

# 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 weight reduction long term in adults and pediatric patients 2 years of age and older with syndromic or monogenic obesity due to:

- Bardet-Biedl syndrome (BBS)
- Pro-opiomelanocortin (POMC), proprotein convertase subtilisin/kexin type 1 (PCSK1), or leptin receptor (LEPR) deficiency as determined by an FDA-approved test 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:

- 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 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:

- 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 body mass index (BMI) and weight
  - Continuation requests (where applicable): Medical record (e.g., chart notes) and growth chart (if continued growth potential) documentation of current BMI and current weight
- Obesity due to Bardet-Biedl Syndrome
  - Initial requests:
    - 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 body mass index (BMI) and weight
  - Continuation requests (where applicable): Medical record (e.g., chart notes) and growth chart documentation of current BMI and current weight

## Coverage Criteria

### Obesity due to POMC, PCSK1, or LEPR Deficiency<sup>1-2,4</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
- 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>1-4</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 clinical diagnosis of BBS as per Beales criteria (member has 4 primary features OR 3 primary and 2 secondary features) (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

### 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:
  - Member has lost at least 5% of baseline body weight
  - Member has continued growth potential and has had a reduction in body mass index (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

### 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 body mass index (BMI) of at least 5% from baseline

## 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
- Hepatic fibrosis

## References

1. Imcivree [package insert]. Boston, MA: Rhythm Pharmaceuticals, Inc.; December 2024.
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.