Clinical Policy: Metreleptin (Myalept)

Reference Number: PA.CP.PHAR.425
Effective Date: 01/2020
Last Review Date: 07/2024

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, without concurrent evidence of 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 PA Health & Wellness® 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. 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 (e.g., AGPAT2, BSCL2, CAV1, PTRF);
   b. Acquired generalized lipodystrophy (Lawrence syndrome);
4. 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: 6 months

B. Other diagnoses/indications

1. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

II. Continued Therapy

A. Leptin Deficiency (must meet all)**:**

1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.PHARM.01) applies;
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 ≤ 40 kg: 0.13 mg/kg per day;
   b. Body weight > 40 kg: 10 mg per day.

Approval duration: 12 months

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

1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.PHARM.01) applies.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

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 – PA.CP.PMN.53;
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 acquired generalized lipodystrophy	Weight ≤ 40 kg: 0.06 to 0.13 mg/kg SC QD (adjust in increments of 0.02 mg/kg) Weight > 40 kg: 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: 0.13 mg/kg/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. Dublin, Ireland: Amryt Pharmaceuticals, Inc; February 2022. Available at http://www.myalept.com. Accessed on May 23, 2024.
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 December 15, 2022. Accessed May 23, 2024.
4. Leptin to treat lipodystrophy (NCT00025883). ClinicalTrials.gov. Available at: https://clinicaltrials.gov/ct2/show/NCT00025883. Accessed May 23, 2024.

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
New Policy Created	01/2020
3Q 2020 annual review: references reviewed and updated.	07/2020
3Q 2021 annual review: no significant changes; references reviewed and updated.	07/2021
3Q 2022 annual review: added prescriber requirement; clarified that leptin deficiency should be confirmed by laboratory testing per clinical study	07/2022

Reviews, Revisions, and Approvals	Date
design; clarified that congenital generalized lipodystrophy should be confirmed by gene mutation; updated HCPCS codes; references reviewed and updated.	
3Q 2023 annual review: no significant changes; references reviewed and updated.	07/2023
3Q 2024 annual review: no significant changes; references reviewed and updated.	07/2024