Imcivree (setmelanotide)

Disclaimer

Clinical guidelines are developed and adopted to establish evidence-based clinical criteria for utilization management decisions. Clinical guidelines are applicable according to policy and plan type. The Plan may delegate utilization management decisions of certain services to third parties who may develop and adopt their own clinical criteria.

Coverage of services is subject to the terms, conditions, and limitations of a member's policy, as well as applicable state and federal law. Clinical guidelines are also subject to in-force criteria such as the Centers for Medicare & Medicaid Services (CMS) national coverage determination (NCD) or local coverage determination (LCD) for Medicare Advantage plans. Please refer to the member's policy documents (e.g., Certificate/Evidence of Coverage, Schedule of Benefits, Plan Formulary) or contact the Plan to confirm coverage.

Imcivree (setmelanotide) 1
- Summary 2
- Definitions 2
- Clinical Indications 3
  - Medical Necessity Criteria for Clinical Review 3
    - General Medical Necessity Criteria 3
  - Medical Necessity Criteria for Initial Clinical Review 4
    - Initial Indication-Specific Criteria 4
      - Acquired Hypothalamic Obesity (HO) 4
      - Bardet-Biedl Syndrome (BBS) 4
      - Pro-opiomelanocortin (POMC), Proprotein Convertase Subtilisin/Kexin Type 1 (PCSK1), or Leptin Receptor (LEPR) Deficiency 5
  - Medical Necessity Criteria for Subsequent Clinical Review 6
      - Acquired Hypothalamic Obesity (HO), Bardet-Biedl Syndrome (BBS), or 6
      - Pro-opiomelanocortin (POMC), Proprotein Convertase Subtilisin/Kexin Type 1 (PCSK1), or Leptin Receptor (LEPR) Deficiency 6
- Experimental / Investigational, or unproven[s] 6
- References 6
- Appendix A 8
- Appendix B 8
- Clinical Guideline Revision / History Information 9

Summary

Imcivree (setmelanotide) injection for subcutaneous (SC or SQ) use is indicated for chronic weight management in adult and pediatric individuals with monogenic,syndromic, or acquired hypothalamic obesity that involve the MC4R pathway.

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.

Bardet-Biedl Syndrome (BBS) is typically an autosomal recessive genetic disorder. Numerous causative gene mutations have been identified, but 20% to 30% of patients lack a known genetic marker, making clinical observation the primary diagnostic tool. 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

Acquired hypothalamic obesity (HO) results from physical damage to the hypothalamus (e.g., due to tumors, surgery, radiation, or trauma), which disrupts the MC4R signaling pathway. This impairment causes persistent weight gain and hyperphagia.

Definitions

"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.

"Weight-for-Age Growth Charts" are available for weight-for-age for those up to 20 years of age. This chart indicates the percentile the weight falls under. CDC Clinical Growth Charts are available at https://www.cdc.gov/growthcharts/clinical_charts.htm.

"[s]" indicates state mandates may apply.

Clinical Indications

Medical Necessity Criteria for Clinical Review

General Medical Necessity Criteria

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, a physician who specializes in metabolic disorders, or additionally for acquired HO a neurologist; *AND*
2. No evidence of end stage renal disease (eGFR less than 15 mL/min/1.73 m^2)*; AND*
3. There is documentation of the member's baseline weight and body mass index (BMI) (in the past 60 days) prior to treatment with Imcivree (setmelanotide)*; AND*
4. Imcivree (setmelanotide) is being prescribed at a dose and frequency that is within FDA approved labeling*; AND*
5. Clinical chart documentation is provided for review to substantiate the listed requirements*; AND*
6. The member meets the applicable Medical Necessity Criteria for Initial Clinical Review or Subsequent Clinical Review listed below.

Medical Necessity Criteria for Initial Clinical Review

Initial Indication-Specific Criteria

Acquired Hypothalamic Obesity (HO)

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

7. The member meets the above General Medical Necessity Criteria; *AND*
8. The member is 4 years of age or older*; AND*
9. The member requires treatment for acquired hypothalamic obesity (HO) AND meets ALL of the following:
    a. The member has or had a hypothalamic lesion, hypothalamic tumor, hypothalamic damage or injury (e.g., craniopharyngioma, astrocytoma, or other malignant or non-malignant hypothalamic-pituitary tumors; surgery, chemotherapy, or radiation for intracranial tumors; traumatic brain injury, hemorrhage, or stroke; inflammation due to infection*); and*
    b. The member is experiencing weight gain associated with the hypothalamic injury that began within the first 12 months after the onset of hypothalamic damage*; AND*
10. The member meets ONE of the following:
    a. IF the member is 18 years of age or older and has a BMI of greater than or equal to (≥) 30 kg/m^2*; or*
    b. IF the member is 4 to less than (<) 18 years of age and has a BMI greater than or equal to (≥) 95th percentile for age and sex on growth chart assessment*; AND*
11. The member meets ALL of the following:
    a. No evidence of ALL of the following:
        i. IF the member is 18 years of age or older and had weight loss >2% in the previous 3 months*; or*
        ii. IF the member is 4 to less (<) than 18 years of age and had >2% reduction in BMI*; AND*
    b. No evidence of bariatric surgery or procedure within the last 2 years.

If the above prior authorization criteria are met, the requested product will be authorized for up to 12-months.[5]

Bardet-Biedl Syndrome (BBS)

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

6. The member meets the above General Medical Necessity Criteria; *AND*
7. The member is 2 years of age or older*; AND*
8. The member requires treatment for monogenic or syndromic obesity due to Bardet-Biedl syndrome (BBS)*; AND*

9. The member meets ONE of the following diagnostic requirements for BBS (see Appendix A, Table 1):
    a. 4 primary features*; or*
    b. 3 primary and 2 secondary features*; AND*
10. The member meets ONE of the following:
    a. IF the member is 16 years of age or older and has a BMI greater than or equal to (≥) 30 kg/m^2*; or*
    b. IF the member is between 2 to 15 years of age and weight is greater than (>) 97th percentile for age and sex on growth chart assessment*; AND*
11. No evidence of prior gastric bypass surgery resulting in greater than (>) 10% weight loss durably maintained from the baseline pre-operative weight with no evidence of weight regain.

If the above prior authorization criteria are met, the requested product will be authorized for up to 12-months.[s]

Pro-opiomelanocortin (POMC), Proprotein Convertase Subtilisin/Kexin Type 1 (PCSK1), or Leptin Receptor (LEPR) Deficiency

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

6. The member meets the above General Medical Necessity Criteria; *AND*
7. The member is 2 years of age or older*; AND*
8. The member requires treatment for monogenic or syndromic obesity due to Pro-opiomelanocortin (POMC), proprotein convertase subtilisin/kexin type 1 (PCSK1), or leptin receptor (LEPR) deficiency*; AND*There is confirmation by genetic testing (by an FDA-approved/cleared test) demonstrating variants in POMC, PCSK1, or LEPR genes that are BOTH:
    a. Homozygous or compound heterozygous (a different gene mutation on each allele)*; and*
    b. Interpreted as pathogenic, likely pathogenic, or of uncertain significance*; AND*
9. The member meets ONE of the following:
    a. IF the member is 18 years of age or older and has a BMI greater than or equal to (≥) 30 kg/m^2*; or*
    b. IF the member is between 2 to 17 years of age with weight greater than or equal to (≥) 95th percentile for age and sex on growth chart assessment*; AND*
10. No evidence of prior gastric bypass surgery resulting in greater than (>) 10% weight loss durably maintained from the baseline pre-operative weight with no evidence of weight regain.

If the above prior authorization criteria are met, the requested product will be authorized for up to 12-months..[s]

Continued Care

Medical Necessity Criteria for Subsequent Clinical Review

Subsequent Medical Necessity Criteria

Acquired Hypothalamic Obesity (HO), Bardet-Biedl Syndrome (BBS), or Pro-opiomelanocortin (POMC), Proprotein Convertase Subtilisin/Kexin Type 1 (PCSK1), or Leptin Receptor (LEPR) Deficiency

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

1. The member meets the above applicable General Medical Necessity Criteria and/or Initial Clinical Review*; AND*
2. Recent (within the last 3 months) chart documentation showing the member meets ONE of the following:
    a. Lost at least 5% of baseline body weight*; or*
    b. 5% of baseline BMI for members aged less than (<) 18 years*; AND*
3. The member is tolerating dosing beyond the recommended initial starting dose AND at a tolerated maintenance dose that does not exceed 3 mg (0.3 mL) (see Appendix B).

If the above reauthorization criteria are met, the requested product will be authorized for up to 12-months.[s]

Experimental / Investigational, or unproven[s]

Imcivree (setmelanotide) for any other indication is consideredExperimental / Investigational, or unproven. Non-covered indications include, but are not limited to, the following:

- 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 (BBS) or acquired hypothalamic obesity (HO).
- 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, Bardet-Biedl syndrome (BBS), or acquired hypothalamic obesity (HO) including obesity associated with other genetic syndromes and general (polygenic) obesity.
- Polygenic or common obesity.
- Weight loss in individuals without rare genetic disorders of obesity.
- Imcivree should not be used in combination with other weight loss agents (e.g., Saxenda, Wegovy, Zepbound, etc.) without other comorbidities.

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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* B. 3 primary and 2 secondary features	• Hypogonadism in males • Learning disabilities • Obesity • Polydactyly • Renal anomalies • Rod-cone dystrophy	• Ataxia/poor coordination/imbalance • Brachydactyly/Syndactyly • Dental crowding/hypodontia/small roots/high arched palate • Developmental delay • Diabetes mellitus • Hepatic fibrosis • Left ventricular hypertrophy/congenital heart disease • Mild spasticity (especially lower limbs) • Polyuria/Polydipsia (nephrogenic diabetes insipidus) • Speech disorder/delay • Strabismus/Cataracts/Astigmatism

Appendix B

The recommended starting dosage injected subcutaneously is the following:

- Adults and pediatric patients aged 4 years and older with acquired HO is 0.5 mg (0.05 mL) once daily for 2 weeks.
- Adults and pediatric patients aged 12 years and older with BBS or POMC, PCSK1, or LEPR deficiency is 2 mg (0.2 mL) once daily for 2 weeks.
- Pediatric patients aged 6 to less than 12 years with BBS or POMC, PCSK1, or LEPR deficiency is 1 mg (0.1 mL) once daily for 2 weeks.
- Pediatric patients aged 2 to less than 6 years with BBS or POMC, PCSK1, or LEPR deficiency is 0.5 mg (0.05 mL) once daily for 2 weeks.
- The recommended dosage in patients with acquired HO, BBS, or POMC, PCSK1, or LEPR Deficiency and mild or moderate renal impairment is the same as in those with normal kidney function (see above for dosing).

In those with severe renal impairment (eGFR of 15 to 29 mL/min/1.73 m 2) the starting dosage is the following:

- Adults and pediatric patients aged with BBS or POMC, PCSK1, or LEPR Deficiency the recommended starting dosage is 0.5 mg (0.05 mL) injected subcutaneously once daily for 2 weeks.
- Imcivree is not recommended for use in adults and pediatric patients aged 4 years and older with acquired HO and severe renal impairment.

The recommended maintenance dosage for adults and pediatric patients aged 6 years and older for all indications is 3 mg (0.3 mL) injected subcutaneously once daily.

Clinical Guideline Revision / History Information

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