

Clinical Policy: Setmelanotide (Imcivree)

Reference Number: CP.PHAR.491

Effective Date: 11.25.20

Last Review Date: 02.22

Line of Business: Commercial, HIM, Medicaid

[Coding Implications](#)

[Revision Log](#)

See [Important Reminder](#) at the end of this policy for important regulatory and legal information.

Description

Setmelanotide (Imcivree[™]) is melanocortin-4 receptor pathway activator.

FDA Approved Indication(s)

Imcivree is indicated for chronic weight management in adult and pediatric patients 6 years of age and older with obesity due to proopiomelanocortin (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).

Limitation(s) of use: Imcivree is not indicated for the treatment of patients with the following conditions as Imcivree 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, including obesity associated with other genetic syndromes and general (polygenic) obesity

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation[®] that Imcivree is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Genetic Obesity Disorders (must meet all):

1. Diagnosis of POMC-, PCSK1-, or LEPR-deficiency obesity;
2. Prescribed by or in consultation with an endocrinologist or expert in rare genetic disorders of obesity;
3. Member must meet one of the following (a or b):
 - a. Age ≥ 6 and < 18 years with weight $> 95^{\text{th}}$ percentile for age on growth chart assessment (*see Appendix D*);
 - b. Age ≥ 18 years of age and body mass index (BMI) ≥ 30 kg/m²;

4. Genetic testing confirms that variants in the following genes are interpreted as pathogenic, likely pathogenic, or of uncertain significance (a, b, or c):
 - a. POMC;
 - b. PCSK1;
 - c. LEPR;
5. Documentation of baseline weight (in past 60 days) in kilograms;
6. Documentation of creatinine clearance ≥ 60 mL/min/1.73 m²;
7. If member has had prior gastric bypass surgery, member meets one of the following (a or b):
 - a. Member has not had > 10% weight loss from baseline pre-operative weight;
 - b. Member has regained weight after an initial response to surgery;
8. Documentation that member is actively enrolled in a weight loss program that involves a reduced calorie diet and increased physical activity adjunct to therapy;
9. Dose does not exceed the following (a and b):
 - a. First 2 weeks (i or ii):
 - i. Age ≥ 6 and < 18 years: 1 mg per day;
 - ii. Age ≥ 18 years: 2 mg per day;
 - b. Maintenance: 3 mg per day.

Approval duration:

New starts: 4 months

Maintenance: 6 months

B. Other diagnoses/indications

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Genetic Obesity Disorders (must meet all):

1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
2. Member is responding positively to therapy as evidenced by one of the following (a, b, or c):
 - a. After 12 weeks of treatment: reduction in weight compared with baseline;
 - b. After 1 year: $\geq 10\%$ reduction in weight compared with baseline;
 - c. After > 1 year: maintenance of $\geq 10\%$ reduction in weight compared with baseline;
3. If request is for a dose increase, new dose does not exceed 3 mg per day.

Approval duration: 6 months

B. Other diagnoses/indications (must meet 1 or 2):

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.

Approval duration: Duration of request or 6 months (whichever is less);

2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

- A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid or evidence of coverage documents;
- B. Obesity disorders not caused by POMC-, PCSK1-, or LEPR-deficiency obesity;
- C. Obesity disorder in patients with POMC, PCSK1, or LEPR genes variants that are interpreted as benign or likely benign.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

BMI: body mass index

FDA: Food and Drug Administration

LEPR: leptin receptor

PCSK1: proprotein convertase

subtilisin/kexin type 1

POMC: pro-opiomelanocortin

Appendix B: Therapeutic Alternatives

Not applicable

Appendix C: Contraindications/Boxed Warnings

None reported

Appendix D: General Information

- Body mass index calculator: <https://globalrph.com/medcalcs/body-mass-index-bmi/>
- CDC Clinical Growth Charts from 3rd to 97th percentiles:
 - 2 to 20 years: Boys Stature-for-age and Weight-for-age percentiles
<https://www.cdc.gov/growthcharts/data/set2clinical/cj41c071.pdf>
 - 2 to 20 years: Girls Stature-for-age and Weight-for-age percentiles
<https://www.cdc.gov/growthcharts/data/set2clinical/cj41c072.pdf>

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
POMC, PCSK1, LEPR deficiency obesity	<p>≥ 12 years and older: 2 mg SC once daily for 2 weeks; if tolerated, titrate up to 3 mg SC once daily</p> <p>Age 6 to 12 years: 1 mg SC once daily for 2 weeks; if tolerated, titrate up to 3 mg SC once daily</p>	3 mg/day

VI. Product Availability

Vial: 10 mg/mL (1 mL multi-dose)

VII. References

1. Imcivree Prescribing Information. Boston, MA: Rhythm Pharmaceuticals, Inc.; November 2020. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/213793Orig1s000RPLlbl.pdf. Accessed September 27, 2021.
2. Styne DM, Arslanian SA, Conner EL, et al. Pediatric Obesity: Assessment, Treatment, and Prevention: An Endocrine Society Clinical Practice Guideline. *J Clin Endocrinol Metab.* 2017; 102: 709–757.
3. Clement 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, multicenter, phase 3 trials. *Lancet Diabetes Endocrinol.* 2020; 8: 960-70. DOI: 10.1016/S2213-8587(20)30364-8.

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J3490; C9399	Injection, setmelanotide, 1 mg

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created pre-emptively	05.19.20	08.20
Drug is now FDA approved - criteria updated per FDA labeling: added PCSK1-deficiency obesity, revised lower age limit from 12 years to 6 years old; revised percentile for age on growth chart assessment from 97 th to 95 th percentile; clarified that genetic variants in POMC, PCSK1, and LEPR should be interpreted as pathogenic, likely pathogenic, or of uncertain significance; clarified that baseline documentation of weight be in kg; revised specialist requirement from bariatric physician to experts in rare genetic disorders of obesity; added creatinine clearance requirement for normal renal function or mild renal impairment; added criteria requiring documentation of weight loss program to align with other weight-loss agent policies; expanded initial approval duration from 12 weeks to 4 months; added in Section III that coverage will be excluded for obesity disorder in patients with POMC, PCSK1, or LEPR genes variants that are interpreted as benign or likely benign; updated reference for HIM off-label use to HIM.PA.154 (replaces HIM.PHAR.21); references reviewed and updated.	01.05.21	02.21
1Q 2022 annual review: no significant changes; references reviewed and updated.	09.27.21	02.22

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. “Health Plan” means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan’s affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

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Note:

For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

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