09-J1000-32

Original Effective Date: 05/01/11

Reviewed: 10/09/19

Revised: 10/01/25

Subject: Tesamorelin (Egrifta) Injection

THIS MEDICAL COVERAGE GUIDELINE IS NOT AN AUTHORIZATION, CERTIFICATION, EXPLANATION OF BENEFITS, OR A GUARANTEE OF PAYMENT, NOR DOES IT SUBSTITUTE FOR OR CONSTITUTE MEDICAL ADVICE. ALL MEDICAL DECISIONS ARE SOLELY THE RESPONSIBILITY OF THE PATIENT AND PHYSICIAN. BENEFITS ARE DETERMINED BY THE GROUP CONTRACT, MEMBER BENEFIT BOOKLET, AND/OR INDIVIDUAL SUBSCRIBER CERTIFICATE IN EFFECT AT THE TIME SERVICES WERE RENDERED. THIS MEDICAL COVERAGE GUIDELINE APPLIES TO ALL LINES OF BUSINESS UNLESS OTHERWISE NOTED IN THE PROGRAM EXCEPTIONS SECTION.

DESCRIPTION:

Lipodystrophy is a disorder of fat metabolism involving a loss of subcutaneous adipose tissue (SAT) from the face, extremities and buttocks as well as an accumulation of fat around the liver, stomach, and other abdominal organs. Although lipodystrophy may result due to a genetic disorder, it has been linked to antiretroviral therapy, specifically protease inhibitors.

Tesamorelin (Egrifta) was approved by the U.S. Food and Drug Administration (FDA) in November 2010 as a daily subcutaneous therapy to reduce abdominal lipodystrophy in HIV-infected individuals. Two multicenter, randomized, double-blind, placebo-controlled studies were conducted in individuals with HIV-associated lipodystrophy and excess abdominal fat. Study 1 randomized 412 participants and Study 2 included 404 randomized participants. Both studies consisted of a 26-week Main Phase and a 26-week Extension Phase. Inclusion criteria were age 18-65 years, a waist circumference ≥ 95 cm (37.4 inches) and a waist-to-hip ratio ≥ 0.94 for men, ≥ 94 cm (37.0 inches) and ≥ 0.88 for women, respectively, and FBG < 150 mg/dL (8.33 mmol/L). Exclusion criteria included BMI ≤ 20 kg/m2, type 1 diabetes, and type 2 diabetes if previously treated with insulin.

At week 26, treatment with tesamorelin resulted in a reduction from baseline in mean abdominal fat of 1.0 kg in Study 1 and 0.8 kg in Study 2, respectively (compared with an increase of 0.4 kg in Study 1 and of 0.2 kg in Study 2, respectively, in individuals receiving placebo). Treatment with tesamorelin resulted in an increase from baseline in mean lean body mass of 1.3 kg in Study 1 and of 1.2 kg in Study 2, respectively (compared with a decrease of 0.2 kg in Study 1 and of 0.03 kg in Study 2, respectively, in individuals receiving placebo). Tesamorelin did not adversely alter antiretroviral effectiveness as measured by mean circulating levels of CD4 counts or HIV-1 RNA (viral load).

In Study 2, the reduction of VAT was approximately 18% ($p<0.001$) and continued for 12 months. Those participants who switched from treatment with tesamorelin to placebo lost the initial improvements in VAT. The decrease in VAT was statistically significant for the treatment group (-10.9%) compared to -0.6% in the placebo group at 6 months ($p<0.0001$). There was no change in abdominal or limb subcutaneous fat. Secondary endpoints were significantly improved for self-rating of belly appearance distress ($p=0.02$) and physician rating of belly profile ($p=0.02$) in the treatment groups compared to the placebo groups. Levels of triglyceride changes from baseline (-51 ± 169 mg/dl, $p<0.001$ compared to baseline) and total cholesterol (-7 ± 36 mg/dl, $p=0.009$ compared to baseline) were maintained in the treatment group. However, there were no significant changes observed in the ratio of total cholesterol to high-density lipoprotein (HDL) cholesterol in the treatment group.

POSITION STATEMENT:

Comparative Effectiveness

The Food and Drug Administration has deemed the drug(s) or biological product(s) in this coverage policy to be appropriate for self-administration or administration by a caregiver (i.e., not a healthcare professional). Therefore, coverage (i.e., administration) in a provider-administered setting such as an outpatient hospital, ambulatory surgical suite, physician office, or emergency facility is not considered medically necessary.

Initiation of tesamorelin (Egrifta®) me**ets the definition of medical necessity** when **ALL** of the following criteria are met:

1. Member is diagnosed with HIV-associated lipodystrophy that is symptomatic (e.g., abdominal pain, shortness of breath) – documentation from the medical record must be provided
2. Member meets all of the following:
    a. Body mass index (BMI) greater than 20 kg/m2
    b. Waist circumference greater than or equal to 95 cm (37.5 in) – documentation from the medical record must be provided
    c. Waist-to-hip ratio greater than or equal to 0.94 – documentation from the medical record must be provided
    d. HIV postive – laboroatory documentation must be provided
    e. Fasting blood glucose (FBG) is less than 150 mg/dL (8.33 mmol/L) – laboroatory documentation must be provided
    f. No history of type 1 diabetes or insulin-treated type 2 diabetes
    g. No active malignancy (e.g. a potential cancer which is being evaluated or a diagnosed cancer which is being treated)
    h. No concomitant use of growth hormone
3. Member is 18 years of age or older
4. Dose does not exceed 2 mg daily

Approval duration: 6 months

Continuation of tesamorelin (Egrifta®) **meets the definition of medical necessity** for members meeting the following criteria:

1. Authorization/reauthorization for tesamorelin has been previously approved by Florida Blue or another health plan in the past two years for the treatment of excess abdominal fat in HIV-infected patients with lipodystrophy **OR** the member currently meets all indication-specific initiation criteria criteria (NOTE: BMI, waist circumference, and waist-to-hip ratio may be evaluated using pre-treatment measurements)
2. Member meets one of the following:
    a. Member has had a reduction of 8% in VAT measured by CT scan – documentation of baseline and on-treatment imaging must be provided
    b. Member has had a decrease in waist circumference – documentation of baseline and on-treatment waist circumference must be provided
    c. Member currently demonstrates a beneficial response to treatment with tesamorelin **AND** has been receiving treatment for a minimum of 12 months
3. Member meets all of the following:
    a. Fasting blood glucose (FBG) is less than 150 mg/dL (8.33 mmol/L) – laboroatory documentation must be provided
    b. No history of type 1 diabetes or insulin-treated type 2 diabetes
    c. No active malignancy (e.g. a potential cancer which is being evaluated or a diagnosed cancer which is being treated)
    d. No concomitant use of growth hormone
4. Dose does not exceed 2 mg daily

Approval duration: 6 months

DOSAGE/ADMINISTRATION:

THIS INFORMATION IS PROVIDED FOR INFORMATIONAL PURPOSES ONLY AND SHOULD NOT BE USED AS A SOURCE FOR MAKING PRESCRIBING OR OTHER MEDICAL DETERMINATIONS. PROVIDERS SHOULD REFER TO THE MANUFACTURER'S FULL PRESCRIBING INFORMATION FOR DOSAGE GUIDELINES AND OTHER INFORMATION RELATED TO THIS MEDICATION BEFORE MAKING ANY CLINICAL DECISIONS REGARDING ITS USAGE.

FDA-approved

- Lipodystrophy in HIV-infected patients: 2 mg subcutaneously once a day.

Drug Availability

- 1 mg single-dose vial with a diluent of 10 mL of Sterile Water for Injection, USP

PRECAUTIONS:

Boxed Warning

None

Contraindications

- Active malignancy
- Known hypersensitivity to tesamorelin and/or mannitol
- Pregnancy
- Disruption of the hypothalamic-pituitary axis due to hypophysectomy, hypopituitarism or primary tumor/surgery, head irradiation or head trauma

Precautions/Warnings

- **Neoplasms:** preexisting malignancy should be inactive and its treatment complete prior to initiation.
- **Elevated IGF-1:** IGF-1 should be monitored regularly; consider discontinuation if elevated levels persist.
- **Fluid retention:** may include edema, arthralgia, and carpal tunnel syndrome
- **Glucose intolerance:** may develop secondary to therapy; evaluate glucose status prior to and during therapy.
- **Hypersensitivity:** seek immediate medical attention if suspected.
- **Injection site reactions:** rotate sites to avoid.
- **Acute critical illness:** consider discontinuation.

BILLING/CODING INFORMATION:

HCPCS Coding

C9399	Unclassified drugs or biologicals (This code should only be used for drugs and biologicals that are approved by the FDA on or after January 1, 2004) (Hospital Outpatient Use ONLY)
J3490	Unclassified drug

ICD-10 Diagnosis Codes That Support Medical Necessity

E88.14	HIV-associated lipodystrophy

REIMBURSEMENT INFORMATION:

Refer to section entitled **POSITION STATEMENT**.

PROGRAM EXCEPTIONS:

Federal Employee Program (FEP): Follow FEP guidelines.

State Account Organization (SAO): Follow SAO guidelines.

Medicare Part D: Florida Blue has delegated to Prime Therapeutics authority to make coverage determinations for the Medicare Part D services referenced in this guideline.

Medicare Advantage: No National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) were found at the time of the last guideline revised date.

If this Medical Coverage Guideline contains a step therapy requirement, in compliance with Florida law 627.42393, members or providers may request a step therapy protocol exemption to this requirement if based on medical necessity. The process for requesting a protocol exemption can be found at Coverage Protocol Exemption Request

DEFINITIONS:

No guideline specific definitions apply.

RELATED GUIDELINES:

Growth Hormone Therapy, 09-J0000-27

Mecasermin (Increlex®), 09-J0000-57

OTHER:

None.

REFERENCES:

1. Clinical Pharmacology [Internet]. Tampa (FL): Gold Standard, Inc.; 2018 [cited 9/29/19]. Available from: http://www.clinicalpharmacology.com/.
2. ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine; 2000 Feb 29 - [cited 9/29/19]. Available from: http://clinicaltrials.gov/.
3. DRUGDEX® System [Internet]. Greenwood Village (CO): Thomson Micromedex; Updated periodically [cited 9/29/19]. Available from: http://www.thomsonhc.com/.
4. EMD Serono, Inc. Egrifta (tesamorelin) kit. 2010 [cited 9/29/19]. In: DailyMed [Internet]. Bethesda (MD): National Library of Medicine. Available from: http://dailymed.nlm.nih.gov/dailymed/lookup.cfm?setid=3de31cec-31dc-4ac4-9717-367a687d22f2/.
5. Orphan Drug Designations and Approval [Internet]. Silver Spring (MD): US Food and Drug Administration; 2019 [cited 9/29/19]. Available from: http://www.accessdata.fda.gov/scripts/opdlisting/oopd/index.cfm/.

COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Medical Policy and Coverage Committee on 05/13/20.

GUIDELINE UPDATE INFORMATION:

05/01/11	New Medical Coverage Guideline.
05/15/12	Review and revision to guideline; consisting of updating references.

03/15/13	Review and revision to guideline; consisting of revising description section and precautions section; updating references.
12/15/13	Review and revision to guideline; consisting of revising dosage/administration, precautions, program exceptions, references.
12/15/14	Review and revision to guideline; consisting of references.
11/15/16	Revision to guideline; consisting of description, position statement, coding, references.
12/15/17	Review and revision to guideline; consisting of references.
11/15/18	Review and revision to guideline; consisting of position statement and references.
11/15/19	Review and revision to guideline; consisting of dosing, references.
06/15/20	Revision to guideline to remove CT from initiation criteria
10/01/25	Revision to guideline to update ICD10.