VENTURA COUNTY
HEALTH CARE PLAN

PRIOR AUTHORIZATION POLICY

POLICY: Lipodystrophy – Egrifta Prior Authorization Policy
- Egrifta® (tesamorelin injection – EMD Serono)

REVIEW DATE: 04/28/2021

OVERVIEW

Egrifta, an analog of human growth hormone-releasing factor, is indicated for the reduction of excess abdominal fat in **patients with human immunodeficiency virus (HIV) who have lipodystrophy**.[1-3] At this time, the long-term cardiovascular safety and potential long-term cardiovascular benefit are not established. Careful consideration should be given to continue Egrifta in patients who do not show a clear efficacy response, as judged by the degree of reduction in visceral adipose tissue.[1] Egrifta has a weight-neutral effect and is not indicated for weight loss management. There are no data supporting improved compliance with anti-retroviral therapies in patients who are HIV-positive and take Egrifta. In the pivotal trial, all patients had lipodystrophy and excess abdominal fat, evidenced by a waist circumference ≥ 95 cm (≥ 94 cm for women) and a waist-to-hip ratio ≥ 0.94 (≥ 0.88 for women). Patients were required to be on a stable antiretroviral regimen for at least 8 weeks. Safety and effectiveness of Egrifta have been established in patients between the ages of 18 and 65 years of age.

Disease Overview

Lipodystrophy is the change in body fat which affects some patients with HIV infection, either due HIV infection or due to medication to treat HIV.[5] Egrifta binds and stimulates human growth hormone-releasing receptors with similar potency as endogenous growth hormone-releasing. This stimulates the synthesis and pulsatile release of endogenous growth hormone, which is both anabolic and lipolytic. Growth hormone exerts its effect by interacting with receptors on a variety of target cells resulting in the pharmacodynamic effect. A decrease in nocturnal secretion of growth hormone and insulin-like growth factor 1 (IGF-1) is associated with increased visceral adipose tissue in patients with HIV-associated lipodystrophy.[2] Egrifta increases secretion of growth hormone and has been shown to decrease visceral adipose tissue and spare subcutaneous adipose tissue.[3-4]

Other Therapies

There are no other therapies approved specifically for treatment of HIV-associated lipodystrophy and treatment options are limited.[5-6] Administration of growth hormone has demonstrated a significant decrease in visceral adipose tissue, but also a decrease in subcutaneous adipose tissue, compared with placebo.[7] Management strategies for lipodystrophy include: switching antiretroviral therapy, exercise and diet, cosmetic procedures (e.g., liposuction, facial fillers), and prevention of lipodystrophy by selection of regimens less likely to cause lipohypertrophy.[6]

Safety

Because the long-term cardiovascular safety and potential long-term cardiovascular benefit are not established, careful consideration should be given whether to continue Egrifta treatment in patients who do not show a clear efficacy response, as judged by the degree of reduction in visceral adipose tissue measured by waist circumference or computerized tomography scan. In the pivotal studies, efficacy of Egrifta was assessed at Week 26. Because Egrifta induces the release of endogenous growth hormone (a known growth factor) and increases serum IGF-1, the benefits of treatment should be weighed against the increased risk of malignancies patients who are HIV-positive. Since the effect of prolonged IGF-1 elevations on the development or progression of malignancies is unknown, monitor IGF-1 levels closely during Egrifta therapy and consider discontinuation in patients with persistent elevations of IGF-1 levels (e.g., > 3 standard

deviation scores), especially if the patient has not experienced a robust response. Egrifta should be used with caution in patients who develop glucose intolerance or diabetes; discontinuation of therapy should be considered for patients who do not show a clear efficacy response.

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of Egrifta. Because of the specialized skills required for evaluation and diagnosis of patients treated with Egrifta as well as the monitoring required for adverse events and long-term efficacy, initial approval requires Egrifta to be prescribed by or in consultation with a physician who specializes in the condition being treated. In the approval indication, as appropriate, an asterisk (*) is noted next to the specified gender. In this context, the specified gender is defined as follows: men are defined as individuals with the biological traits of a man, regardless of the individual's gender identity or gender expression. All approvals are provided for the duration noted below. When approvals are authorized in months, 1 month is equal to 30 days.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

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

FDA-Approved Indications

1. **Lipodystrophy Associated with Human Immunodeficiency Virus (HIV) Infection.** Approve for the duration noted if the patient meets ONE of the following (A or B):
   - **A)** Initial Therapy. Approve for 6 months if the patient meets ALL of the following criteria (i, ii, iii, iv, and v):
     - **i.** Patient is ≥ 18 years of age; AND
     - **ii.** The medication is prescribed for the reduction of excess abdominal fat; AND
     - **iii.** Patient meets ONE of the following (1 or 2):
       - **(1)** If male*, waist circumference is ≥ 95 cm (37.4 in) and waist-to-hip ratio is ≥ 0.94; OR
       - **(2)** If female*, waist circumference is ≥ 94 cm (37 in) and waist-to-hip ratio is ≥ 0.88; AND
     - **iv.** Patient has been stable on an anti-retroviral regimen for at least 8 weeks; AND
       Note: Examples include antiretroviral regimens containing protease inhibitors, nucleoside reverse-transcriptase inhibitors, and/or nonnucleoside reverse-transcriptase inhibitors.
     - **v.** The medication is prescribed by or in consultation with an endocrinologist or a physician specializing in the treatment of human immunodeficiency virus (HIV) infection (e.g., infectious disease [ID], oncology).
   - **B)** Patient is Currently Receiving Egrifta. Approve for 1 year if the patient has responded, as determined by the prescriber.
     Note: Examples of a response include reduction in visceral adipose tissue measured by waist circumference or computed tomography (CT) scan.

***** Refer to the Policy Statement.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Egrifta is not recommended in the following situations:

1. **Abdominal Obesity in a Patient without Human Immunodeficiency Virus (HIV) Infection.** More data are needed. Egrifta has been studied in a very limited number patients who have abdominal obesity without HIV infection.[8] To be eligible for the published trial, patients were required to have a peak stimulated GH no higher than 9 µg/L on a standardized GH-releasing hormone (GHRH)-arginine stimulation test. Patients (n = 60) were randomized in a 1:1 ratio to treatment with Egrifta 2 mg once daily or placebo. The primary endpoint was the change in visceral adipose tissue from baseline. Over 12 months (using last observation carried forward), visceral adipose tissue improved significantly in patients treated with Egrifta compared with placebo (net treatment effect vs. placebo: -35 [95% confidence interval: -58, -12]; P = 0.003). Treatment with Egrifta increased IGF-1 by 90%, decreased triglycerides by 20%, and decreased log C-reactive protein by 24% compared with placebo. There was no effect on total cholesterol, high-density lipoprotein cholesterol (HDL-C), or low-density lipoprotein cholesterol (LDL-C) in the treatment groups.

2. **Human Immunodeficiency Virus (HIV)-Related Cachexia, Weight Loss, or Fat Distribution other than Lipodystrophy.** Egrifta has not been studied in these conditions.

3. **Patient is > 65 Years of Age.** There is no information on the use of Egrifta in patients greater than 65 years of age with HIV and lipodystrophy.[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.

REFERENCES

1. Egrifta® injection [prescribing information]. Montreal, Quebec, Canada: Theratechnologies; July 2019.
2. Wang Y, Tomlinson B. Tesamorelin, a human growth hormone releasing factor analogue. *Expert Opin Investig Drugs*. 2009;18(3):303-310.
3. Falutz J, Allas S, Blot K, et al. Metabolic effects of a growth hormone-releasing factor in patients with HIV. *N Engl J Med*. 2007;357(23):2359-2370.
4. Falutz J, Potvin D, Mamputu JC, et al. Effects of tesamorelin, a growth hormone-releasing factor, in HIV-infected patients with abdominal fat accumulation: a randomized placebo-controlled trial with a safety extension. *J Acquir Immune Defic Syndr*. 2010;53(3):311-322.
5. HIV and Lipodystrophy. US Department of Health and Human Services. Updated October 10, 2017. Available at: https://aidsinfo.nih.gov/understanding-hiv-aids/fact-sheets/22/61/hiv-and-lipodystrophy. Accessed March 19, 2018.
6. Pierone Jr, G. HIV lipodystrophy. AIDS Research & Treatment Center of the Treasure Coast; October 26-27, 2012. Printed January 7, 2013.
7. Sivakumar T, Mechanic O, Fehmie DA, Paul B. Growth hormone axis treatments for HIV-associated lipodystrophy: a systematic review of placebo-controlled trials. *HIV Med*. 2011;12(8):453-462.
8. Makimura H, Feldpausch MN, Rope AM, et al. Metabolic effects of a growth hormone-releasing factor in obese subjects with reduced growth hormone secretion: a randomized controlled trial. *J Clin Endocrinol Metab*. 2012;97(12):4769-4779.