Oscar Clinical Guideline: Imcivree (setmelanotide) (PG088, Ver. 7)

# Imcivree (setmelanotide)



## Summary

Imcivree (setmelanotide) injection for subcutaneous (SC or SQ) use is indicated for chronic weight management in adult and pediatric individuals 2 years of age and older with monogenic or syndromic obesity due to:

1. 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)
2. Bardet-Biedl syndrome (BBS)

Imcivree (setmelanotide) is NOT indicated for the treatment of those with the following conditions asImcivree (setmelanotide) 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 POMC, PCSK1 or LEPR deficiency or BBS, including obesity associated with other genetic syndromes and general (polygenic) obesity

Melanocortin 4 (MC4) receptors in the brain are involved in regulation of hunger, satiety, and energy expenditure. POMC, PCSK1, and LEPR deficiencies, though extremely rare, are associated with

insufficient activation of the MC4 receptors. Imcivree (setmelanotide) addresses the underlying cause of obesity in these rare instances, when gene variation is interpreted as pathogenic, likely pathogenic, or of uncertain significance, by restoring MC4 receptor activity resulting in reduced hunger and enhanced weight loss through decreased caloric intake and increased energy expenditure. Information on an FDA-approved test for the detection of variants in the POMC, PCSK1, or LEPR is available at http://www.fda.gov/CompanionDiagnostics.

## Definitions

"Bardet-Biedl syndrome (BBS)" is a rare disorder caused by genetic changes in many genes that affects many parts of the body. Signs and symptoms for this condition vary depending on the person, but it may cause problems such as loss of vision, obesity, extra fingers or toes (polydactyly), abnormalities of the genitalia, kidney abnormalities, and learning difficulties.

"Body Mass Index (BMI)" is a value that is calculated based on an individual's weight and height and helps determine whether a person is underweight, overweight, or normal weight.

"Deficiency" is the state of lacking a required amount of something or possessing defective versions which results in decreased function.

"Genetic variation" is a permanent alteration in the sequence, number, structure, or function of the unit of inheritance, also known as a gene.

"Heterozygous" describes a genetic disorder inherited from one parent.

"Homozygous" describes a rare genetic disorder inherited from both parents.

"Monogenic" means involving or controlled by a single gene.

"No evidence of" indicates that the reviewer has not identified any records of the specified item or condition within the submitted materials or claims history. In the absence of such evidence, the member is considered eligible. If any evidence of the item or condition is present upon review of the request, the applicant does not qualify.

"Obesity" is a condition diagnosed when a person has a body mass index (BMI) of 30 $kg/m^2$ or higher.

"Pathogenic" describes a condition that causes or is capable of causing disease or dysfunction.

"Syndromic" means occuring or associated with a syndrome, such as Alström syndrome, Bardet-Biedl syndrome, or Prader-Willi syndrome.

## Medical Necessity Criteria for Initial Authorization

The Plan considers Imcivree (setmelanotide) medically necessary when ALL of the following criteria are met:

1. The medication is prescribed by or in consultation with an endocrinologist, a geneticist, or a physician who specializes in metabolic disorders; *AND*
2. The member is 2 years of age or older*; AND*
3. The member requires treatment for monogenic or syndromic obesity due to ONE (1) of the following:
    a. Bardet-Biedl syndrome (BBS) meeting BOTH of the following:
        i. At least ONE (1) of the following diagnostic requirements for BBS (see Appendix A, Table 1):
            1. 4 primary features*; or*
            2. 3 primary and 2 secondary features*; and*
        ii. Meets ONE (1) of the following:
            1. Is 16 years of age or older and has a BMI greater than or equal to (≥) 30 $kg/m^2$*; or*
            2. Is between 2 to 15 years of age and weight is greater than (>) $97^{th}$ percentile for age and sex on growth chart assessment*; or*
    b. Pro-opiomelanocortin (POMC), proprotein convertase subtilisin/kexin type 1 (PCSK1), or leptin receptor (LEPR) deficiency AND BOTH of the following:
        i. Has been confirmed by genetic testing (by an FDA-approved/cleared test) demonstrating variants in POMC, PCSK1, or LEPR genes that are BOTH:
            1. Homozygous or compound heterozygous (a different gene mutation on each allele)*; and*
            2. Interpreted as pathogenic, likely pathogenic, or of uncertain significance*; and*
        ii. Meets ONE (1) of the following:
            1. Is 18 years of age or older and has a BMI greater than or equal to (≥) 30 $kg/m^2$*; or*
            2. Is between 2 to 17 years of age with weight greater than or equal to (≥) $95^{th}$ percentile for age and sex on growth chart assessment*; AND*
4. The member meets ALL of the following:
    a. No evidence of prior gastric bypass surgery resulting in >10% weight loss durably maintained from the baseline pre-operative weight with no evidence of weight regain*; or*
    b. No evidence of end stage renal disease (eGFR less than 15 mL/min/1.73 $m^2$)*; AND*
5. Clinical chart documentation is provided for review to substantiate the above listed requirements.

If the above prior authorization criteria are met, Imcivree (setmelanotide) will be approved for:

- Up to 12-months for Obesity and a Clinical Diagnosis of BBS; *or*
- Up to 4-months for Obesity Due to POMC, PCSK1, or LEPR Deficiency

## Medical Necessity Criteria for Reauthorization

Reauthorization for up to 12 months will be granted if BOTH of the following are met:

1. The member still meets the applicable initial criteria*; AND*
2. Recent (within the last 3 months) chart documentation shows ONE (1) of the following:
    a. For Obesity and a Clinical Diagnosis of BBS - the member lost at least 5% of baseline body weight or 5% of baseline BMI for members aged less than 18 years*; or*
    b. For Obesity Due to POMC, PCSK1, or LEPR Deficiency - the member lost at least 5% of baseline body weight or 5% of baseline BMI for members with continued growth potential.

## Experimental or Investigational / Not Medically Necessary

Imcivree (setmelanotide) for any other indication is considered not medically necessary by the Plan, as it is deemed to be experimental, investigational, or unproven. Imcivree (setmelanotide) is not approved and is considered experimental/investigational for the treatment of general obesity or weight loss in individuals without confirmed pathogenic variants in POMC, PCSK1, or LEPR genes, or without a clinical diagnosis of Bardet-Biedl syndrome. This includes use for:

1. Polygenic or common obesity.
2. Obesity associated with other genetic syndromes not specified in the FDA-approved indications.
3. Weight loss in individuals without rare genetic disorders of obesity.

## References


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## Appendix A

Table 1: Diagnostic criteria for Bardet-Biedl syndrome (BBS)

| Requirement | Primary/major features | Secondary/minor features |
|---|---|---|
| A. 4 primary features*; or*<br>B. 3 primary and 2 secondary features | • Hypogonadism in males<br>• Learning disabilities<br>• Obesity<br>• Polydactyly<br>• Renal anomalies<br>• Rod-cone dystrophy | • Ataxia/poor coordination/imbalance<br>• Brachydactyly/Syndactyly<br>• Dental crowding/hypodontia/small roots/high arched palate<br>• Developmental delay<br>• Diabetes mellitus<br>• Hepatic fibrosis<br>• Left ventricular hypertrophy/congenital heart disease |

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|---|---|---|
| | | • Mild spasticity (especially lower limbs)<br>• Polyuria/Polydipsia (nephrogenic diabetes insipidus)<br>• Speech disorder/delay<br>• Strabismus/Cataracts/Astigmatism |

## Clinical Guideline Revision / History Information

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