BlueCross BlueShield
Federal Employee Program
Blue Cross Blue Shield Association
750 9th St NW, Suite 900
Washington, D.C. 20001
1-800-624-5060
Fax 1-877-378-4727

5.60.048

Section:	Prescription Drugs	**Effective Date:**	July 1, 2026
Subsection:	Central Nervous System Drugs	**Original Policy Date:**	January 29, 2021
Subject:	Imcivree	**Page:**	1 of 6

Last Review Date: June 11, 2026

Imcivree

Description

Imcivree (setmelanotide)

Background
Imcivree (setmelanotide) is a melanocortin 4 (MC4) receptor agonist with 20-fold less activity at the melanocortin 3 (MC3) and melanocortin 1 (MC1) receptors. MC4 receptors in the brain are involved in regulation of hunger, satiety, and energy expenditure. Imcivree may re-establish MC4 receptor pathway activity in patients with proopiomelanocortin (POMC), proprotein convertase subtilisin/kexin type 1 (PCSK1), or leptin receptor (LEPR) deficiency, Bardet-Biedl syndrome (BBS), or acquired hypothalamic obesity (HO) associated with insufficient activation of the MC4 receptor, reducing hunger and decreasing body mass index (BMI) through decreased caloric intake and increased energy expenditure (1).

Regulatory Status
FDA-approved indications: Imcivree is a melanocortin 4 (MC4) receptor agonist indicated to reduce excess body weight and maintain weight reduction long term in adults and pediatric patients aged: (1-2)

- 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: (1-2)

- 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 HO, BBS or POMC, PCSK1 or LEPR deficiency, including obesity associated with other genetic syndromes and general (polygenic) obesity.

Select patients for treatment with Imcivree who have genetically confirmed or suspected deficiency of POMC, PCSK1, or LEPR. Treat patients with variants in POMC, PCSK1, or LEPR genes that are interpreted as pathogenic, likely pathogenic, or of uncertain significance (VUS) in the clinical context of the patient (1).

Select patients for treatment with Incivree who have a clinical diagnosis of acquired HO or BBS (1).

Imcivree may cause depression or suicidal ideation. Patients should be monitored for new onset or worsening of depression. Discontinuation of therapy may be considered if patients experience suicidal thoughts or behaviors (1).

The safety and effectiveness of Imcivree in pediatric patients less than 2 years of age with BBS, POMC, PCSK1, or LEPR deficiency have not been established. The safety and effectiveness of Imcivree in pediatric patients less than 4 years of age with acquired hypothalamic obesity have not been established (1).

Related policies
Weight Loss Medications

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Imcivree may be considered **medically necessary** if the conditions indicated below are met.

Imcivree may be considered **investigational** for all other indications.

Prior-Approval Requirements

Diagnosis

Patient must have **ONE** of the following:

1. POMC, PCSK1, or LEPR deficiency as confirmed by genetic testing
    a. 2 years of age or older
    b. Variants in POMC, PCSK1, or LEPR genes are pathogenic, likely pathogenic, **OR** of uncertain significance (VUS)
2. Bardet-Biedl syndrome (BBS)
    a. 2 years of age or older
3. Acquired hypothalamic obesity (HO)
    a. 4 years of age or older

AND ALL of the following:

1. Patient has the following:
    a. Age 18+: Body mass index (BMI) ≥ 30 kg/m^2
    b. Age 2-17: Body mass index (BMI) ≥ 95^{th} percentile for their age
2. Prescriber agrees to monitor patient's BMI
3. Prescriber agrees to monitor for depression and suicidal ideation
4. **NO** dual therapy with another Prior Authorization (PA) medication for weight loss (see Appendix 1)

Prior – Approval *Renewal* Requirements

Diagnosis

Patient must have **ONE** of the following:

1. POMC, PCSK1, or LEPR deficiency as confirmed by genetic testing
    a. 2 years of age or older
2. Bardet-Biedl syndrome (BBS)
    a. 2 years of age or older
3. Acquired hypothalamic obesity (HO)
    a. 4 years of age or older

AND ALL of the following:

1. Patient has the following:

a. Age 18+, must have **ONE** of the following:
    i. Body mass index (BMI) is <30 kg/m^2
    ii. Patient has lost ≥ 5% of body mass index (BMI) from baseline
b. Age 6-17, must have **ONE** of the following:
    i. Body mass index (BMI) is < 95th percentile for their age
    ii. Patient has lost ≥ 5% of body mass index (BMI) from baseline

2. Prescriber agrees to monitor patient's BMI
3. Prescriber agrees to monitor for depression and suicidal ideation
4. **NO** dual therapy with another Prior Authorization (PA) medication for weight loss (see Appendix 1)

Policy Guidelines

Pre - PA Allowance

None

Prior - Approval Limits

Quantity 30 vials per 90 days

Duration 12 months

Prior – Approval *Renewal* Limits

Quantity 30 vials per 90 days

Duration 12 months

Rationale

Summary

Imcivree (setmelanotide) is a melanocortin 4 (MC4) receptor agonist. MC4 receptors in the brain are involved in regulation of hunger, satiety, and energy expenditure. Imcivree may re-establish MC4 receptor pathway activity in patients with POMC, PCSK1, or LEPR deficiency, BBS, or acquired HO, thereby reducing hunger and decreasing body mass index (BMI) through decreased caloric intake and increased energy expenditure. Imcivree may cause depression or suicidal ideation (1).

Prior authorization is required to ensure the safe, clinically appropriate, and cost-effective use of Imcivree while maintaining optimal therapeutic outcomes.

References

1. Imcivree [package insert]. Boston, MA: Rhythm Pharmaceuticals, Inc.; March 2026.
2. Centers for Disease Control and Prevention. About Adult BMI. Retrieved from: https://www.cdc.gov/healthyweight/assessing/bmi/adult_bmi/index.html.

Policy History

Date	Action
January 2021	Addition to PA
March 2021	Annual review
June 2022	Annual review and reference update
July 2022	Per PI update, addition of diagnosis of Bardet-Biedl syndrome (BBS). Also added requirement for an FDA-approved test to POMC, PCSK1, or LEPR deficiency indication
September 2022	Annual review
December 2022	Annual review. Addition of requirement “no dual therapy with another PA medication for weight loss.” Addition of Appendix 1
June 2023	Annual review
December 2023	Annual review
March 2024	Annual review and reference update
December 2024	Annual review
June 2025	Annual editorial review and reference update
January 2026	Removed from PA
April 2026	Added back to PA. Per PI update, added indication of acquired hypothalamic obesity, decreased age limit of BBS, POMC, PCSK1, and LEPR deficiency from 6 years of age or older to 2 years of age or older, changed FDA-approved test to genetic test
June 2026	Annual review and reference update

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on June 11, 2026 and is effective on July 1, 2026.

Appendix 1 - List of PA Weight Loss Medications

Generic Name	Brand Name
benzphetamine	N/A
carboxymethylcellulose-cellulose-citric acid	Plenity
diethylpropion	N/A
liraglutide	Saxenda
naltrexone/bupropion	Contrave
orlistat	Xenical
phendimetrazine	N/A
phentermine	Adipxex-P/Lomaira
phentermine/topiramate ER	Qsymia
semaglutide	Wegovy
setmelanotide	Imcivree
tirzepatide	Zepbound