Drug Use Research & Management Program
Oregon State University, 500 Summer Street NE, E35
Salem, Oregon 97301-1079
Phone 503-947-5220 | **Fax** 503-947-2596

Orphan Drug Evaluation: Myalept® (metreleptin) subcutaneous injection

Date of Review: April 2026
Generic Name: metreleptin

End Date of Literature Search: 01/16/2026
Brand Name (Manufacturer): MYALEPT (Chiesi)

Dossier Received: Yes

Purpose for Review:

- To review evidence of safety and effectiveness of metreleptin in people with lipodystrophy due to leptin deficiency and to establish prior authorization (PA) criteria to support medical appropriateness and necessity for metreleptin.

Plain Language Summary:

- Lipodystrophy (also called fat redistribution) is a rare condition that affects how the body stores fat. Some people with lipodystrophy do not have enough leptin, a hormone that affects appetite and energy use. Diabetes, liver disease, and high blood triglyceride levels are linked to having low levels of leptin.
- Diet, exercise, and medicines that manage diabetes (insulin, metformin) and high triglycerides (fibrates, statins) are the current preferred treatments for people with lipodystrophy.
- Metreleptin mimics the effects of leptin in the body and is approved by the Food and Drug Administration (FDA) in people who have low levels of leptin and generalized lipodystrophy (either the inherited or acquired form). Metreleptin is injected under the skin (subcutaneously) once a day.
- Metreleptin is not approved for use in people with human immunodeficiency virus (HIV)-related lipodystrophy or serious liver disease.
- Side effects with metreleptin include headaches, feeling tired, low blood sugar, decreased weight, stomach pain, and nausea. Metreleptin has been linked to a certain type of cancer called T-cell lymphoma and is only available through the manufacturer's restricted safety program.
- The recommendation for the Oregon Health Plan is that metreleptin be covered for people diagnosed with generalized lipodystrophy due to low leptin levels and when other treatments have been prescribed to treat diabetes and high triglycerides.

Research Questions:

1. What is the efficacy and safety of metreleptin in people with generalized lipodystrophy?
2. Are there populations based on demographic characteristics (e.g., age), symptom severity, type of lipodystrophy for which metreleptin is more effective or safe?

Conclusions:

- The clinical trial that supported FDA approval is not published, but study details are included in the prescribing information.[1]
- A phase 2 study evaluated metreleptin dosing and the subsequent open-label, single site, long-term extension study (n=66) conducted over 14 years provides evidence for the safety and efficacy of metreleptin in treating patients with congenital or acquired generalized lipodystrophy due to leptin

Author: Deanna Moretz, PharmD, BCPS

deficiency.[2] The co-primary efficacy endpoints were change in HbA1c and percent change in fasting serum triglycerides from baseline to 12 months. Metreleptin treatment led to a reduction in mean hemoglobin A1c (HbA1c) at 12 months, from 8.6% at baseline to 6.4% (95% Confidence interval [CI] not reported; p<0.001), and mean fasting triglycerides decreased from 1,302 mg/dL at baseline to 398 mg/dL at 12 months (95% CI not reported; p<0.001); (low-quality evidence for both endpoints).[2]

- The most common adverse events included: weight decrease (26%), abdominal pain (17%), hypoglycemia (15%), headache (12%) and decreased appetite (12%).[2] The label for metreleptin carries two black boxed warnings: 1) T-cell lymphoma has been reported in patients with acquired generalized lipodystrophy, in those both treated and untreated with metreleptin, and 2) anti-metreleptin antibodies with neutralizing activity have been identified in patients treated with metreleptin.[1]
- Metreleptin has been studied in patients with partial lipodystrophy but has not received FDA approval for use in this population because the results did not show efficacy in reducing HbA1c and triglycerides.[1,3] Patients with HIV-related lipodystrophy, non-alcoholic steatohepatitis (NASH) and obesity or metabolic disease not associated with leptin-deficient lipodystrophy are also not approved for metreleptin therapy.[1]

Recommendations:

- Implement prior authorization proposed in **Appendix 2** to ensure standard of care in patients diagnosed with lipodystrophy due to leptin deficiency.

Background:

Leptin is a naturally occurring hormone predominantly secreted by adipose tissue that plays a central role in the neurohormonal regulation of energy homeostasis and fat and glucose metabolism.[4] Lipodystrophy syndromes due to leptin deficiency are rare diseases of the adipose tissue characterized by a complete or selective deficiency of body fat.[5] Instead of being stored in adipocytes, lipids are stored in the liver and muscles which results in diabetes, insulin resistance, and metabolic comorbidities (e.g., hepatic steatosis, hypertriglyceridemia).[5] The lack of leptin can lead to hyperphagia (constant hunger) which also contributes to metabolic abnormalities.[5] The lipodystrophy syndrome can be classified as autoimmune (acquired) or congenital, and subclassified based on the extent of fat pattern loss as generalized or partial.[5] Acquired lipodystrophies are associated with immunological abnormalities including dermatomyositis, autoinflammatory disorders, tissue specific autoimmunity, and myeloid disorders (e.g. myelosuppression and lymphoma).[4] Generalized lipodystrophy is usually associated with very low levels of leptin and severe metabolic disease; partial lipodystrophy is associated with a range of leptin levels and may or may not be accompanied by metabolic disease.[4] Complications of lipodystrophy include multi-organ damage affecting the heart, liver, kidneys and pancreas, leading to high morbidity and premature death.[6]

- Diagnosis of lipodystrophy is based on history, physical examination, body composition, and metabolic status.[6] There are no defined serum leptin levels that establish or rule out diagnosis of lipodystrophy.[6]
- Standard of care for leptin-deficient lipodystrophy includes a balanced diet (50-60% carbohydrates, 20-30% fat, and 20% protein), exercise, and pharmacological treatment of diabetes (insulin, metformin) and hyperlipidemias (fibrates, statins).[6]
- The prevalence of lipodystrophy depends on the subtype but overall is around 2.5 per 1 million of the overall population.[7] Generalized lipodystrophy has an estimated prevalence of 0.23 to 0.96 people per million and partial lipodystrophy has an estimated prevalence of 1.67 to 2.84 people per people per million.[8] Acquired generalized lipodystrophy is more common in females than males (3:1 ratio) and usually appears before adolescence.[6]
- In the Oregon Health Plan, 62 people had a diagnosis of lipodystrophy in the past year. Most of the patients (n=53) are enrolled in a Coordinated Care Organization (CCO) and 5 patients are enrolled in fee-for-service (FFS).

- Metreleptin is a recombinant analog of leptin and differs by one amino acid compared with native human leptin.[4] Metreleptin dosing is based on weight and gender. Gender dimorphism of leptin levels has been identified in healthy subjects, with women having higher leptin levels than men even after adjustment for differences in body composition.[4]
- Metreleptin is the only medication approved by FDA as an adjunct to diet as replacement therapy in patients with congenital or acquired generalized lipodystrophy due to leptin deficiency.[1] According to FDA, the effectiveness of metreleptin for the treatment of metabolic complications of partial lipodystrophy have not been established.[1]
- The annual wholesale acquisition cost (WAC) for metreleptin is $6,695 per 11.3 mg vial. Since the dosing is weight-based, the cost may vary depending on the dose the patient is prescribed ranging from one vial per day to one vial every 3 days. The annual cost could range from 0.8 to 2.4 million dollars.
- Canada's Drug Agency (CDA)[8] and the National Institute for Health and Care Excellence (NICE)[7] have evaluated the safety and efficacy of metreleptin in leptin-deficient lipodystrophy patients.
    - CDA recommends metreleptin as an adjunct to diet as replacement therapy when prescribed by an endocrinologist to treat complications of leptin deficiency in lipodystrophy patients:
        - with confirmed congenital generalized lipodystrophy (Berardinelli-Seip syndrome) or acquired generalized lipodystrophy (Lawrence syndrome) in adults and children 2 years of age and older with at least one metabolic abnormality of diabetes, insulin resistance, or high levels of triglycerides: OR
        - with confirmed familial partial lipodystrophy or acquired partial lipodystrophy (Barraquer-Simons syndrome) in adults and children aged 12 years and older with persistent significant metabolic disease for whom standard treatments for a 12-month period have failed to achieve adequate metabolic control, defined as hemoglobin A1c (HbA1c) higher than 6.5% or fasting triglycerides higher than 5.65 mmol/L (101.8 mg/dL).[8]
        - Patients should not be pregnant, lactating, or have HIV-associated lipodystrophy.[8]
        - Maximum duration of initial authorization is 12 months.[8]
        - Renewal after initial authorization requires documentation of beneficial metabolic effect defined as:
            - HbA1c reduction of at least 0.5% from baseline; or
            - Reduction of fasting triglycerides by at least 15% from baseline.[8]
    - NICE guidance recommends metreleptin as an option for treating complications of leptin deficiency in lipodystrophy for:
        - People who are 2 years of age and have generalized lipodystrophy.
        - People who are 12 years of age with partial lipodystrophy do not have metabolic control despite standard treatments. Metreleptin is only recommended if the HbA1c level is higher than 7.5% or fasting triglycerides higher than 5.0 mmol/L (90 mg/dL).[7] (The European Medicines Agency (EMA) label for metreleptin includes people aged 12 years and older with partial lipodystrophy.[6])

Drug Information

See **Appendix 1** for **Highlights of Prescribing Information** from the manufacturer, including Boxed Warnings and Risk Evaluation Mitigation Strategies (if applicable), indications, dosage and administration, formulations, contraindications, warnings and precautions, adverse reactions, drug interactions and use in specific populations.

Clinical Efficacy and Safety:
The clinical trial that supported FDA approval is not published, but study details are included in the prescribing information. The published clinical trial to support the safety and efficacy of metreleptin is described and evaluated in **Table 1**.

Noteworthy trial design and patient characteristics include:

- Long-term Extension Trial Duration: 14 years
- Number of Participants: 66 adults and children
- Comparator: Single-arm study at one site. There are no trials that compare metreleptin with standard supportive care.
- Baseline disease severity and population characteristics:
    - Most of the patients were female (77%) and the median age was 15 years.[2]
    - The majority of patients had congenital lipodystrophy (68%), while 21% had acquired lipodystrophy.[2]
    - The mean baseline HbA1c was 8.6% and the fasting triglyceride level was 1,284 mg/dL.[2]
    - Eighty percent of patients were taking diabetic medications and 52% were taking lipid-lowering medications.[2]

Efficacy:

- Co-primary efficacy endpoints: Change in HbA1c and percent change in fasting serum triglycerides from baseline to 12 months.
- Metreleptin treatment led to a 2.2% mean reduction in HbA1c at 12 months from 8.6% at baseline to 6.4% (95% CI not reported; $p<0.001$) and fasting triglycerides decreased from a mean of 1,302 mg/dL at baseline to a mean of 398.6 mg/dL at 12 months (95% CI not reported; $p<0.001$).[2]

Safety:

- Adverse Effects:
    - Most common adverse events included: weight decrease (26%), abdominal pain (17%), hypoglycemia (15%), headache (12%), and decreased appetite (12%).
    - Ten patients (15.2%) developed a neoplasm during the study; one case of anaplastic large-cell lymphoma was assessed as treatment-related.[2]
- The label for metreleptin carries a boxed warning that T-cell lymphoma has been reported in patients with acquired generalized lipodystrophy, in those both treated and untreated with metreleptin.[1] Patients with acquired generalized lipodystrophy appear to be at a higher risk for lymphoma than the general population, likely due to underlying autoimmunity.[2] In addition, a second boxed warning notes that anti-metreleptin antibodies with neutralizing activity have been identified in patients treated with metreleptin.[1] The consequences are not well characterized but could include inhibition of endogenous leptin action and loss of metreleptin efficacy.[1] Worsening metabolic control and severe infection have been reported.[1] The manufacturer recommends testing for anti-metreleptin antibodies with neutralizing activity in patients who develop severe infections or show signs suspicious for loss of efficacy during metreleptin therapy.[1]
- Metreleptin is available only through a restricted distribution program under a Risk Evaluation and Mitigation Strategy (REMS) because of the risks associated with the development of anti-metreleptin antibodies that neutralize endogenous leptin and the risk of lymphoma.[1]

Other Populations:
Metreleptin is not approved to treat partial lipodystrophy, HIV-related lipodystrophy, NASH, obesity, or metabolic disease not associated with leptin-deficient lipodystrophy.[1]

See **Table 1** for major evidence limitations including:

- Single-arm, open label study design in small number of patients with generalized lipodystrophy, a rare condition. Population was mostly female, which reflects prevalence of the condition.
- Large number of dropouts and missing data. Last observation carried forward (LOCF) imputed for missing results that were 6 months post baseline assessments.
- Primary efficacy outcomes surrogate metabolic endpoints: change from baseline in HbA1c and fasting triglycerides. No evidence from this study that metreleptin helps improve hyperphagia or health-related quality of life.

Table 1. Comparative Evidence Table.

Ref./ Study Design	Drug Regimens/ Duration	Patient Population	N	Efficacy Endpoints	ARR/ NNT	Safety Outcomes	ARR/ NNH	Risk of Bias/ Applicability
1. Brown RJ, et al.[2] Phase 2 Pilot: NCT00005905 Phase 3 Extension: NCT00025883 Open-label, single-arm, single-center study	1. Metreleptin SC 0.08 to 0.10 mg/kg/day in females aged 5 years and older; 0.06 mg/kg/day in all males and females aged less than 5 years. Dose could be increased in increments of 0.02 mg/kg/day in females aged ≥ 10 yo and 0.01 mg/kg/day in all other patients. Dose capped at 0.24 mg/kg/day.	Demographics: -Congenital LD: n = 45 -Acquired LD: n = 21 -Mean fasting leptin: 1.3 ng/mL -Mean baseline HbA1c: 8.6% -Mean fasting TG: 1,284 mg/dL -Mean FPG: 185.6 mg/dL -Female: 77% -Median Age: 15 yrs -Race: --White: 47% --Black: 24% --Hispanic: 17% --Asian: 4.5% --Native American: 3% -Taking diabetic medications: 80% -Taking lipid-lowering medications: 51.5% Key Inclusion Criteria: -Aged 6 mos and older -Diagnosis of LD -Serum leptin < 12 ng/mL (females) and < 8 ng/mL (males) -At least one metabolic abnormality: --Diabetic or fasting insulin > 30 micro units/mL and/or --Fasting TG > 200 mg/dL or non-fasting TG > 500 mg/dL	ITT: 66 PP: 43 Attrition: 23 (35%)	Co-primary Endpoints: Change from baseline in mean HbA1c and mean fasting TG levels at 12 months. n = 59 Baseline HbA1c: 8.6% HbA1c at 12 mos: 6.4% Mean change: -2.2% (95% CI NR; p<0.001) n = 57 Baseline fasting TG: 1,302 mg/dL Fasting TG at 12 mos: 398.6 mg/dL Mean change: -69% (95% CI NR; p<0.001) Secondary Endpoint: Mean change from baseline in FBG at 12 months n=59 Baseline FPG: 183.8 mg/dL FPG at 12 mos: 126.1 mg/dL Mean change: -3.0% (95% CI NR; p<0.001)	NA NA NA	SAEs 19 (29%) TEAEs: 59 (89.4%) Death: 3 (4.5%) p-values and CI not reported	NA for all	**Risk of Bias (low/high/unclear)**: Selection Bias: High. Open-label, single arm study. No randomization performed. Performance Bias: High. No blinding of patients, caregivers, or investigators. Detection Bias: High. No comparator was used to evaluate therapy. Attrition Bias: High. Significant attrition due to nonadherence, lack of efficacy, transfer to another study, and death. Reporting Bias: High. LOCF used for missing data ≥ 6 mos post baseline. Patients with no observational data before 6 mos were excluded from final analysis, therefore mITT population was analyzed. Other Bias: Unclear. Study funded by NIH. Manufacturer provided funding for medical writing of manuscript. Several authors report serving as consultants and/or receiving funding from the manufacturer. **Applicability**: Patient: Small study population due to the nature of the rare condition. Population was mostly female, which reflects the prevalence of the condition. Intervention: Metreleptin dosing studied in Phase 2 phase of the open-label extension study. FDA has approved dosing used in this study. Comparator: Single-arm study design, no comparator. Outcomes: Surrogate outcomes included changes in HbA1C and fasting TG levels from baseline to 12 mos. Metabolic changes are the clinically accepted metrics used to evaluate complications of leptin deficiency.

		Key Exclusion Criteria: -HIV -Infectious liver disease -Taking weight loss drugs						Setting: Single site at the NIH in Bethesda, Maryland with patients originating from the United States, European Union, South America, Canada, India, Pakistan, and Saudi Arabia

Abbreviations: CI = confidence interval; dL = deciliters; DM = diabetes mellitus; FDA = Food and Drug Administration; FPG = fasting blood glucose; GL = generalized lipodystrophy; HbA1c = hemoglobin A1C; HIV = human immunodeficiency virus; ITT = intention to treat; kg = kilograms; LOCF = last observation carried forward; LD = lipodystrophy; mg = milligrams; mITT = modified intention to treat; mL = milliliters; mmol = millimoles; mos = months; N = number of subjects; NA = not applicable; ng = nanograms; NIH = National Institutes of Health; NNH = number needed to harm; NNT = number needed to treat; NR = not reported; PP = per protocol; SAEs = serious adverse events; SC = subcutaneous; TEAEs = treatment-emergent adverse events; TG = triglycerides; yo = years old; yrs = years

References:

1. MYALEPT (metreleptin) for subcutaneous injection. Prescribing Information. Cambridge, MA; Aegerion Pharmaceuticals, Inc. 3/2024.
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3. Oral EA, Gorden P, Cochran E, et al. Long-term effectiveness and safety of metreleptin in the treatment of patients with partial lipodystrophy. *Endocrine*. 2019/06/01 2019;64(3):500-511. doi:10.1007/s12020-019-01862-8
4. Food and Drug Administration. Center for Drug Evaluation and Research. Application Number: 125390Orig1s000. Summary Review. https://www.accessdata.fda.gov/drugsatfda_docs/nda/2014/125390Orig1s000SumR.pdf Accessed January 20, 2026.
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7. Metreleptin for treating lipodystrophy. London: National Institute for Health and Care Excellence (NICE); 2021 Feb 24. PMID: 40811586. https://www.nice.org.uk/guidance/hst14.
8. Metreleptin (Myalepta): Therapeutic area: Leptin deficiency in lipodystrophy: Reimbursement Review . Ottawa (ON): Canadian Agency for Drugs and Technologies in Health; 2024 Oct. Report No.: SR0784-Clinical Review. PMID: 39652691. https://www.cda-amc.ca/sites/default/files/DRR/2024/SR0784REC-Myalepta.pdf Accessed January 16, 2026.

Appendix 1: Prescribing Information Highlights

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use MYALEPT safely and effectively. See full prescribing information for MYALEPT.

MYALEPT® (metreleptin) for injection, for subcutaneous use
Initial U.S. Approval: 2014

WARNING: RISK OF ANTI-METRELEPTIN ANTIBODIES WITH NEUTRALIZING ACTIVITY AND RISK OF LYMPHOMA

See full prescribing information for complete boxed warning.

Anti-metreleptin antibodies with neutralizing activity have been identified in patients treated with MYALEPT. The consequences are not well characterized but could include inhibition of endogenous leptin action and loss of MYALEPT efficacy. Worsening metabolic control and/or severe infection have been reported. Test for anti-metreleptin antibodies with neutralizing activity in patients with severe infections or loss of efficacy during MYALEPT treatment. Contact Chiesi Farmaceutici S.p.A. at 1-866-216-1526 for neutralizing antibody testing. (4.1, 5.1)

T-cell lymphoma has been reported in patients with acquired generalized lipodystrophy, both treated and not treated with MYALEPT. Carefully consider the benefits and risks of treatment with MYALEPT in patients with significant hematologic abnormalities and/or acquired generalized lipodystrophy. (5.2)

MYALEPT is available only through a restricted program called the MYALEPT REMS PROGRAM. (5.3)

INDICATIONS AND USAGE

MYALEPT is a leptin analog indicated as an adjunct to diet as replacement therapy to treat the complications of leptin deficiency in patients with congenital or acquired generalized lipodystrophy. (1)

Limitations of Use

- The safety and effectiveness of MYALEPT for the treatment of complications of partial lipodystrophy have not been established. (1)
- The safety and effectiveness of MYALEPT for the treatment of liver disease, including nonalcoholic steatohepatitis (NASH), have not been established. (1)
- MYALEPT is not indicated for use in patients with HIV-related lipodystrophy. (1)
- MYALEPT is not indicated for use in patients with metabolic disease, without concurrent evidence of generalized lipodystrophy. (1)

DOSAGE AND ADMINISTRATION

Administer as a subcutaneous injection once daily after the lyophilized cake is reconstituted with Bacteriostatic Water for Injection (BWFI) or preservative-free sterile Water for Injection (WFI). (2.1)

The recommended daily dosages are:

- Body weight 40 kg or less: starting dose 0.06 mg/kg/day, increase or decrease by 0.02 mg/kg to a maximum daily dose of 0.13 mg/kg. (2.1)
- Males greater than 40 kg body weight: starting dose 2.5 mg/day, increase or decrease by 1.25 mg to 2.5 mg/day to a maximum dose of 10 mg/day. (2.1)
- Females greater than 40 kg body weight: starting dose 5 mg/day, increase or decrease by 1.25 mg to 2.5 mg/day to a maximum dose of 10 mg/day. (2.1)

DOSAGE FORMS AND STRENGTHS

MYALEPT is supplied as a sterile, white, solid, lyophilized cake of 11.3 mg metreleptin per vial to deliver 5 mg per mL when reconstituted in 2.2 mL of BWFI or WFI. (3)

CONTRAINDICATIONS

- General obesity not associated with congenital leptin deficiency. (4.1)
- Hypersensitivity to metreleptin. (4.2)

WARNINGS AND PRECAUTIONS

- Anti-metreleptin antibodies with neutralizing activity: Could inhibit endogenous leptin action and/or result in loss of MYALEPT efficacy. Test for neutralizing antibodies in patients with severe infections or loss of efficacy during MYALEPT treatment. (5.1)
- T-cell lymphoma: Carefully consider benefits and risks of treatment with MYALEPT in patients with significant hematologic abnormalities and/or acquired generalized lipodystrophy. (5.2)
- Hypoglycemia: A dose adjustment, including possible large reductions, of insulin or insulin secretagogue may be necessary. Closely monitor blood glucose in patients on concomitant insulin or insulin secretagogue therapy. (5.4)
- Autoimmunity: Autoimmune disorder progression has been observed in patients treated with MYALEPT. Carefully consider benefits and risks of MYALEPT treatment in patients with autoimmune disease. (5.5)
- Hypersensitivity: Hypersensitivity reactions (e.g., anaphylaxis, urticaria or generalized rash) have been reported. Patient should promptly seek medical advice regarding suspected reactions. (5.6)
- Benzyl Alcohol Toxicity: Preservative-free sterile WFI recommended for neonates and infants. (5.7)

ADVERSE REACTIONS

Most common in clinical trials (≥10%): headache, hypoglycemia, decreased weight, abdominal pain. (5.4, 6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Chiesi Farmaceutici S.p.A. at 1-888-661-9260 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

See 17 for PATIENT COUNSELING INFORMATION and Medication Guide

Revised: 03/2024

Appendix 2: Proposed Prior Authorization Criteria

Metreleptin (MYALEPT®)

Goal(s):

- Promote evidence-based standard of care in patients diagnosed with lipodystrophy due to leptin deficiency.
- Limit to populations in which metreleptin has been studied and approved by the Food and Drug Administration.

Length of Authorization:

- Up to 12 months

Requires PA:

- Metreleptin (pharmacy and physician administered claims)

Covered Populations: FFS patients

Covered Alternatives:

- Current PMPDP preferred drug list per OAR 410-121-0030 at www.orpdl.org
- Searchable site for Oregon FFS Drug Class listed at www.orpdl.org/drugs/

Approval Criteria		
1. What diagnosis is being treated?	Record ICD10 code.	
2. Is the request for a patient with a prior FFS approval for the requested drug?	**Yes**: Go to **Renewal Criteria**	**No:** Go to #3
3. Is this an FDA approved age and indication?	**Yes**: Go to #4	**No:** Pass to RPh. Deny; medical appropriateness

Approval Criteria		
4. Does the patient have any of the following diagnoses: • Partial lipodystrophy • Non-alcoholic steatohepatitis (NASH) or metabolic dysfunction-associated steatohepatitis (MASH) • General obesity not associated with congenital leptin deficiency • HIV-related lipodystrophy or • Metabolic disease (diabetes, hypertriglyceridemia) without evidence of generalized lipodystrophy?	**Yes:** Pass to RPh. Deny; medical appropriateness	**No:** Go to #5
5. Is the drug prescribed by an endocrinologist or a provider with experience in managing lipodystrophy due to leptin deficiency?	**Yes**: Go to #6	**No:** Pass to RPh. Deny; medical appropriateness
6. Are there documented baseline assessments for all of the following within the past year: • Serum leptin level • Hemoglobin A1C • Fasting triglycerides	**Yes**: Go to #7 Document date and lab results_____	**No:** Pass to RPh. Deny; medical appropriateness
7. Does the patient have: • Persistent hyperglycemia (HbA1c > 6.5%) despite dietary interventions AND • Persistent fasting hypertriglyceridemia (TG > 200 mg/dL) despite dietary interventions	**Yes:** Go to #8	**No:** Pass to RPh. Deny; medical appropriateness

Approval Criteria		
8. Is the patient on maximally tolerated therapy for diagnosed diabetes and hypertriglyceridemia when applicable with the following medications: • Optimized diabetes therapy (insulin, metformin, GLP-1 antagonist, or SGLT-2 inhibitor) at maximum tolerated dose for at least 6 months • Optimized therapy with at least 2 triglyceride-lowering agents (e.g., fibrates, statins) at maximum tolerated doses for at least 6 months • Or do they have documented age or co-morbidity contraindication to these medications	**Yes**: Approve for 6 months	**No:** Pass to RPh. Deny; medical appropriateness

Renewal Criteria		
1. Is there documented evidence of adherence and tolerance to therapy based on claims history and provider assessment?	**Yes:** Go to #2	**No:** Pass to RPh. Deny; medical appropriateness
2. Has the provider re-evaluated the following baseline assessments based upon pre-existing diagnoses within the past 6 months? • HbA1c • Serum triglycerides	**Yes:** Go to #3 Document date and lab values_____	**No:** Pass to RPh. Deny; medical appropriateness
3. Has A1C reduced by at least 0.5% from baseline or have fasting triglycerides reduced by at 15%?	**Yes:** Approve for 12 months	**No:** Pass to RPh. Deny; medical appropriateness

P&T/DUR Review: 4/26 (DM)
Implementation: 6/1/26