Clinical Criteria

Subject:	Imcivree (setmelanotide)		
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Table of Contents

Overview

This document addresses the use of Imcivree (setmelanotide). Imcivree is a melanocortin-4 receptor (MC4R) agonist that is intended to treat certain individuals with obesity by partially or completely restore signaling at the MC4 receptor. Imcivree is indicated for adult and pediatric patients 6 years of age or older with obesity due to proopiomelanocortin (POMC), Proprotein convertase subtilisin/kexin type 1 (PCSK 1), or Leptin receptor (LEPR) deficiency. Patients should be selected for therapy based on genetic testing demonstrating gene variants that are interpreted as pathogenic, likely pathogenic, or of uncertain significance (VUS).

Imcivree is the first FDA approved treatment for chronic weight management in obese patients with confirmed POMC, PCSK1, and LEPR deficiency. Individuals with these specific genetic aberrations experience excessive appetite and weight gain, resulting in morbid obesity, even as early as infancy. Individuals may experience other disorders of the endocrine system due to involvement in various hormone signaling pathways. Comorbidities may include postprandial hypoglycemia, hypogonadism, hypothyroidism, adrenal insufficiency, and high risk of infection. Historically, patients have relied on management of excessive appetite with calorie restrictions, lifestyle modification, and close supervision to control weight. Imcivree can partially or completely restore signaling at the MC4 receptor resulting in appetite suppression and weight loss in certain individuals.

Imcivree was studied in two open label, single-arm, multicenter, multi-phase trials which enrolled individuals with genetically confirmed or suspected POMC, PCSK1, or LEPR deficiency. Individuals were classified as obese based on ≥BMI 30 kg/m^2 for adults or weight ≥95th percentile using growth chart assessments for pediatric patients. Pediatric BMI may be assessed using tools on the CDC website located here. After 1 year of treatment, results showed that 8/10 individuals with POMC/PSCK1 variants (80%) and 5/11 individuals with LEPR variants (45.5%) achieved at least 10% weight loss after treatment with Imcivree.

Imcivree labeling includes warnings for disturbances in sexual arousal, skin pigmentation, and depression and suicidal ideation. Individuals with suicidal ideation/behavior or history of suicide attempt were excluded from clinical trials; and individuals should be monitored for new onset or worsening depression during treatment. Response to Imcivree treatment should be monitored closely, initially after 12-16 weeks of therapy. Treatment should be discontinued if individual does not lose at least 5% of baseline bodyweight or 5% of baseline BMI in patients with continued growth potential.

Clinical Criteria

When a drug is being reviewed for coverage under a member's medical benefit plan or is otherwise subject to clinical review (including prior authorization), the following criteria will be used to determine whether the drug meets any applicable medical necessity requirements for the intended/prescribed purpose.

Imcivree (setmelanotide)

Initial requests for Imcivree (setmelanotide) may be approved if the following criteria are met:

I. Individual is 6 years of age or older; **AND**
II. Documentation is provided that individual has a diagnosis of obesity, defined as:
    A. BMI of 30 kg/m^2 or greater for adults; **OR**
    B. Bodyweight of more than the 95th percentile for age on growth chart assessment for pediatric individuals (<18 years of age); **AND**

III. Documentation is provided that obesity is due to Proopiomelanocortin (POMC), Proprotein convertase subtilisin/kexin type 1 (PCSK 1), or Leptin receptor (LEPR) deficiency, confirmed by genetic testing; **AND**
IV. Genetic testing demonstrates that variants in POMC, PCSK1, or LEPR genes are pathogenic, likely pathogenic, or of uncertain significance; **AND**
V. Individual is NOT receiving two medications for weight loss at the same time.

Initial Authorization Period: 16 weeks.

Requests for subsequent authorization for Imcivree (setmelanotide) may be approved if the individual meets ALL of the following criteria:

I. Documentation is provided that individual has achieved/maintained weight loss of at least 5% of baseline body weight or 5% of baseline BMI for patients with continued growth potential; **AND**
II. Individual is NOT receiving two medications for weight loss at the same time.

Subsequent Authorization Period: 16 weeks.

Requests for Imcivree (setmelanotide) may not be approved for any of the following:

I. All other indications not included above; **OR**
II. Obesity with POMC, pCSK1, or LEPR variants classified as benign or likely benign; **OR**
III. Individual has an estimated glomerular filtration rate (eGFR) less than 60 mL/min/1.73 m^2.

Quantity Limits

Imcivree (setmelanotide) Quantity Limit

Drug	Limit
Imcivree 10 mg/mL multi-dose vial	9 vials per 30 days

Coding

The following codes for treatments and procedures applicable to this document are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

HCPCS

J3490	Unclassified drugs
J3590	Unclassified biologics

ICD-10 Diagnosis

	All diagnosis pend

Document History

Reviewed: 05/20/2022
Document History:

- 05/20/2022 – Annual Review: No Changes. Coding Reviewed: No changes.
- 08/01/2021 – Administrative update to add documentation.
- 02/19/2021 – Annual Review: Add new clinical criteria document for Imcivree. Coding Reviewed: Added J3490, J3590. All Diagnosis pend.

References

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3. DrugPoints® System [electronic version]. Truven Health Analytics, Greenwood Village, CO. Updated periodically.
4. Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc.; 2022; Updated periodically.
5. Clément K, van den Akker E, Argente J, et al. Efficacy and safety of setmelanotide, an MC4R agonist, in individuals with severe obesity due to LEPR or POMC deficiency: single-arm, open-label, multicentre, phase 3 trials. *Lancet Diabetes Endocrinol*. 2020 Dec;8(12):960-970. doi: 10.1016/S2213-8587(20)30364-8. Epub 2020 Oct 30. PMID: 33137293.
6. "About Child & Teen BMI." *Centers for Disease Control and Prevention*, Centers for Disease Control and Prevention, 29 June 2020, www.cdc.gov/healthyweight/assessing/bmi/childrens_bmi/about_childrens_bmi.html.

Federal and state laws or requirements, contract language, and Plan utilization management programs or polices may take precedence over the application of this clinical criteria.