PRIOR AUTHORIZATION POLICY

POLICY: Lipodystrophy – Myalept Prior Authorization Policy
- Myalept® (metreleptin subcutaneous injection – Aegerion)

REVIEW DATE: 11/09/2022

OVERVIEW

Myalept, a recombinant analog of human leptin, is indicated as an adjunct to diet as replacement therapy to treat complications of leptin deficiency in patients with **congenital or acquired generalized lipodystrophy**.[1] Limitations of Use: The safety and efficacy of Myalept have not been established for the treatment of complications of partial lipodystrophy, liver disease (including nonalcoholic steatophepatitis [NASH]), human immunodeficiency virus (HIV)-related lipodystrophy, or metabolic disease (including diabetes mellitus and hypertriglyceridemia) without concurrent evidence of generalized lipodystrophy.

Guidelines

Guidelines on the diagnosis and management of lipodystrophy syndromes were published in 2016 and endorsed by multiple groups of endocrine experts, including the Endocrine Society, the Pediatric Endocrine Society, the American Diabetes Association, and the American Association of Clinical Endocrinologists.[2] These guidelines note that lipodystrophy is an incurable condition and no treatment will regrow adipose tissue. Myalept is the only drug specifically indicated for the treatment of lipodystrophy. Myalept, along with diet, is recommended as the first-line treatment for metabolic and endocrine abnormalities in patients with generalized lipodystrophy. In children, Myalept may also be used to prevent the development of comorbidities.

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of Myalept. Because of the specialized skills required for evaluation and diagnosis of patients treated with Myalept, as well as the monitoring required for adverse events and long-term efficacy, approval requires Myalept to be prescribed by or in consultation with a physician who specializes in the condition being treated. All approvals are provided for the duration noted below.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Myalept is recommended in those who meet the following criteria:

FDA-Approved Indication

1. **Generalized Lipodystrophy (Congenital or Acquired):** Approve for 1 year if the medication is prescribed by, or in consultation with, an endocrinologist or a geneticist physician specialist.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Myalept is not recommended in the following situations:

1. **General Obesity not associated with Congenital Leptin Deficiency.** Myalept is contraindicated in patients with general obesity not associated with congenital leptin deficiency.[1] Myalept was previously evaluated in two clinical development programs for obesity, both as monotherapy (n > 1,100) and in combination with Symlin® (pramlintide acetate for injection; n > 600).[3] Published studies on the effects of leptin therapy in these patients without leptin deficiency yielded conflicting efficacy results.[4,5] The studies involving obese patients (some with type 2 diabetes mellitus), with the exception of one dose-escalation trial, failed to show significant weight loss with Myalept therapy and resulted in clinically insignificant changes in other metabolic parameters, such as insulin sensitivity.[6-10] One additional randomized, double-blind, placebo-controlled crossover study evaluated the efficacy of leptin administration to promote further weight reduction in patients who had undergone Roux-en-Y gastric bypass surgery.[11] Following 16 weeks of therapy, Myalept was not found to promote additional decreases in body weight compared with placebo.

2. **Human Immunodeficiency Virus (HIV)-related Lipodystrophy.** Myalept is not indicated for the treatment of patients with HIV-related lipodystrophy.[1] Results from four small studies of patients with HIV-associated lipodystrophy and leptin deficiency showed mixed results with Myalept therapy.[12-15] One study found significantly improved fasting insulin levels, insulin resistance and high-density lipoprotein (HDL) levels, but no significant differences in fasting glucose levels, free-fatty acid levels, or low-density lipoprotein (LDL) levels when Myalept was compared with placebo.[12] Another demonstrated improved fasting insulin levels, but no difference in intravenous glucose disappearance, fasting serum glucose concentration, glycosylated hemoglobin (HbA_{1C}) levels, body mass index (BMI), or lipid parameters after treatment with Myalept.[13] Two additional studies found that therapy with Myalept improved some, but not all metabolic parameters in patients infected with HIV.[14,15] More information is needed to determine if Myalept is a safe and effective treatment for HIV-related lipodystrophy.

3. **Partial Lipodystrophy.** The safety and efficacy of Myalept in the treatment of the complications of partial lipodystrophy have not been established.[1] The effects of Myalept therapy in patients with partial lipodystrophy have been evaluated; the pivotal trial of Myalept included a subset of patients (n = 24) with partial lipodystrophy.[16] Overall, patients with partial lipodystrophy had milder baseline metabolic abnormalities than patients with generalized lipodystrophy. Following 12 months of Myalept therapy, patients experienced a reduction in HbA_{1C}, fasting plasma glucose, and fasting triglycerides; however, the magnitude of the improvements was less than those observed in patients with generalized lipodystrophy. There are data showing sustained improvements out to 36 months as well.[17] Additional data also highlight the heterogeneity of partial lipodystrophy; Myalept may provide improvement in some metabolic parameters in certain patients with partial lipodystrophy, but more data are needed to confirm these benefits.[18-20] Current lipodystrophy guidelines (2016) outline certain patients with partial lipodystrophy that may benefit from Myalept therapy, but indicate a lower level of evidence to support use in this patient population compared with generalized lipodystrophy.[2] Myalept prescribing information continues to list partial lipodystrophy as a limitation of use.[1]

4. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

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