Egrifta (tesamorelin) Prior Authorization with Quantity Limit Program Summary

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

This is a FlexRx Standard and GenRx Standard program.

POLICY REVIEW CYCLE

Effective Date	Date of Origin
9/1/2023	11/1/2019

FDA APPROVED INDICATIONS AND DOSAGE

Agent(s)	FDA Indication(s)	Notes	Ref#
Egrifta SV® (tesamorelin) Subcutaneous injection	Reduction of excess abdominal fat in HIV-infected adult patients with lipodystrophy		1

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

CLINICAL RATIONALE

Overview	Due to the successes of antiretroviral therapy (ART), persons with human immunodeficiency virus infection (HIV) are living longer and experiencing conditions commonly associated with aging (i.e., cardiovascular disease, neurocognitive dysfunction, physical function impairments, falls). Although multiple factors contribute to the development of these disease processes, an accumulation of visceral adipose tissue (VAT) may play a central role. VAT accumulation is associated with HIV, ART, and diet and physical activity, and may contribute to the low-level, chronic inflammatory state persistent in HIV infection despite virologic suppression. Several studies have shown strong associations between VAT or central adiposity and cardiovascular disease, neurocognitive dysfunction, and frailty among those with HIV. VAT tends to accumulate with increasing age. The deposition of this ectopic adipose tissue in organs including the liver, epicardium, and skeletal muscle has been associated with organ-specific disease development including liver steatosis and fibrosis, myocardial infarction, and physical function limitations or falls. The combination of age-associated and HIV-associated VAT accumulation may accentuate the effects of organ-specific diseases and frailty among people aging with HIV. Furthermore, therapeutic options to reverse VAT accumulation are limited.(5) In November 2010, the United Stated Food and Drug Administration (FDA) approved tesamorelin for the treatment of excessive abdominal fat in persons with HIV. Tesamorelin is a synthetic analog of human growth hormone-releasing factor that acts on the anterior pituitary gland to stimulate the endogenous growth hormone secretion.(1,5) Tesamorelin is a synthetic analog of human growth hormone-releasing factor that acts on the anterior pituitary gland to stimulate the endogenous growth hormone secretion.(1,5) The clinical evidence for the efficacy of tesamorelin was derived from 2 randomized, double-blind, placebo-controlled studies conducted in HIV-infected patients with lipodystrophy and excess abdominal fat (abdominal lipohypertrophy). Both studies (Study 1 and 2) consisted of a 26-week Main Phase and a 26-week Extension Phase.

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	Main inclusion criteria were age 18-65 years, a waist circumference greater than or equal to 95 cm for men and greater than or equal to 94 cm for women, a waist-to-hip ratio greater than or equal to 0.94 for men and greater than or equal to 0.88 for women, and fasting blood glucose less than 150 mg/dL. Patients were on a stable ART regimen for at least 8 weeks prior to randomization. The primary efficacy assessment for each of these studies was the percent change from baseline to Week 26 (Main Phase) in visceral adipose tissue (VAT), as assessed by CT scan at L4-L5 vertebral level.(1,3,4) Study 1 randomized 412 HIV-infected patients with lipodystrophy and excess abdominal fat, to receive either tesamorelin (N equal to 273) or placebo (N equal to 137). The percent change from baseline to week 26 in VAT was significantly greater in the tesamorelin group, which had a decrease of 27.8 cm^2 (-18% mean change), as compared with an increase of 4 cm^2 (2% mean change) in the placebo group. The percent change from week 26 to week 52 in VAT was significantly greater in the tesamorelin group, which had an increase of 3 cm^2 (0%) as compared with an increase of 25 cm^2 (22%) in the placebo group. Waist circumference in the treatment group decreased 3 cm versus 1 cm decrease in placebo, at 26 weeks. At 52 weeks, treatment group waist circumference decreased 0.2 cm while increasing 2.4 cm in placebo group.(1,4) Study 2 randomized 404 HIV-infected patients with lipodystrophy and excess abdominal fat to receive either tesamorelin (N equal to 270) or placebo (N equal to 126). The percent change from baseline to week 26 in visceral adipose tissue was significantly greater in the tesamorelin group, which had a decrease of 21 cm^2 (-14% mean change), as compared with a decrease of 0 cm^2 (-2% mean change) in the placebo group. In the extension phase, the percent change from week 26 to week 52 in visceral adipose tissue was significantly greater in the tesamorelin group, which had a decrease of 11 cm^2 (-5% mean change), as compared with an increase of 24 cm^2 (16% mean change) in the placebo group. Waist circumference in the treatment group decreased 2 cm versus 1 cm decrease in placebo, at 26 weeks. At 52 weeks, treatment group waist circumference decreased 1.1 cm while increasing 0.2 cm in placebo group.(1,3) The FDA review noted that tesamorelin is clearly effective on modifying the biomarker of VAT by 8-10%, which was the decrease needed to support approval. What the clinical benefit is with this degree of VAT reduction is uncertain, and benefit based on patient reported outcomes (PRO) measures in this population appears to be modest at best. PRO was the only secondary endpoint identified by the FDA for which the applicant needed to show a positive effect on to support the primary endpoint of VAT reduction. In particular, the applicant had to demonstrate an improvement on belly appearance distress (BAD), as this was considered a consequential component of PRO whereas other PRO measures (belly size evaluation or belly profile) were considered supportive. Neither of the supportive PRO measures were significantly different between the two groups.(2) A post hoc analysis compared tesamorelin non-responders to responders (defined as those with greater than or equal to 8% reduction in visceral adipose tissue [VAT]) for reduction in triglyceride levels, and glucose homeostasis. The study reported that compared to non-responders, HIV-infected patients receiving tesamorelin with greater than or equal to 8% reduction in VAT have significantly improved triglyceride levels, adiponectin levels, and preservation of glucose homeostasis.(4)
SAFETY (1)	Tesamorelin is contraindicated in the following: • Patients with disruption of the hypothalamic-pituitary axis due to hypophysectomy, hypopituitarism, pituitary tumor/surgery, head irradiation, or head trauma • Patients with active malignancy (either newly diagnosed or recurrent) • Patients with a known hypersensitivity to tesamorelin or any of the agent's excipients

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	• Pregnant women

REFERENCES

Number	Reference
1	Egrifta SV prescribing information. Theratechnologies Inc. October 2019.
2	Egrifta FDA Review. Center for Drug Evaluation and Research. Available at: http://www.accessdata.fda.gov/drugsatfda_docs/nda/2010/022505Orig1s000SumR.pdf
3	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 Synd 2010;53(3):311-322.
4	Stanley TL, Feldpausch MN, Oh J, et al. Effect of Tesamorelin on Visceral Fat and Liver Fat in HIV-Infected Patients with Abdominal Fat Accumulation: A Randomized Clinical Trial. JAMA 2014;312(4):380-389.
5	Adrian S, Scherzinger A, Sanyal A, et al. The Growth Hormone Releasing Hormone Analogue, Tesamorelin, Decreases Muscle Fat and Increases Muscle Area in Adults with HIV. J Frailty Aging 2019;8(3):154-159.

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POLICY AGENT SUMMARY PRIOR AUTHORIZATION

Target Brand Agent(s)	Target Generic Agent(s)	Strength	Targeted MSC	Available MSC	Final Age Limit	Preferred Status
Egrifta ; Egrifta sv	Tesamorelin Acetate For Inj ; tesamorelin acetate for inj	2 ; 2 MG	M ; N ; O ; Y	N		

POLICY AGENT SUMMARY QUANTITY LIMIT

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	QL Amount	Dose Form	Day Supply	Duration	Addtl QL Info	Allowed Exceptions	Targeted NDCs When Exclusions Exist
Egrifta ; Egrifta sv	Tesamorelin Acetate For Inj 2 MG (Base Equiv)	2 ; 2 MG	30	Vials	30	DAYS			

CLIENT SUMMARY – PRIOR AUTHORIZATION

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Egrifta ; Egrifta sv	Tesamorelin Acetate For Inj ; tesamorelin acetate for inj	2 ; 2 MG	FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx

CLIENT SUMMARY – QUANTITY LIMITS

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Egrifta ; Egrifta sv	Tesamorelin Acetate For Inj 2 MG (Base Equiv)	2 ; 2 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(s)** will be approved when ALL of the following are met: 1. The patient has a diagnosis of human immunodeficiency virus (HIV) infection **AND** 2. The requested agent is being prescribed to reduce excess abdominal fat in HIV-associated lipodystrophy **AND** 3. If the patient has an FDA approved indication, ONE of the following: A. The patient's age is within FDA labeling for the requested indication for the requested agent **OR** B. The prescriber has provided information in support of using the requested agent for the patient's age for the requested indication **AND** 4. The prescriber has measured and recorded baseline (prior to initiating therapy with the requested agent) visceral adipose tissue (VAT) and waist circumference **AND**

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Module	Clinical Criteria for Approval
	5. The patient is currently being treated with anti-retroviral therapy (ART) **AND** 6. The prescriber is a specialist in the area of the patient's diagnosis (e.g., infectious disease, HIV specialist) or the prescriber has consulted with a specialist in the area of the patient's diagnosis **AND** 7. The patient does NOT have any FDA labeled contraindications to the requested agent **Length of Approval:** 6 months NOTE if Quantity Limit applies, please refer to Quantity Limit criteria **Renewal Evaluation** **Target Agent(s)** will be approved when ALL 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 patient is currently being treated with anti-retroviral therapy (ART) **AND** 3. The patient has had improvements or stabilization with the requested agent as indicated by ONE of the following: A. The patient has achieved or maintained an 8% decrease in visceral adipose tissue (VAT) from baseline (prior to initiating therapy with the requested agent) **OR** B. The patient has maintained or decreased waist circumference from baseline (prior to initiating therapy with the requested agent) **AND** 4. The prescriber is a specialist in the area of the patient's diagnosis (e.g., infectious disease, HIV specialist) or the prescriber has consulted with a specialist in the area of the patient's diagnosis **AND** 5. The patient does NOT have any FDA labeled contraindications to the requested agent **Length of Approval:** 12 months NOTE: If Quantity Limit applies, please refer to Quantity Limit criteria

QUANTITY LIMIT CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
	Quantity limit for the Target Agent(s) will be approved when **ONE** of the following is met: 1. The requested quantity (dose) does NOT exceed the program quantity limit **OR** 2. ALL of the following: A. The requested quantity (dose) is greater than the program quantity limit **AND** B. The requested quantity (dose) does NOT exceed the maximum FDA labeled dose for the requested indication **AND** C. The requested quantity (dose) cannot be achieved with a lower quantity of a higher strength that does NOT exceed the program quantity limit **Length of Approval:** Initial: 6 months Renewal: 12 months

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