Myalept (metreleptin) Prior Authorization Program Summary

This program applies to FlexRx Closed, FlexRx Open, FocusRx, GenRx Closed, GenRx Open, Health Insurance Marketplace, and KeyRx.

This is a FlexRx Standard and GenRx Standard program.

POLICY REVIEW CYCLE

Effective Date	Date of Origin
1/1/2024	4/1/2016

FDA APPROVED INDICATIONS AND DOSAGE

Agent(s)	FDA Indication(s)	Notes	Ref#
Myalept® (metreleptin) Subcutaneous injection	Adjunct to diet as replacement therapy to treat the complications of leptin deficiency in patients with congenital or acquired generalized lipodystrophy Limitations of Use: - Safety and effectiveness for the treatment of complications of partial lipodystrophy have not been established - Safety and effectiveness for the treatment of liver disease, including nonalcoholic steatohepatitis (NASH), have not been established - Not indicated for use in patients with HIV-related lipodystrophy - Not indicated for use in patients with metabolic disease, including diabetes mellitus and hypertriglyceridemia, without concurrent evidence of congenital generalized lipodystrophy (CGL) or acquired generalized lipodystrophy (AGL)		1

See package insert for FDA prescribing information: https://dailymed.nlm.nih.gov/dailymed/index.cfm

CLINICAL RATIONALE

Lipodystrophy	Lipodystrophy is a rare, heterogeneous group of syndromes characterized by the complete or partial loss or absence of subcutaneous adipose tissue. The loss or absence of adipose tissue results in decreased levels of leptin, which is an important hormone regulating appetite. Lipodystrophy is often, although not always, accompanied by metabolic derangements, including insulin resistance, diabetes mellitus, hepatic steatosis or steatohepatitis, and dyslipidemia. Metabolic derangements associated with lipodystrophy can be severe and lead to substantial comorbidities, including acute pancreatitis (due to severe hypertriglyceridemia), hepatic cirrhosis, and premature cardiovascular disease.(2-5) Lipodystrophy can generally be classified based on extent or pattern of fat loss (generalized or partial) and whether the disease is genetic or acquired. There are 4 major lipodystrophy subtypes: congenital generalized lipodystrophy (CGL), acquired generalized lipodystrophy (AGL), familial partial lipodystrophy (FPL), and acquired partial lipodystrophy (APL).(2-4)

	Initial treatment of metabolic disturbances associated with lipodystrophy (e.g., diabetes, hypertriglyceridemia) is the same as in patients without lipodystrophy. Diabetes is treated with hyperglycemic drugs as well as insulin (although high doses are often required). Hypertriglyceridemia may be treated with statins, fibric acid derivatives, or omega-3 fatty acids. Individuals with CGL and AGL are encouraged to maintain a healthy weight by following a low-fat diet and engaging in regular exercise. If metabolic disturbances persist, metreleptin is recommended, along with careful monitoring, in these patients.(2,3,5)
Efficacy (1)	Metreleptin is a recombinant human leptin analog that functions by binding to and activating the human leptin receptor which studies suggest causes an increase in insulin sensitivity and a reduction in food intake. The efficacy of metreleptin was evaluated in an open label single arm study of 48 patients with congenital (n=32) or acquired (n=16) generalized lipodystrophy who also had at least one of the metabolic abnormalities [diabetes mellitus, hypertriglyceridemia > 200 mg/dL, and/or increased fasting insulin (greater than or equal to 30 µU/mL)]. At baseline, 37 (77%) patients had HbA1c values of 7% or greater, 19 (40%) had HbA1c values of 9% or greater, 33 (69%) had fasting plasma glucose values of 126 mg/dL or greater, 17 (35%) had fasting triglyceride values of 500 mg/dL or greater, and 11 (23%) had fasting triglyceride values of 1000 mg/dL or greater. The metreleptin treatment duration was 3.6 months to 10.9 years (median = 2.7 years) and metreleptin was administered either once or twice daily. At year 1, patients treated with metreleptin had mean/median reductions in HbA1c (-2%), fasting glucose (-49 mg/dL), and triglycerides (-55%). Concomitant anti-hyperglycemic and lipid-altering medications dosing regimens were not held constant throughout the study.
Safety (1)	Metreleptin has the following boxed warning for risk of anti-metreleptin antibodies with neutralizing activity and risk of lymphoma: • Anti-metreleptin antibodies with neutralizing activity have been identified in patients treated with metreleptin. The consequences are not well characterized but could include inhibition of endogenous leptin action and loss of metreleptin efficacy. Worsening metabolic control and/or severe infection have been reported. Test for anti-metreleptin antibodies with neutralizing activity in patients who develop severe infections or show signs suspicious for loss of efficacy during metreleptin treatment • T-cell lymphoma has been reported in patients with acquired generalized lipodystrophy, both treated and not treated with metreleptin. Carefully consider the benefits and risks of treatment with metreleptin in patients with significant hematologic abnormalities and/or acquired generalized lipodystrophy Due to the issues included in the boxed warning, metreleptin is available only through a restricted REMS program. Metreleptin is contraindicated in the following: • Patients with general obesity not associated with congenital leptin deficiency. It 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 metreleptin • Patients with prior severe hypersensitivity reactions to metreleptin or to any of the product components

REFERENCES

Number	Reference
1	Myalept prescribing information. Aegerion Pharmaceuticals, Inc. February 2022.

Number	Reference
2	Handelsman Y, Oral EA, Bloomgarden Z. The Clinical Approach to the Detection of Lipodystrophy – An AACE Consensus Statement. *Endocr Pract* 2013;19(1):107-116.
3	Brown R, Araujo-Vilar D, Pik T, et al. The Diagnosis and Management of Lipodystrophy Syndromes: A Multi-Society Practice Guideline. *J Clin Endocrinol Metab* 2016 Dec;101(12):4500-4511.
4	Araujo-Vilar D, Santini F. Diagnosis and Treatment of Lipodystrophy: A Step-By-Step Approach. *J Endocrinol Invest* 2019;42(1):61-73.
5	National Organization for Rare Disorders (NORD). Physician Guide to the Lipodystrophy Disorders. 2014. Available at: https://rarediseases.org/physician-guide/lipodystrophy-disorders/.

POLICY AGENT SUMMARY PRIOR AUTHORIZATION

Target Brand Agent(s)	Target Generic Agent(s)	Strength	Targeted MSC	Available MSC	Final Age Limit	Preferred Status
Myalept	metreleptin for subcutaneous inj	11.3 MG	M ; N ; O ; Y	N		

CLIENT SUMMARY – PRIOR AUTHORIZATION

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Myalept	metreleptin for subcutaneous inj	11.3 MG	FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx

PRIOR AUTHORIZATION CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
	Initial Evaluation **Target Agent** will be approved when ALL of the following are met: 1. The patient has a diagnosis of either congenital generalized lipodystrophy (CGL) or acquired generalized lipodystrophy (AGL) **AND** 2. The patient has a diagnosis of leptin deficiency AND the patient does NOT have any of the following: partial lipodystrophy, liver disease (including non-alcoholic steatohepatitis [NASH]), HIV-related lipodystrophy, or metabolic disease (e.g., diabetes mellitus, hypertriglyceridemia) without evidence of generalized lipodystrophy **AND** 3. The prescriber is a specialist in the area of the patient's diagnosis (e.g., endocrinologist) or the prescriber has consulted with a specialist in the area of the patient's diagnosis **AND** 4. The patient has baseline HbA_{1C}, triglycerides, and fasting insulin levels measured prior to initiating the requested agent **AND** 5. The patient has complications related to lipodystrophy [e.g., diabetes mellitus, hypertriglyceridemia (greater than or equal to 200 mg/dL), and/or high fasting insulin (greater than or equal to 30 µU/mL)] **AND** 6. The patient has tried and had an inadequate response to maximum tolerable dose of a conventional agent for complications related to lipodystrophy **AND** 7. The patient has had an inadequate response to lifestyle modification (i.e., diet modification and exercise) AND will continue lifestyle modifications with the requested agent **AND**

Module	Clinical Criteria for Approval
	8. The patient does NOT have any FDA labeled contraindications to the requested agent **AND** 9. The requested quantity (dose) does NOT exceed the maximum FDA labeled dose for the requested indication **Length of Approval:** 12 months **Renewal Evaluation** **Target Agent** will be approved when ALL of the following are met: 1. The patient has been previously approved for the requested agent through the plan's Prior Authorization process **AND** 2. The prescriber is a specialist in the area of the patient's diagnosis (e.g., endocrinologist) or the prescriber has consulted with a specialist in the area of the patient's diagnosis **AND** 3. The patient has had stabilization and/or reduction from baseline in at least ONE of the following: HbA_{1C}, triglycerides, and/or fasting insulin **AND** 4. The patient will continue lifestyle modifications (i.e., diet and exercise) with the requested agent **AND** 5. The patient does NOT have any FDA labeled contraindications to the requested agent **AND** 6. The requested quantity (dose) does NOT exceed the maximum FDA labeled dose for the requested indication **Length of Approval:** 12 months

