

Clinical Policy: Metreleptin (Myalept)

Reference Number: CP.PHAR.425

Effective Date: 11.16.16

Last Review Date: 08.25

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

Metreleptin (Myalept[®]) is a recombinant human leptin analog.

FDA Approved Indication(s)

Myalept is indicated as an adjunct to diet as replacement therapy to treat the complications of leptin deficiency in patients with congenital or acquired generalized lipodystrophy.

Limitation(s) of use:

- The safety and effectiveness of Myalept for the treatment of complications of partial lipodystrophy have not been established.
- The safety and effectiveness of Myalept for the treatment of liver disease, including nonalcoholic steatohepatitis (NASH), have not been established.
- Myalept is not indicated for use in patients with HIV-related lipodystrophy.
- Myalept is not indicated for use in patients with metabolic disease, including diabetes mellitus and hypertriglyceridemia, without concurrent evidence of congenital or acquired generalized lipodystrophy.

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 Myalept is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria**A. Leptin Deficiency** (must meet all):

1. Diagnosis of leptin deficiency as evidenced by baseline leptin level < 12 ng/mL;
2. Prescribed by or in consultation with an endocrinologist or geneticist;
3. Age ≥ 1 year;
4. Member has one of the following (a or b):
 - a. Congenital generalized lipodystrophy (Berardinelli-Seip syndrome) as evidenced by presence of at least one gene mutation (i.e., AGPAT2, BSCL2, CAV1, PTRF, CAVIN1);
 - b. Acquired generalized lipodystrophy (Lawrence syndrome);
5. Dose does not exceed (a or b):
 - a. Body weight ≤ 40 kg: 0.13 mg/kg per day;
 - b. Body weight > 40 kg: 10 mg per day.

Approval duration:

Medicaid/HIM – 6 months

Commercial – 6 months or to the member's renewal date, whichever is longer

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. Leptin Deficiency (must meet all):

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;
3. If request is for a dose increase, new dose does not exceed (a or b):
 - a. Body weight $\leq$ 40 kg: 0.13 mg/kg per day;
 - b. Body weight $>$ 40 kg: 10 mg per day.

Approval duration:

Medicaid/HIM – 12 months

Commercial – 6 months or to the member's renewal date, whichever is longer

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. General obesity not associated with congenital leptin deficiency;
- C. HIV-related lipodystrophy;
- D. Liver disease, including NASH.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

FDA: Food and Drug Administration

HIV: human immunodeficiency virus

NASH: nonalcoholic steatohepatitis

Appendix B: Therapeutic Alternatives

Not applicable

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s):
 - General obesity not associated with congenital leptin deficiency: Myalept has not been shown to be effective in treating general obesity, and the development of anti-metreleptin antibodies with neutralizing activity has been reported in obese patients treated with Myalept
 - Hypersensitivity to metreleptin
- Boxed warning(s): risk of anti-metreleptin antibodies with neutralizing activity and risk of lymphoma
 - Because of these risks, Myalept is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the Myalept REMS Program

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Complications of leptin deficiency in patients with congenital or	<u>Weight ≤ 40 kg:</u> 0.06 to 0.13 mg/kg SC QD (adjust in increments of 0.02 mg/kg)	Weight ≤ 40 kg: 0.13 mg/kg/day

Indication	Dosing Regimen	Maximum Dose
acquired generalized lipodystrophy	<u>Weight > 40 kg:</u> Males: 2.5 to 10 mg SC QD (adjust in increments of 1.25 to 2.5 mg/day) Females: 5 to 10 mg SC QD (adjust in increments of 1.25 to 2.5 mg/day)	Weight > 40 kg: 10 mg/day

VI. Product Availability

Lyophilized cake in vial to be reconstituted: 11.3 mg/vial (5 mg/mL after reconstitution)

VII. References

1. Myalept Prescribing Information. Cary, NC: Chiesi USA, Inc; March 2024. Available at www.myalept.com. Accessed on May 6, 2025.
2. Brown RJ, Araujo-Vilar D, Cheung PT, et al. The diagnosis and management of lipodystrophy syndromes: A multi-society practice guideline. *J Clin Endocrinol Metab*. 2016; 101(12): 4500-4511. doi: 10.1210/jc.2016-2466.
3. National Organization for Rare Disorders. Congenital generalized lipodystrophy. Available at: <https://rarediseases.org/rare-diseases/congenital-generalized-lipodystrophy>. Last updated April 16, 2025. Accessed May 6, 2025.
4. Leptin to treat lipodystrophy (NCT00025883). ClinicalTrials.gov. Available at: <https://clinicaltrials.gov/ct2/show/NCT00025883>. Accessed May 6, 2025.

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	Unclassified drugs

Reviews, Revisions, and Approvals	Date	P&T Approval Date
3Q 2021 annual review: no significant changes; references to HIM.PHAR.21 revised to HIM.PA.154; references reviewed and updated.	03.18.21	08.21
3Q 2022 annual review: added prescriber requirement; clarified that leptin deficiency should be confirmed by laboratory testing per clinical study design; clarified that congenital generalized lipodystrophy should be confirmed by gene mutation; updated HCPCS codes; references reviewed and updated.	03.29.22	08.22
Template changes applied to other diagnoses/indications and continued therapy section.	09.23.22	
3Q 2023 annual review: no significant changes; references reviewed and updated.	04.14.23	08.23

Reviews, Revisions, and Approvals	Date	P&T Approval Date
3Q 2024 annual review: no significant changes; references reviewed and updated.	05.08.24	08.24
3Q 2025 annual review: updated limitations of use per PI; clarified genes associated with congenital generalized lipodystrophy; references reviewed and updated.	5.06.25	08.25

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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