Oscar Clinical Guideline: Imcivree (setmelanotide) (PG088, Ver. 6)

Imcivree (setmelanotide)

Summary

Imcivree (setmelanotide) injection for subcutaneous (SC or SQ) use is indicated for chronic weight management in adult and pediatric patients 6 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 patients with the following conditions as Imcivree (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.

"**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 member is 6 years of age or older***; AND***
2. The member requires treatment for monogenic or syndromic obesity due to **ONE** of the following:
    a. Bardet-Biedl syndrome (BBS) meeting **BOTH** of the following:
        i. At least **ONE** of the following diagnostic requirements for BBS (see Table 1):
            1. 4 primary features***; or***
            2. 3 primary and 2 secondary features***; and***
        ii. Meets **ONE** 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 6 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** 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 6 to 17 years of age with weight greater than or equal to (≥) 95^{th} percentile for age and sex on growth chart assessment***; AND***
3. The member does **NOT** have **ANY** of the following:
    a. 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. Severe renal impairment (eGFR 15 to 29 mL/minute/1.73 m^2) AND is 6 to less than 12 years of age***; or***

c. End stage renal disease (eGFR less than 15 mL/min/1.73 m^2)***; AND***

4. 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:

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

Medical Necessity Criteria for Reauthorization

Reauthorization for 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 month) chart documentation shows **ONE** 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 patients 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 patients with continued growth potential.

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

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.

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