

PRIOR AUTHORIZATION POLICY

POLICY: Lipodystrophy – Egrifta® (tesamorelin injection – EMD Serono)

TAC APPROVAL DATE: 04/10/2019

OVERVIEW

Egrifta is an analog of human growth hormone-releasing factor (GRF), indicated for the reduction of excess abdominal fat in human immunodeficiency virus (HIV)-infected patients with lipodystrophy.¹⁻³ At this time, the long-term cardiovascular (CV) safety and potential long-term CV benefit are not established and 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 HIV-positive patients who take Egrifta.

Disease Overview

Lipodystrophy is the change in body fat which affects some patients with HIV infection, either due to HIV infection or due to medication to treat HIV.⁵ Egrifta binds and stimulates human GRF receptors with similar potency as endogenous GRF. GRF stimulates the synthesis and pulsatile release of endogenous growth hormone (GH), which is both anabolic and lipolytic. GH exerts its effect by interacting with receptors on a variety of target cells resulting in the pharmacodynamic effect. A decrease in nocturnal secretion of GH and insulin-like growth factor 1 (IGF-1) is associated with increased visceral adipose tissue (VAT) in patients with HIV-associated lipodystrophy.² Egrifta increases secretion of GH and has been shown to decrease VAT and spare subcutaneous adipose tissue (SAT).³⁻⁴ Egrifta is contraindicated in patients with disruption of the hypothalamic-pituitary axis due to hypophysectomy, hypopituitarism, pituitary tumor or surgery, head irradiation, or head trauma; patients with known hypersensitivity to Egrifta or mannitol; pregnant women; and in patients with an active malignancy.¹ Any pre-existing malignancy should be inactive; patients should complete treatment prior to beginning Egrifta.

Other Therapies

There are no other therapies approved specifically for treatment of HIV-associated lipodystrophy and treatment options are limited.⁵⁻⁶ Administration of GH has demonstrated a significant decrease in VAT, but also a decrease in SAT, 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 CV safety and potential long-term CV 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 CT scan. In the pivotal studies, efficacy of Egrifta was assessed at Week 26. Because Egrifta induces the release of endogenous GH (a known growth factor) and increases serum IGF-1, the benefits of treatment should be weighed against the increased risk of malignancies in HIV-positive patients. 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 [SDS]), 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. The FDA-approved indication is authorized for an initial 6-month duration (where 1 month is equal to 30 days), then for a 3-year approval duration for patients currently receiving Egrifta.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

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

FDA-Approved Indications

- 1. Lipodystrophy in Human Immunodeficiency Virus (HIV)-Infected Patients.** 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, and iii):
 - i.** The patient is an adult \geq 18 years of age; AND
 - ii.** Egrifta 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); AND
 - iii.** Egrifta is prescribed for the reduction of excess abdominal fat.
 - B) Patient is Currently Receiving Egrifta.** Approve for 3 years if the patient has responded (e.g., reduction in visceral adipose tissue measured by waist circumference or computed tomography [CT] scan), as determined by the prescriber. The patient may not have a full response, but there should have been response to Egrifta.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Egrifta has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. Rationale for non-coverage for these specific conditions is provided below. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval.)

- 1. Abdominal Obesity in Patients without Human Immunodeficiency Virus (HIV) Infection.** More data are needed. Egrifta has been studied in a very limited number of 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 μ g/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 (QD) or placebo. The primary endpoint was the change

in VAT from baseline. Over 12 months (using last observation carried forward [LOCF]), VAT improved significantly in patients treated with Egrifta compared with placebo (net treatment effect vs. placebo: -35 [95% confidence interval {CI}: -58, -12]; P = 0.003). Treatment with Egrifta increased IGF-1 by 90%, decreased triglycerides by 20%, and decreased log C-reactive protein (CRP) 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. 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, Inc; July 2018.
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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.

OTHER REFERENCES UTILIZED

- Panel on Antiretroviral Therapy and Medical Management of HIV-Infected Children. Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection. Updated December 14, 2018. Available at: <http://aidsinfo.nih.gov/contentfiles/lvguidelines/pediatricguidelines.pdf>. Accessed March 26, 2019.
- Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents. Department of Health and Human Services. Updated October 25, 2018. Available at: <http://aidsinfo.nih.gov/contentfiles/lvguidelines/adultandadolescentgl.pdf>. Accessed March 26, 2019. [pages K 19].
- Mangili A, Falutz J, Mamputu JC, et al. Predictors of treatment response to tesamorelin, a growth hormone-releasing factor analog, in HIV-infected patients with excess abdominal fat. *PLoS One*. 2015;10(10):e0140358.

HISTORY

Type of Revision	Summary of Changes*	TAC Approval Date
Annual revision	No criteria changes.	03/08/2017
Annual revision	No criteria changes.	04/04/2018
Annual revision	No criteria changes.	04/10/2019

TAC – Therapeutic Assessment Committee; * For a further summary of criteria changes, refer to respective TAC minutes available at: <http://esidepartments/sites/Dep043/Committees/TAC/Forms/AllItems.aspx>.