the following:
  - BMI greater than or equal to 30 kg/m<sup>2</sup> in members 18 years of age or older
  - BMI greater than or equal to 95<sup>th</sup> percentile for age on growth chart assessment in members less than 18 years of age

## Obesity due to Bardet-Biedl Syndrome<sup>1-6</sup>

Authorization of 12 months may be granted to reduce excess body weight and maintain weight reduction long term for members with obesity due to Bardet-Biedl syndrome (BBS) when all of the following criteria are met:

- The member has a diagnosis of BBS defined as one of the following:
  - Member has 4 primary features of the Beales criteria (see Appendix)
  - Member has 3 primary and 2 secondary features of the Beales criteria (see Appendix)
  - Member has had genetic testing confirming a variant in both alleles of one of the core genes associated with Bardet-Biedl syndrome (e.g., BBS1, BBS2, ARL6 ) and 1 primary feature of the Beales criteria (see Appendix)
- The member is 2 years of age or older
- The member has obesity defined as one of the following:
  - BMI greater than or equal to 30 kg/m<sup>2</sup> in members 18 years of age or older
  - BMI greater than or equal to 95<sup>th</sup> percentile for age on growth chart assessment in members less than 18 years of age

## Continuation of Therapy

### Acquired Hypothalamic Obesity

- Authorization of up to 12 months may be granted for continued treatment in members requesting reauthorization when the member has received less than 12 months of therapy.
- Authorization of 12 months may be granted for continued treatment in members requesting reauthorization when the member has received 12 months of therapy or more and the member has had a reduction in BMI of at least 5% from baseline or has achieved or sustained clinically meaningful weight loss.

### Obesity due to POMC, PCSK1, or LEPR Deficiency

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization when one of the following is met:

- The member has received less than 12 months of therapy and one of the following is met:

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- Member has lost at least 5% of baseline body weight
- Member is less than 18 years of age and has had a reduction in BMI of at least 5% from baseline
- Member has received 12 months of therapy or more and has achieved or sustained clinically meaningful weight loss
- The member is 2 years of age or older.

## Obesity due to Bardet-Biedl Syndrome

- Authorization of up to 12 months may be granted for continued treatment in members requesting reauthorization when the member has received less than 12 months of therapy.
- Authorization of 12 months may be granted for continued treatment in members requesting reauthorization when the member has received 12 months of therapy or more and one of the following is met:
  - Member has lost at least 5% of baseline body weight
  - Member is less than 18 years of age and has had a reduction in BMI of at least 5% from baseline
- The member is 2 years of age or older.

## Appendix<sup>3</sup>

### Beales Diagnostic Criteria

#### Primary features

- Rod-cone dystrophy
- Polydactyly
- Obesity
- Learning disability
- Hypogonadism in males
- Renal abnormalities

#### Secondary features

- Speech disorder/delay
- Strabismus/cataracts/astigmatism
- Brachydactyly/syndactyly
- Developmental delay
- Polyuria/polydipsia (nephrogenic diabetes insipidus)
- Ataxia/poor coordination/imbalance
- Mild spasticity (especially lower limbs)
- Diabetes mellitus
- Dental crowding/hypodontia/small roots/high arched palate
- Left ventricular hypertrophy/congenital heart disease

Reference number(s)
4378-A

- Hepatic fibrosis

## References

1. Imcivree [package insert]. Boston, MA: Rhythm Pharmaceuticals, Inc.; March 2026.
2. Clément K, van den Akker E, Argente J, et al. Efficacy and safety of setmelanotide, an MC4R agonist, in individuals with severe obesity due to LEPR or POMC deficiency: single-arm, open-label, multicentre, phase 3 trials. *Lancet Diabetes Endocrinol.* 2020;8(12):960-970. doi:10.1016/S2213-8587(20)30364-8
3. Beales P, Elcioglu N, Woolf AS, et al. New criteria for improved diagnosis of Bardet-Biedl syndrome: results of a population survey. *J Med Genet.* 1999;36(6):437-446.
4. Argente J, Verge CF, Okorie U, et al. Setmelanotide in patients aged 2-5 years with rare MC4R pathway-associated obesity (VENTURE): a 1 year, open-label, multicenter, phase 3 trial. *Lancet Diabetes Endocrinol.* 2025;13:29-37.
5. Dollfus H, Lilien MR, Maffei P et al. Bardet-Biedl syndrome improved diagnosis criteria and management: Inter European Reference Networks consensus statement and recommendations. *European Journal of Human Genetics.* 2024; 32: 1347-1360.
6. Centers for Disease Control and Prevention. Childhood Obesity Facts. Updated April 2024. Available at: <https://www.cdc.gov/obesity/childhood-obesity-facts/childhood-obesity-facts.html>. Accessed on February 12, 2026.
7. Mueller HL, Tanaka T, Hasegawa T et al. Diagnostic criteria for acquired hypothalamic obesity – international expert guidance document. *Endocr J.* 2026; 73 (2): 341-353.
8. Rose SR, Horne VE, Bingham N, Jenkins T, Black J, Inge T. Hypothalamic Obesity: 4 years of the international registry of hypothalamic obesity disorders. *Obesity (Silver Spring).* 2018; 26 (11): 1727-1732.