

## PHARMACY COVERAGE GUIDELINE

### MYALEPT® (metreleptin) subcutaneous injection Generic Equivalent (if available)

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#### **This Pharmacy Coverage Guideline (PCG):**

- Provides information about the reasons, basis, and information sources we use for coverage decisions
- Is not an opinion that a drug (collectively “Service”) is clinically appropriate or inappropriate for a patient
- Is not a substitute for a provider’s judgment (Provider and patient are responsible for all decisions about appropriateness of care)
- Is subject to all provisions e.g. (benefit coverage, limits, and exclusions) in the member’s benefit plan; and
- Is subject to change as new information becomes available.

#### **Scope**

- This PCG applies to Commercial and/or Marketplace plans
- This PCG does not apply to the Federal Employee Program, Medicare Advantage, Medicaid or members of out-of-state Blue Cross and/or Blue Shield Plans

#### **Instructions & Guidance**

- To determine whether a member is eligible for the Service, read the entire PCG.
  - This PCG is used for FDA approved indications including, but not limited to, a diagnosis and/or treatment with dosing, frequency, and duration.
  - Use of a drug outside the FDA approved guidelines, refer to the appropriate Off-Label Use policy.
  - The “Criteria” section outlines the factors and information we use to decide if the Service is medically necessary as defined in the Member’s benefit plan.
  - The “Description” section describes the Service.
  - The “Definition” section defines certain words, terms or items within the policy and may include tables and charts.
  - The “Resources” section lists the information and materials we considered in developing this PCG
  - **We do not accept patient use of samples as evidence of an initial course of treatment, justification for continuation of therapy, or evidence of adequate trial and failure.**
  - Information about medications that require prior authorization is available at [www.azblue.com/pharmacy](http://www.azblue.com/pharmacy). You must fully complete the [request form](#) and provide chart notes, lab workup and any other supporting documentation. The prescribing provider must sign the form. Fax the form to BCBSAZ Pharmacy Management at (602) 864-3126 or email it to [Pharmacyprecert@azblue.com](mailto:Pharmacyprecert@azblue.com).
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## Medical Necessity Requirements for MYALEPT (metreleptin)

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### **Criteria for Initial Therapy:**

#### **Prescriber Qualifications**

- Prescribed by a physician specializing in the diagnosis or in consultation with an Endocrinologist

#### **Indication**

- An adjunct to diet to treat leptin deficiency complications in congenital or acquired generalized lipodystrophy
- Complications must include **ONE** of the following:

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- Diabetes mellitus requiring high doses of insulin (greater than 200 units/day or greater than 2 units/kg/day or currently taking U 500 insulin)
- Hyperinsulinemia or insulin resistance with persistent hemoglobin A1C greater than 7 despite dietary intervention, metformin, and other therapy for diabetes mellitus
- Persistent hypertriglyceridemia (greater than 250 mg/dL) despite dietary intervention and optimal therapy with at least two triglyceride lowering agents from different classes (fibrate, omega 3 fatty acid, statin)

#### Age Requirement

- 1 year of age or older

#### Baseline Clinical Evaluation

- Confirmed diagnosis of congenital or acquired generalized lipodystrophy
- A low fat diet is used to manage complications related to leptin deficiency which will be continued
- Fasting leptin concentration at baseline is below the normal range (lab result must be submitted)
- Completed **ALL** of the following baseline tests:
  - Blood glucose
  - Hemoglobin A1C
  - Triglycerides
  - Fasting leptin concentration at baseline is below the normal range (lab result must be submitted)

#### Alternative Therapies

- Failure (trial for at least three months duration), contraindication, intolerance, or is not a candidate for:
  - Fibrate
  - Omega 3 fatty acid
  - Statin

#### Brand Specific Criteria

- Have failure, contraindication, or intolerance with **THREE** generic equivalents (if available) for at least three months each. **Note:** Any failure, contraindication, or intolerance to the generic drugs should be reported to the FDA (see Definitions section)

#### Safety

- No concomitant drug use that may interfere with therapy
- Does not have **ANY** of the following:
  - Liver disease including nonalcoholic steatohepatitis (NASH/MASH)
  - HIV related lipodystrophy
  - General obesity not associated with leptin deficiency
  - Complications of partial lipodystrophy
  - Metabolic disease without concurrent evidence of generalized lipodystrophy

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#### Documentation Requirements

- A completed request form must be submitted including:
  - Chart notes
  - Lab results (fasting leptin concentration, blood glucose, hemoglobin A1C, triglycerides)
  - Supporting clinical documentation

#### Initial Therapy Criteria Approval Duration

- 6 months OR end of plan year
- 

#### Criteria for Continuation of Therapy (renewal therapy):

**Note: Manufacturer assistance (e.g., coupons, samples, etc.) are not considered for continuation of therapy.**

#### Prescriber Qualification

- Continues to be seen by a physician specializing in or is in consultation with an Endocrinologist

#### Clinical Response

- Positive clinical response defined as achieving and maintaining **ALL** of the following:
  - At least 20 percent reduction in hemoglobin A1C over baseline
  - At least 25 percent reduction in fasting glucose over baseline
  - At least 50 percent reduction in triglycerides over baseline

#### Adherence

- Adherence to the prescribed therapy regimen has been documented (includes adherence with continued use of low fat diet to treat the complications of leptin deficiency)

#### Brand Specific Criteria

- Have failure, contraindication, or intolerance with **THREE** generic equivalents (if available) for at least three months each. **Note:** Any failure, contraindication, or intolerance to the generic drugs should be reported to the FDA (see Definitions section)

#### Safety

- Does not have **ANY** of the following:
  - Liver disease including nonalcoholic steatohepatitis (NASH/MASH)
  - HIV related lipodystrophy
  - General obesity not associated with leptin deficiency
  - Complications of partial lipodystrophy
  - Metabolic disease without concurrent evidence of generalized lipodystrophy
- No development of contraindications or significant adverse drug effects including:
  - Loss of efficacy due to anti metreleptin antibodies with neutralizing activity
  - T cell lymphoma
  - Autoimmune disorders (e.g., autoimmune hepatitis, membranoproliferative glomerulonephritis)

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- Severe hypoglycemia

#### Documentation Requirements

- Chart notes
- Supporting clinical documentation with evidence of improvement in given indication
- Lab values confirming safe use (hemoglobin A1C, fasting glucose, triglycerides)

#### Continuation Therapy Criteria Approval Duration

- 12 months OR end of plan year
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#### Criteria for Off-Label Use Requests:

Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

1. Off-Label Use of Non-Cancer Medications
  2. Off-Label Use of Cancer Medications
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#### Description:

Myalept (metreleptin) is a recombinant human leptin analog indicated as an adjunct to diet as replacement therapy to treat the complications of leptin deficiency in individuals with generalized lipodystrophy (congenital or acquired). Metreleptin binds to and activates the leptin receptor. Generalized lipodystrophy is a condition associated with a lack of fat tissue and very low leptin levels, a hormone made by fat tissue.

Lipodystrophy is accompanied by other hormonal abnormalities and is often accompanied by metabolic derangements, including insulin resistance, diabetes mellitus, hepatic steatosis or steatohepatitis, and dyslipidemia. In addition, fat may be deposited in other areas such as in the liver and muscle. Hyperglycemia and hypertriglyceridemia that are resistant to treatment or the use of very high doses of insulin may be important clues of lipodystrophy in the clinical setting.

Adipocytes store lipids to meet the fuel requirements of non-adipose tissues during fasting. In patients with generalized lipodystrophy, the deficiency of adipose tissue leads to hypertriglyceridemia and ectopic deposition of fat in liver and muscle, contributing to metabolic abnormalities including insulin resistance. Native leptin is a hormone predominantly secreted by adipose tissue that informs the central nervous system of the status of energy stores in the body. In patients with generalized lipodystrophy, leptin deficiency, resulting from the loss of adipose tissue, contributes to excess caloric intake, which exacerbates the metabolic abnormalities.

There are four major subtypes of lipodystrophy: congenital generalized lipodystrophy (CGL), acquired generalized lipodystrophy (AGL), familial partial lipodystrophy (FPL), and acquired partial lipodystrophy (APL). Human immunodeficiency virus-associated lipodystrophy has been categorized as a type of APL.

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Individuals with CGL are born with little or no fat tissue over their entire body. CGL is also known as Berardinelli-Seip syndrome, an autosomal recessive disorder. Individuals with AGL are born with normal fat distribution but lose fat tissue over time, starting in childhood or adolescence. There is a progressive loss of fat affecting the whole-body including palms and soles. AGL is also known as Lawrence syndrome.

Therapeutic options for the metabolic management of lipodystrophy consist of lifestyle modifications (diet and exercise), conventional anti-hyperglycemic and lipid-lowering medications, and leptin replacement therapy. Metformin, sulfonylureas (glyburide, glipizide, and others), thiazolidinediones (pioglitazone, rosiglitazone), and insulin can be used to manage hyperglycemia, while fibrates, omega-3 fatty acids, and/or statins can be used to manage hypertriglyceridemia. Myalept (metreleptin) is used as leptin replacement therapy, in addition to diet, in individuals with CGL or AGL.

Clinical studies in patients with generalized lipodystrophy suggest that metreleptin increases insulin sensitivity and reduces food intake. Improvements in insulin sensitivity and reductions in food intake are consistent with lower HbA1c, fasting glucose, and fasting triglyceride values that were seen in the clinical trials.

Myalept (metreleptin) is contraindicated in patients with general obesity not associated with congenital leptin deficiency.

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

Because of the risks associated with the development of neutralizing antibodies and lymphoma, Myalept (metreleptin) is available only through the Myalept Risk Evaluation and Mitigation Strategy (REMS) Program.

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#### **Definitions:**

U.S. Food and Drug Administration (FDA) MedWatch Forms for FDA Safety Reporting  
[MedWatch Forms for FDA Safety Reporting | FDA](#)

#### **Risk Evaluation and Mitigation Strategies (REMS):**

Use of Myalept is subject to a Risk Evaluation and Mitigation Strategies (REMS) program that requires provider, patient, and dispensing pharmacy be enrolled into the program. Only providers and Pharmacies enrolled into the REMS may prescribe and dispense the drug, respectively, to individuals who are also in the program. A REMS program attempts to manage known or potentially serious risks associated with a drug product and is required by the Food and Drug Administration (FDA) for some drugs to ensure that the benefits of a drug outweigh its risks. Under this REMS program, prescribers must be certified with the program by enrolling in and completing training. Pharmacies must be certified with the program and only dispense Myalept after receipt of the Myalept REMS Prescription Authorization Form for each new prescription.

#### **Fibric acid derivatives:**

Choline fenofibrate  
Fenofibrate

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Fenofibric acid  
 Gemfibrozil

**Omega-3 fatty acids derivatives:**

Lovaza or generic  
 Triklo  
 Vascepa

**Statins:**

Atorvastatin  
 Fluvastatin  
 Lovastatin  
 Pitavastatin  
 Pravastatin  
 Rosuvastatin  
 Simvastatin

**American Association of Clinical Endocrinologist Criteria – Clinical Suspicion of Lipodystrophy:**

Core clinical characteristic for lipodystrophy	<ul style="list-style-type: none"> <li>• Loss or absence of subcutaneous body fat in a partial or generalized fashion</li> </ul>
Core clinical characteristic for Familial partial lipodystrophy	<ul style="list-style-type: none"> <li>• Loss of subcutaneous body fat, typically occurring around or shortly after puberty, occurring in the extremities and/or gluteal region with sparing of fat loss or accumulation of excess fat in the face and neck or intra-abdominal area</li> </ul>
Supportive clinical characteristics for lipodystrophy	<ul style="list-style-type: none"> <li>• Presence of diabetes with evidence of severe insulin resistance               <ul style="list-style-type: none"> <li>• Diabetes mellitus with requirement for high doses of insulin, e.g., requiring <math>\geq 200</math> units/d, or <math>\geq 2</math> units/kg/d, or currently taking U-500 insulin</li> <li>• Ketosis-resistant diabetes</li> </ul> </li> <li>• Other evidence of severe insulin resistance               <ul style="list-style-type: none"> <li>• Acanthosis nigricans</li> <li>• Polycystic Ovarian Syndrome (PCOS) or PCOS-like symptoms (hyperandrogenism, oligomenorrhea, and/or polycystic ovaries)</li> </ul> </li> <li>• Presence of hypertriglyceridemia               <ul style="list-style-type: none"> <li>• Severe hypertriglyceridemia (<math>\geq 500</math> mg/dL)</li> <li>• Triglyceride levels (<math>\geq 250</math> mg/dL) that are nonresponsive to therapy and/or modifications to diet</li> <li>• History of pancreatitis associated with hypertriglyceridemia</li> </ul> </li> <li>• Evidence of hepatic steatosis or steatohepatitis               <ul style="list-style-type: none"> <li>• Hepatomegaly and/or elevated transaminases in the absence of a known cause of liver disease (e.g., viral hepatitis) may be consistent with nonalcoholic fatty liver disease</li> <li>• Radiographic evidence of hepatic steatosis (e.g., on ultrasound or computed tomography)</li> </ul> </li> <li>• Family history of similar physical appearance and/or history of fat loss</li> <li>• Prominent muscularity and phlebomegaly (enlarged veins) in the extremities</li> <li>• Disproportionate hyperphagia (cannot stop eating, waking up to eat, fighting for food)</li> <li>• Secondary hypogonadism in a male or primary/secondary amenorrhea in a female patient</li> </ul>

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#### **Resources:**

Myalept (metreleptin) subcutaneous injection product information, revised by Chiesi USA, Inc. 03-2024. Available at DailyMed <http://dailymed.nlm.nih.gov>. Accessed October 24, 2025.

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Fourman LT, Grinspoon SK. Approach to the patient with lipodystrophy. *J Clin Endocrinol Metab.* 2022 Jun; 107(6): 1714–1726. Accessed January 21, 2024. Re-evaluated October 31, 2025.

Mosbah H, Vantighem M-C, Nobécourt E, et al.: Therapeutic indications and metabolic effects of metreleptin in patients with lipodystrophy syndromes: Real-life experience from a national reference network. *Diabetes Obes Metab.* 2022;24(8):1565-1577. Accessed January 21, 2024. Re-evaluated October 31, 2025.