

Preemptive policy: This is a P&T approved policy and can be used after the drug is FDA approved until it is superseded by an updated policy



Clinical Policy: Setmelanotide (Imcivree)

Reference Number: CP.PHAR.491

Effective Date: **FDA Approval Date**

Last Review Date: 11.25

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) [Pending]^

Imcivree is indicated for the treatment of acquired hypothalamic obesity (HO).

^Pre-emptive policy: Following FDA approval, criteria for the above pre-emptive indication will be merged with the existing clinical policy of the same policy reference number above for this drug product and its existing FDA-approved indications.

Limitation(s) of use: [XXX]

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. Acquired Hypothalamic Obesity (must meet all):*

**Criteria will mirror the clinical information from the prescribing information once FDA-approved*

1. Diagnosis of acquired HO as evidenced by all of the following (a, b, and c):*
 - a. Evidence of hypothalamic injury (i.e., hypothalamic lesions) assessed by magnetic resonance imaging (MRI);
 - b. Diagnosis of craniopharyngioma or other brain tumors affecting the hypothalamic region (see *Appendix D*);
 - c. Member has undergone surgery, chemotherapy, or radiation for ≥ 6 months;
2. Prescribed by or in consultation with an endocrinologist;*
3. Member meets one of the following (a or b):*
 - a. Age ≥ 4 and < 18 years with body mass index (BMI) $\geq 95^{\text{th}}$ percentile for age and sex;
 - b. Age ≥ 18 years with BMI ≥ 30 kg/m²;
4. Weight ≥ 15 kg;
5. Documentation of baseline weight (in the past 60 days) in kilograms;
6. Documentation of creatinine clearance ≥ 30 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. For age \geq 6 years: 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 3 mg per day.*

Approval duration: 12 months

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

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
 - a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
 - b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Acquired Hypothalamic Obesity (must meet all):*

**Criteria will mirror the clinical information from the prescribing information once FDA-approved*

1. Member meets one of the following (a or b):
 - a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
 - b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B*);
2. Member is responding positively to therapy as evidenced by one of the following (a or b):*
 - a. Initial re-authorization: After 1 year of treatment, reduction of at least 5% of baseline body weight or 5% of baseline BMI;
 - b. Subsequent re-authorizations: Maintenance of \geq 5% reduction in weight or BMI compared with baseline;
3. If request is for a dose increase, new dose does not exceed 3 mg per day.*

Approval duration: 12 months

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

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
 - a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
 - b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: 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 disorder in patients with POMC, PCSK1, or LEPR gene variants that are interpreted as benign or likely benign.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

BBS: Bardet-Biedl syndrome

BMI: body mass index

FDA: Food and Drug Administration

HO: hypothalamic obesity

LEPR: leptin receptor

PCSK1: proprotein convertase
subtilisin/kexin type 1

POMC: pro-opiomelanocortin

VUS: variant of uncertain significance

Appendix B: Therapeutic Alternatives

Not applicable

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): hypersensitivity to setmelanotide or any of its excipients
- Boxed warning(s): 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:
 - Stature-for-age and Weight-for-age percentiles

- Boys 2 to 20 years:
<https://www.cdc.gov/growthcharts/data/set2clinical/cj41c071.pdf>
- Girls 2 to 20 years:
<https://www.cdc.gov/growthcharts/data/set2clinical/cj41c072.pdf>
- BMI-for-age
 - Boys 2 to 20 years:
<https://www.cdc.gov/growthcharts/data/set2clinical/cj41c073.pdf>
 - Girls 2 to 20 years:
<https://www.cdc.gov/growthcharts/data/set2clinical/cj41c074.pdf>
- Acquired hypothalamic obesity is a rare subtype of obesity caused by acquired, non-genetic hypothalamic dysfunction caused by structural injury to the hypothalamus.
 - This may occur as a result of tumors impacting the hypothalamus.
 - Among those with tumors, 72% had a craniopharyngioma; Other tumor types include astrocytoma, germinomas, gliomas, hamartomas, pituitary macroadenoma.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Acquired HO	Pending	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.; December 2024. Available at: <https://www.imcivree.com>. Accessed January 9, 2025.
2. Clinicaltrials.gov. Open-label study of setmelanotide in hypothalamic obesity. Available at: <https://clinicaltrials.gov/study/NCT04725240>. Accessed October 1, 2025.
3. Clinicaltrials.gov. A trial of setmelanotide in acquired hypothalamic obesity. Available at: <https://clinicaltrials.gov/study/NCT05774756>. Accessed October 1, 2025.
4. Roth CL, Scimia C, Shoemaker AH, et al. Setmelanotide for the treatment of acquired hypothalamic obesity: a phase 2, open-label multicentre trial. *Lancet Diabetes Endocrinol.* 2024 Jul;12(6):380-389.
5. Roth CL and McCormack SE. Acquired hypothalamic obesity: A clinical overview and update. *Diabetes Obes Metab.* 2024;26(Suppl. 2):34-45.
6. van Santen HM and Muller HL. Management of acquired hypothalamic dysfunction and the hypothalamic syndrome; It is more than obesity. *Endocrine Reviews* 2025; 00(0): 1-17.
7. Rose SR, Horne VE, Bingham N, et al. Hypothalamic obesity: Four years of the international registry of hypothalamic obesity disorders. *Obesity* 2018;26(11): 1727-1732.

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
C9399	Unclassified drugs or biologicals
J3490	Unclassified drugs

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created pre-emptively for acquired HO.	10.21.25	11.25

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.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members, and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

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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