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| **Section:** | Prescription Drugs | **Effective Date:** | January 1, 2025 |
| **Subsection:** | Central Nervous System Drugs | **Original Policy Date:** | January 29, 2021 |
| **Subject:** | Imcivree | **Page:** | 1 of 6 |

***Last Review Date:*** December 13, 2024

# 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, or Bardet-Biedl syndrome (BBS) 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 indicated for chronic weight management in adult patients with a BMI of 30 kg/m$^2$ or higher and in pediatric patients 6 years of age and older with a BMI at or above the 95$^{th}$ percentile due to: (1-2)

- 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).
- Bardet-Biedl syndrome (BBS)

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)

- BMI of 30 kg/m$^2$ in adults or BMI at or above the 95$^{th}$ percentile in pediatric patients due to suspected POMC, PCSK1, or LEPR deficiency with *POMC*, *PCSK1*, or *LEPR* variants classified as benign or likely benign.
- BMI of 30 kg/m$^2$ in adults or BMI at or above the 95$^{th}$ percentile in pediatric patients not related to POMC, PCSK1, or LEPR deficiency or BBS, including high BMI associated with other genetic syndromes and general (polygenic) high BMI.

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 BBS (1).

Patients should be periodically assessed for response to Imcivree therapy. For patients with POMC, PCKS1, or LEPR deficiency, evaluate decrease in BMI after 12-16 weeks of treatment. For patients with BBS, evaluate decrease in BMI after 1 year of treatment. If a patient has not shown an appropriate decrease in BMI, discontinue Imcivree as it is unlikely that the patient will achieve and sustain clinically meaningful decrease in BMI with continued treatment (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 6 years of age 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

**Age** 6 years of age or older

**Diagnosis**

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

1. POMC, PCSK1, or LEPR deficiency as determined by an FDA-approved test
    a. Variants in POMC, PCSK1, or LEPR genes are pathogenic, likely pathogenic, **OR** of uncertain significance (VUS)
2. Bardet-Biedl syndrome (BBS)

**AND ALL** of the following:

1. Patient has the following:
    a. Age 18+: Body mass index (BMI) ≥ 30 kg/$m^2$
    b. Age 6-17: 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

**Age** 6 years of age or older

**Diagnosis**

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

1. POMC, PCSK1, or LEPR deficiency as determined by an FDA-approved test
2. Bardet-Biedl syndrome (BBS)

**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 < 95$^{th}$ 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** | POMC, PCSK1, or LEPR deficiency | 6 months |
| | BBS | 12 months |

### Prior – Approval *Renewal* Limits

| | | |
|---|---|---|
| **Quantity** | 30 vials per 90 days | |
| **Duration** | POMC, PCSK1, LEPR deficiency, or BBS | 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, or BBS, 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.; November 2023.
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 |

## Keywords

**This policy was approved by the FEP® Pharmacy and Medical Policy Committee on December 13, 2024 and is effective on January 1, 2025.**

## 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 |