HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use EGRIFTA WR safely and effectively. See full prescribing information for EGRIFTA WR.

EGRIFTA WR™ (tesamorelin) for injection, for subcutaneous use
Initial U.S. Approval: 2010

RECENT MAJOR CHANGES

Dosage and Administration (2) 3/2025

INDICATIONS AND USAGE

EGRIFTA WR is a growth hormone-releasing factor (GHRF) analog indicated for the reduction of excess abdominal fat in HIV-infected adult patients with lipodystrophy. (1)

Limitations of use:

- Long-term cardiovascular safety of EGRIFTA WR has not been established. (1)
- Not indicated for weight loss management. (1)
- There are no data to support improved compliance with anti-retroviral therapies in HIV-positive patients taking EGRIFTA WR. (1)

DOSAGE AND ADMINISTRATION

- The recommendations in this prescribing information only apply to EGRIFTA WR (tesamorelin) for injection 11.6 mg per vial formulation. For recommendations for tesamorelin for injection 2 mg per vial formulation, see the EGRIFTA SV prescribing information. These two formulations and strengths have differences in the dosage, the number of vials required to prepare a dose, reconstitution instructions, and storage requirements. EGRIFTA WR and EGRIFTA SV are not substitutable. (2.1).
- The dose of EGRIFTA WR is 1.28 mg (0.16 mL of the reconstituted solution) injected subcutaneously once daily. (2.1)
- Inject EGRIFTA WR into the abdomen, rotating injection sites. (2.1,5.6)
- Use only the diluent provided, Bacteriostatic Water for Injection, USP, to reconstitute EGRIFTA WR. (2.2)
- Reconstitute one vial of lyophilized powder with 1.3 mL of diluent. Move the vial in a circle (swirl) to mix all the powder and liquid. Do not shake. (2.2)
- Inspect the reconstituted vial visually for particulate matter and discoloration. Use only if the solution is clear, colorless and without particulate matter. (2.2)
- One reconstituted vial provides daily doses for 7 days. Discard unused solution of EGRIFTA WR vial 7 days after mixing. (2.2)

DOSAGE FORMS AND STRENGTHS

- For injection: 11.6 mg of tesamorelin as a lyophilized powder in single-patient-use vial for reconstitution. (3)

CONTRAINDICATIONS

EGRIFTA WR is contraindicated in:

- Patients with disruption of the hypothalamic-pituitary axis (4)
- Patients with active malignancy (4)
- Patients with known hypersensitivity to tesamorelin or excipients in EGRIFTA WR (4)
- Pregnancy (4)

WARNINGS AND PRECAUTIONS

- *Increased risk of neoplasms:* Preexisting malignancy should be inactive and its treatment complete prior to starting EGRIFTA WR**.** Discontinue EGRIFTA WR if there is any evidence of recurrent malignancy. (5.1)
- *Elevated IGF-1:* EGRIFTA WR stimulates GH production and increases serum IGF-1, a growth factor. The effects of prolonged elevations in IGF-1 levels are unknown Monitor IGF-1 levels during EGRIFTA WR therapy. Consider discontinuing in patients with persistent elevations. (5.2)
- *Fluid retention:* May occur with EGRIFTA WR and may include edema, arthralgia, and carpal tunnel syndrome. (5.3)
- *Glucose intolerance or diabetes mellitus:* May develop with EGRIFTA WR use. Evaluate glucose prior to and during therapy. (5.4)
- *Hypersensitivity reactions:* Have occurred in clinical trials. Advise patients to seek immediate medical attention and discontinue treatment if suspected. (5.5)
- *Increased mortality in patients with acute critical illness:* Consider discontinuation in critically ill patients**.** (5.7)

ADVERSE REACTIONS

Most commonly reported adverse reactions (>5%): Arthralgia, injection site erythema, injection site pruritus, pain in extremity, peripheral edema, and myalgia. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact THERA patient support® toll free at 1-833-23THERA (1-833-238-4372) or FDA at 1-800-FDA-1088 or *www.fda.gov/medwatch*

DRUG INTERACTIONS

- *Cytochrome P450-metabolized drugs*: Monitor patients for potential interactions when administering with EGRIFTA WR. (7.1)
- *Glucocorticoids*: Patients receiving glucocorticoid replacement for previously diagnosed hypoadrenalism may require an increase in maintenance or stress doses following initiation of EGRIFTA WR. (7.2)

USE IN SPECIFIC POPULATIONS

- *Lactation:* HIV-1 infected mothers should not breastfeed to avoid potential postnatal transmission of HIV-1. (8.2)

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.

Revised: 3/2025

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FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

EGRIFTA WR is indicated for the reduction of excess abdominal fat in HIV-infected adult patients with lipodystrophy.

Limitations of Use:

- Long-term cardiovascular safety of EGRIFTA WR has not been established. Consider risk/benefit of continuation of treatment in patients who have not had a reduction in visceral adipose tissue.
- EGRIFTA WR is not indicated for weight loss management as it has a weight neutral effect.
- There are no data to support improved compliance with anti-retroviral therapies in HIV-positive patients taking EGRIFTA WR.

2 DOSAGE AND ADMINISTRATION

2.1 Recommended Dosage and Administration Instructions

- There are two EGRIFTA formulations (EGRIFTA WR and EGRIFTA SV) with different recommended dosages. These two formulations and strengths have differences in the dosage, the number of vials required to prepare a dose, reconstitution instructions, and storage requirements.
- EGRIFTA WR and EGRIFTA SV are not substitutable.
- The dosage and administration recommendations in this prescribing information only apply to EGRIFTA WR (tesamorelin) for injection 11.6 mg per vial formulation. For dosage and administration recommendations for tesamorelin for injection 2 mg per vial formulation, see the EGRIFTA SV prescribing information.
- The recommended dosage of EGRIFTA WR is 1.28 mg subcutaneously once daily.
- Inject EGRIFTA WR into the abdomen. Rotate injection sites to different areas of the abdomen *[see Warnings and Precautions (5.6)]*. Do not inject into scar tissue, bruises or the navel.

2.2 Reconstitution Procedure

- Instruct patients to read the Instructions for Use enclosed in the EGRIFTA WR Injection Box.
- Use only the diluent provided, Bacteriostatic Water for Injection, to reconstitute EGRIFTA WR.
- Reconstitute 1 vial of EGRIFTA WR lyophilized powder with 1.3 mL of diluent (8 mg per mL). Move the vial in a circle (swirl) to mix all the powder and liquid. Do not shake.
- Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. EGRIFTA WR is a clear, colorless solution. Do not use if solid particles appear or if the solution is cloudy or colored.
- One reconstituted EGRIFTA WR vial provides daily doses for 7 consecutive days. One dose of EGRIFTA WR is 1.28 mg in 0.16 mL of the reconstituted solution.
- Store reconstituted EGRIFTA WR at room temperature at 20°C to 25°C (68°F to 77°F). Discard unused solution of EGRIFTA WR 7 days after mixing. Do not freeze.

3 DOSAGE FORMS AND STRENGTHS

For injection: 11.6 mg of tesamorelin as a white to off-white lyophilized powder in a single-patient-use vial for reconstitution and a diluent of 30 mL of multiple-dose Bacteriostatic Water for Injection, USP.

4 CONTRAINDICATIONS

EGRIFTA WR is contraindicated in:

- Patients with disruption of the hypothalamic-pituitary axis due to hypophysectomy, hypopituitarism, pituitary tumor/surgery, head irradiation or head trauma.
- Patients with active malignancy. Any preexisting malignancy should be inactive and its treatment complete prior to instituting therapy *[see Warnings and Precautions (5.1)]*.
- Patients with known hypersensitivity to tesamorelin or the excipients in EGRIFTA WR *[see Warnings and Precautions (5.5)]*.
- Pregnant women because modifying visceral adipose tissue offers no benefit in a pregnant woman and could result in fetal harm *[see Use in Specific Populations (8.1)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Increased Risk of Neoplasms

New Malignancy

Carefully consider the decision to start treatment with EGRIFTA WR based on the increased background risk of malignancies in HIV-positive patients.

Active Malignancy

EGRIFTA WR induces the release of endogenous growth hormone (GH), a known growth factor. Do not treat patients with active malignancy with EGRIFTA WR *[see Contraindications (4)]*.

History of Malignancy

For patients with a history of non-malignant neoplasms, initiate EGRIFTA WR therapy after careful evaluation of the potential benefit of treatment. For patients with a history of treated and stable malignancies, initiate EGRIFTA WR therapy only after careful evaluation of the potential benefit of treatment relative to the risk of re-activation of the underlying malignancy. Discontinue EGRIFTA WR if there is any evidence of recurrent malignancy.

5.2 Elevated IGF-1 Levels

EGRIFTA WR stimulates GH production and increases serum IGF-1, a growth factor. The effects of prolonged elevations in IGF-1 levels are unknown. Monitor IGF-1 levels during EGRIFTA WR therapy. Consider discontinuing EGRIFTA WR in patients with persistent elevations of IGF-1 levels (e.g., >3 SDS), particularly if the efficacy response is not robust.

Among patients who received EGRIFTA for 26 weeks, 47% had IGF-1 levels greater than 2 standard deviation scores (SDS), and 36% had SDS >3, with this effect seen as early as 13 weeks of treatment. Among those patients who remained on EGRIFTA for a total of 52 weeks, at the end of treatment, 34% had IGF-1 SDS >2 and 23% had IGF-1 SDS >3.

5.3 Fluid Retention

Fluid retention may occur during EGRIFTA WR therapy and is thought to be related to the induction of GH secretion. This manifests as increased tissue turgor and musculoskeletal discomfort resulting in adverse reactions (e.g. edema, arthralgia, and carpal tunnel syndrome) which are either transient or resolve with discontinuation of treatment.

5.4 Glucose Intolerance or Diabetes Mellitus

EGRIFTA WR treatment can result in glucose intolerance. During clinical trials, the percentages of patients with elevated HbA_{1c} ($\geq$ 6.5%) from baseline to Week 26 were 5% and 1% in the EGRIFTA and placebo groups, respectively. An increased risk of developing diabetes with EGRIFTA (HbA_{1c} level $\geq$ 6.5%) relative to placebo was observed [intent-to-treat hazard odds ratio of 3.3 (CI 1.4, 9.6)].

Evaluate glucose status prior to initiating EGRIFTA WR. Monitor all patients treated with EGRIFTA WR periodically to diagnose those who develop impaired glucose tolerance or diabetes. If patients treated with EGRIFTA WR develop glucose intolerance or diabetes, consider discontinuing EGRIFTA WR in patients who do not show a clear efficacy response.

EGRIFTA WR increases IGF-1, monitor patients with diabetes who are receiving treatment with TESAMORELIN for injection at regular intervals for potential development or worsening of retinopathy.

5.5 Hypersensitivity Reactions

Hypersensitivity reactions occurred in 4% of patients treated with EGRIFTA in clinical trials. Reactions included pruritus, erythema, flushing, urticaria, and rash. In cases of suspected hypersensitivity reactions, advise patients to seek prompt medical attention and immediately discontinue treatment with EGRIFTA WR.

5.6 Injection Site Reactions

EGRIFTA WR treatment may cause injection site reactions, including injection site erythema, pruritus, pain, irritation, and bruising. The incidence of injection site reactions was 25% in EGRIFTA treated patients and 14% in placebo-treated patients during the first 26 weeks of treatment in clinical trials. Rotate injection sites to different areas of the abdomen to decrease injection site reactions *[see Dosage and Administration (2.1)]*.

5.7 Increased Mortality in Patients with Acute Critical Illness

Increased mortality in patients with acute critical illness due to complications following open heart surgery, abdominal surgery or multiple accidental trauma, or those with acute respiratory failure has been reported after treatment with pharmacologic amounts of growth hormone. EGRIFTA WR is a growth hormone-releasing hormone (GHRH) and since it stimulates growth hormone production, consider discontinuing EGRIFTA WR in critically ill patients.

6 ADVERSE REACTIONS

The following important adverse reactions are also described elsewhere in the labeling:

- Increased risk of neoplasms *[see Warnings and Precautions (5.1)]*
- Elevated IGF-1 levels *[see Warnings and Precautions (5.2)]*
- Fluid retention *[see Warnings and Precautions (5.3)]*
- Glucose intolerance or diabetes mellitus *[see Warnings and Precautions (5.4)]*
- Hypersensitivity reactions *[see Warnings and Precautions (5.5)]*
- Injection site reactions *[see Warnings and Precautions (5.6)]*

6.1 Clinical Trial Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

The safety of EGRIFTA WR (11.6 mg/vial formulation) has been established based on clinical trials conducted with EGRIFTA (1 mg/vial formulation). Adverse reactions for the 1.28 mg dose (11.6 mg/vial formulation) of EGRIFTA WR are expected to be similar to those observed with the 2 mg dose (1 mg/vial formulation) of EGRIFTA *[see Clinical Pharmacology 12.3)].*

Seven hundred and forty (740) HIV-infected patients with lipodystrophy and excess abdominal fat were treated with EGRIFTA in clinical trials; of these, 543 received EGRIFTA during the initial 26-week placebo-controlled phase.

The most commonly reported adverse reactions were hypersensitivity reactions (e.g., rash, urticaria), edema-related reactions (e.g., arthralgia, extremity pain, peripheral edema, and carpal tunnel syndrome), hyperglycemia, and injection site reactions (injection site erythema, pruritus, pain, urticaria, irritation, swelling, and hemorrhage).

Adverse reactions that occurred more frequently with EGRIFTA relative to placebo and had an incidence ≥1% during the first 26 weeks across all studies are presented in Table 1.

Table 1. Adverse Reactions Reported in ≥ 1% and More Frequent in EGRIFTA–treated than Placebo Patients during the 26-Week Phase (Combined Studies)

Preferred Term	Placebo (N=263)	EGRIFTA (N=543)
Injection site reaction*	6	17
Arthralgia	11	13
Pain in extremity	5	6
Myalgia	2	6
Edema peripheral	2	6
Paresthesia	2	5
Hypoesthesia	2	4
Rash	2	4
Dyspepsia	1	2

Preferred Term	Placebo (N=263)	EGRIFTA (N=543)
Musculoskeletal pain	1	2
Pain	1	2
Pruritus	1	2
Vomiting	0	3
Musculoskeletal stiffness	0	2
Blood creatine phosphokinase increased	0	1
Carpal tunnel syndrome	0	1
Joint swelling	0	1
Muscle strain	0	1
Night sweats	0	1
Palpitations	0	1

*Injection site reaction includes: Injection site erythema, Injection site pruritus, Injection site rash, Injection site urticaria, Injection site pain, Injection site swelling, Injection site irritation, Injection site hemorrhage.

In the EGRIFTA clinical trials, mean baseline HbA_{1c} was 5.3% among patients in both the EGRIFTA and placebo groups. Patients receiving EGRIFTA had an increased risk of developing diabetes (HbA_{1c} level ≥ 6.5%) compared with placebo (5% vs. 1%), with a hazard ratio of 3.3 (CI 1.4, 9.6).

7 DRUG INTERACTIONS

7.1 Cytochrome P450-Metabolized Drugs

Co-administration of tesamorelin with simvastatin, a CYP3A substrate had no significant impact on the pharmacokinetics profiles of simvastatin in healthy subjects *[see Clinical Pharmacology (12.3)]*.

EGRIFTA WR stimulates GH production. Published data indicate that GH may modulate cytochrome P450 (CYP450) mediated antipyrine clearance. These data suggest that GH may alter the clearance of compounds known to be metabolized by CYP450 liver enzymes (e.g., corticosteroids, sex steroids, anticonvulsants, and cyclosporine). Monitor patients for potential interactions when administering EGRIFTA WR in combination with other drugs known to be metabolized by CYP450 liver enzymes.

7.2 Glucocorticoids

GH inhibits 11β-hydroxysteroid dehydrogenase type 1 (11βHSD-1), a microsomal enzyme required for conversion of cortisone to its active metabolite, cortisol, in hepatic and adipose tissue. EGRIFTA WR stimulates GH production; therefore, patients receiving glucocorticoid replacement for previously diagnosed hypoadrenalism may require an increase in maintenance or stress doses following initiation of EGRIFTA WR. Patients treated with cortisone acetate and prednisone may be affected more than others because conversion of these drugs to their biologically active metabolites is dependent on the activity of 11βHSD-1.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

EGRIFTA WR is contraindicated in pregnant women because modifying visceral adipose tissue offers no benefit in pregnant women and could result in fetal harm *[see Clinical Considerations and Contraindications (4)]*. Administration of tesamorelin acetate to rats during organogenesis resulted in hydrocephaly in offspring at a dose of approximately two and four times the clinical dose, based on measured drug exposure (AUC). If EGRIFTA WR is used during pregnancy, or if the patient becomes pregnant while taking it, discontinue EGRIFTA WR.

The estimated background risk of major birth defects and miscarriage for the indicated population is unknown. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

Clinical Considerations

Disease-associated maternal and/or embryo/fetal risk

During pregnancy, visceral adipose tissue increases due to normal metabolic and hormonal changes. Modifying pregnancy-associated physiologic changes in visceral adipose tissue with EGRIFTA WR offers no known benefit and could result in fetal harm.

Data

Animal Data

Tesamorelin acetate administration to rats during organogenesis and lactation resulted in hydrocephaly in offspring at a dose of approximately two and four times the clinical dose, respectively, based on measured drug exposure (AUC). Actual animal dose was 1.2 mg/kg. During organogenesis, lower doses approximately 0.1 to 1-times the clinical dose caused delayed skull ossification in rats. Actual animal doses were 0.1 to 0.6 mg/kg. No adverse developmental effects occurred in rabbits using doses up to approximately 500 times the clinical dose.

8.2 Lactation

Risk Summary

The Centers for Disease Control and Prevention recommend that HIV-infected mothers in the United States not breastfeed their infants to avoid risking postnatal transmission of HIV-1 infection. There are no data on the presence of tesamorelin in human milk, the effects on the breastfed child, or the effects on milk production. Because of both the potential for (1) HIV-1 infection transmission (in HIV-negative infants), (2) developing viral resistance (in HIV-positive patients), and (3) any possible adverse effects of tesamorelin, mothers should not breastfeed if they receive EGRIFTA WR.

Reference ID: 5557578

8.4 Pediatric Use

The safety and effectiveness of EGRIFTA WR in pediatric patients have not been established.

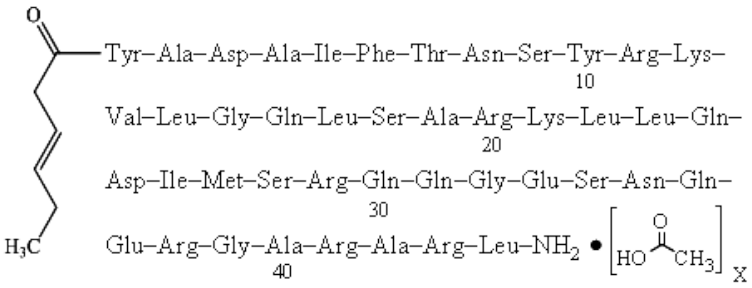
In pediatric patients with open epiphyses, treatment with EGRIFTA WR may result in linear growth acceleration and excessive growth. EGRIFTA WR is not indicated for use in pediatric patients with open or closed epiphyses.

8.5 Geriatric Use

There is no information on the use of EGRIFTA WR in patients greater than 65 years of age.

11 DESCRIPTION

Tesamorelin is a human growth hormone-releasing factor (GRF) analog produced synthetically. It is comprised of the 44 amino acid sequence of human GRF and a hexenoyl moiety, a C6 chain with a double bond at position 3, attached to the tyrosine residue at the N-terminal part of the molecule. Tesamorelin is prepared as an acetate salt. The molecular formula of tesamorelin acetate is $C_{221}H_{366}N_{72}O_{67}S \bullet x\ C_2H_4O_2$ ($x \approx 7$) and its molecular weight (as free base equivalent) is 5135.9 Da. The structural formula of tesamorelin acetate is:



EGRIFTA WR (tesamorelin) for injection is a sterile, white to off-white, preservative-free lyophilized powder for subcutaneous injection. Each single-patient-use vial of EGRIFTA WR contains tesamorelin 11.6 mg (equivalent to approximately 11.9 mg of tesamorelin acetate) and the following inactive ingredients: 145 mg hydroxypropyl betadex, 43.5 mg mannitol. Hydrochloric acid and/or sodium hydroxide may be used to adjust the pH. The pH of EGRIFTA WR is between 4.5 and 7.4. After reconstitution with 1.3 mL of Bacteriostatic Water for Injection, USP, resultant concentration is 8 mg/mL and the solution is clear and colorless. Bacteriostatic Water for Injection, USP contains benzyl alcohol as preservative.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

In vitro, tesamorelin binds and stimulates human GRF receptors with similar potency as the endogenous GRF *[see Clinical Pharmacology (12.2)]*.

Growth hormone-releasing factor (GHRF), also known as growth hormone-releasing hormone (GHRH), is a hypothalamic peptide that acts on the pituitary somatotroph cells to stimulate the synthesis and pulsatile release of endogenous growth hormone (GH), which is both anabolic and lipolytic. GH exerts its effects by interacting with specific receptors on a variety of target cells, including chondrocytes, osteoblasts, myocytes, hepatocytes, and adipocytes, resulting in a host of pharmacodynamic effects. Some, but not all these effects, are primarily mediated by IGF-1 produced in the liver and in peripheral tissues.

12.2 Pharmacodynamics

Tesamorelin stimulates growth hormone secretion, and subsequently increases IGF-1 and IGFBP-3 levels. No clinically significant changes in the levels of other pituitary hormones, including thyroid-stimulating hormone (TSH), luteinizing hormone (LH), adrenocorticotropic hormone (ACTH) and prolactin, were observed in patients receiving EGRIFTA in clinical trials.

12.3 Pharmacokinetics

Absorption

The absolute bioavailability of tesamorelin after subcutaneous administration of a 2 mg dose of EGRIFTA (1 mg/vial formulation) was determined to be less than 4% in healthy adult subjects.

Single and multiple dose pharmacokinetics have been characterized in healthy subjects and HIV-infected patients without lipodystrophy using a 2 mg dose of EGRIFTA (1 mg/vial formulation). Tesamorelin mean extent of absorption (AUC) was 34% higher in HIV-infected patients than healthy subjects. Tesamorelin peak plasma concentration (C_{max}) was similar in HIV-infected patients and healthy subjects. The median peak plasma tesamorelin concentration (T_{max}) was 0.15 h in both populations.

Following single dose of subcutaneous administration of 1.28 mg of EGRIFTA WR (11.6 mg/vial formulation) in healthy subjects, the mean [coefficient of variation (CV)] $AUC_{0\text{-}inf}$ was 1172 (48%) pg.h/mL. The mean (CV) C_{max} value was 3831 (40%) pg/mL and the median T_{max} was 0.15 h.

The systemic exposure (C_{max} and AUCs) of tesamorelin is similar between the 1.28 mg dose of EGRIFTA WR (11.6 mg/vial formulation) and the 2 mg dose of EGRIFTA (1 mg/vial formulation).

Distribution

The mean volume of distribution (±SD) of tesamorelin following a single subcutaneous administration of the 1.28 mg dose of EGRIFTA WR (11.6 mg/vial formulation) was 4.8 ± 1.9 L/kg in healthy subjects.

Metabolism

No formal metabolism studies have been performed in humans.

Elimination

Mean elimination half-life ($t_{1/2}$) of tesamorelin was 11 minutes in healthy subjects after single dose subcutaneous administration of the 1.28 mg of EGRIFTA WR (11.6 mg/vial formulation).

Specific Populations

Pharmacokinetics of tesamorelin in patients with renal or hepatic impairment, in pediatric patients, or in elderly patients has not been established.

Drug Interactions

Simvastatin

The effect of multiple dose administration of EGRIFTA on the pharmacokinetics of simvastatin and simvastatin acid was evaluated in healthy subjects. Co-administration with simvastatin (a CYP3A substrate) resulted in 8% decrease in extent of absorption (AUC_{inf}) and 5% increase in rate of absorption (C_{max}) of simvastatin. For simvastatin acid there was a 15% decrease in AUC_{inf} and 1% decrease in C_{max} *[see Drug Interactions (7.1)]*.

Ritonavir

The effect of multiple dose administration of EGRIFTA on the pharmacokinetics of ritonavir was evaluated in healthy subjects. Co-administration with ritonavir resulted in 9% decrease in AUC_{inf} and 11% decrease in C_{max} of ritonavir *[see Drug Interactions (7.1)]*.

12.6 Immunogenicity

The observed incidence of anti-drug antibodies is highly dependent on the sensitivity and specificity of the assay. Differences in assay methods preclude meaningful comparisons of the incidence of anti-drug antibodies in the studies described below with the incidence of the anti-drug antibodies in other studies, including those of EGRIFTA WR or other growth hormone-releasing factor analog.

In the clinical trials with the EGRIFTA 1 mg/vial formulation, anti-tesamorelin IgG antibodies were detected in 50% of patients who received EGRIFTA for 26 weeks and 47% of patients who received EGRIFTA for 52 weeks. In the subset of patients with hypersensitivity reactions, anti-tesamorelin IgG antibodies were detected in 85%. Cross-reactivity to endogenous growth hormone-releasing hormone (GHRH) was observed in approximately 60% of patients who developed anti-tesamorelin antibodies. Patients with and without anti-tesamorelin IgG antibodies had similar mean reductions in visceral adipose tissue (VAT) and IGF-1 response. In a group of patients who had antibodies to tesamorelin after 26 weeks of treatment (56%) and were re-assessed 6 months later, after stopping EGRIFTA treatment, 18% were still antibody positive.

Neutralizing antibodies to tesamorelin and human GHRH (hGHRH) were detected in vitro at Week 52 in 10% and 5% of EGRIFTA-treated patients, respectively. Changes in VAT and IGF-1 levels in patients with or without in vitro neutralizing antibodies were comparable.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Life-time carcinogenicity studies in rodents have not been conducted with tesamorelin acetate. No potential mutagenicity of tesamorelin acetate was revealed in a battery of tests including induction of gene mutations in bacteria (the Ames test), gene mutations in mammalian cells grown in vitro (hamster CHOK1 cells), and chromosomal damage in intact animals (bone marrow cells in mice). There was no effect on fertility in male or female rats following administration of tesamorelin acetate at doses up to 0.6 mg/kg (approximately equal to clinical exposure) for 28 days in males or 14 days in females.

14 CLINICAL STUDIES

The safety and effectiveness of EGRIFTA WR (11.6 mg/vial formulation) has been established based on adequate and well controlled studies with EGRIFTA (1 mg/vial formulation), as well as a demonstration of comparable bioavailability between the 1.28 mg EGRIFTA WR dose (11.6 mg/vial formulation) and the 2 mg EGRIFTA dose (1 mg/vial formulation) *[see Clinical Pharmacology (12.3)]*.

Reference ID: 5557578

Two multicenter, randomized, double-blind, placebo-controlled studies were conducted in HIV-infected patients with lipodystrophy and excess abdominal fat (abdominal lipohypertrophy). Study 1 and Study 2 consisted of a 26-week Main Phase and a 26-week Extension Phase, respectively. Main inclusion criteria were age 18 to 65 years, a waist circumference ≥95 cm (37.4 inches) and a waist-to-hip ratio ≥0.94 for men and ≥94 cm (37.0 inches) and ≥0.88 for women, respectively, and fasting blood glucose (FBG) <150 mg/dL (8.33 mmol/L). Main exclusion criteria included BMI ≤ 20 kg/m^2, type 1 diabetes mellitus, type 2 diabetes mellitus, previous treatment with insulin or with oral hypoglycemic or insulin-sensitizing agents, history of malignancy, and hypopituitarism. Patients were on a stable anti-retroviral regimen for at least 8 weeks prior to randomization. Patients meeting the inclusion/exclusion criteria were randomized in a 2:1 ratio to receive a 2 mg dose of EGRIFTA (1 mg/vial formulation) or placebo subcutaneously daily for 26 weeks. The primary efficacy assessment for each of these studies was the percent change from baseline to Week 26 in visceral adipose tissue (VAT), as assessed by computed tomography (CT) scan at L4-L5 vertebral level. Secondary endpoints included changes from baseline in patient-reported outcomes related to body image, triglycerides, ratio of total cholesterol to HDL cholesterol, IGF-1 levels, and safety parameters. Other endpoints included changes from baseline in waist circumference, abdominal subcutaneous tissue (SAT), trunk fat, and lean body mass. In both studies, EGRIFTA-treated patients completing the 26-week treatment period were re-randomized to blinded therapy with either daily placebo or a 2 mg dose of EGRIFTA (1 mg/vial formulation) for an additional 26-week treatment period (Extension Phase) in order to assess maintenance of VAT reduction and to gather long-term safety data. For inclusion in the Extension Phase studies, subjects must have completed the Main Phase with FBG ≤ 150 mg/dL.

Main Phase (Baseline to Week 26):

Study 1 (NCT 00123253)
This study randomized 412 HIV-infected patients with lipodystrophy and excess abdominal fat to receive either a 2 mg dose of EGRIFTA (1 mg/vial formulation) (N=273) or placebo (N=137). At baseline for the two groups combined, mean age was 48 years; 86% were male; 75% were white, 14% were Black/African American, and 8% were Hispanic; mean weight was 90 kg; mean BMI was 29 kg/m^2; mean waist circumference was 104 cm; mean hip circumference was 100 cm; mean VAT was 176 cm^2; mean CD4 cell count was 606 cells/mm^3; 69% had undetectable viral load (<50 copies/mL); and 33.7% randomized to EGRIFTA and 36.6% randomized to placebo had impaired glucose tolerance, while 5.6% randomized to EGRIFTA and 6.7% randomized to placebo had diet-controlled diabetes mellitus. The twenty-six week completion rate in Study 1 was 80%.

Study 2 (NCT 00435136)
This study randomized 404 HIV-infected patients with lipodystrophy and excess abdominal fat to receive either a 2 mg dose of EGRIFTA (1 mg/vial formulation) (N=270) or placebo (N=126). At baseline for the two groups combined, mean age was 48 years; 84% were male; 77% were white, 12% were Black/African American, and 9% were Hispanic; mean weight was 88 kg; mean BMI was 29 kg/m^2; mean waist circumference was 105 cm; mean hip circumference was 100 cm; mean VAT was 189 cm^2; mean CD4 cell count was 592 cells/mm^3; 83% had undetectable viral load (<50 copies/mL); and 44% randomized to EGRIFTA and 40% randomized to placebo had impaired glucose tolerance, while 9% randomized to EGRIFTA and 10% randomized to placebo had diet-controlled type 2 diabetes mellitus. The twenty-six week completion rate in Study 2 was 74%.

Results for the Main Phases of Studies 1 and 2 are presented in Tables 2 and 3.

Table 2: Changes from Baseline to Week 26 in Visceral Adipose Tissue (cm^2) by Treatment Group (Intent-To-Treat Population with Last Observation Carried Forward)

MAIN PHASE (Baseline-Week 26)

Reference ID: 5557578

	Study 1		Study 2	
	2 mg EGRIFTA (1 mg/vial) (N=273)	Placebo (N=137)	2 mg EGRIFTA (1 mg/vial) (N=270)	Placebo (N=126)
Baseline (cm^2)	178 (77)	171 (77)	186 (87)	195 (95)
Change (cm^2)	-27	4	-21	-0
Mean treatment difference (95% CI)	-31 (-39,-24)		-21 (-29,-12)	
Mean change (%)[1]	-18	2	-14	-2
Mean treatment difference (95% CI)[1]	-20 (-24, -15)		-12 (-16, -7)	

Baseline data are expressed as mean (SD); Change refers to least-squares mean (LSM); CI: confidence interval.

[1] Results derived from the statistical model: Ln(VAT Week 26/VAT Baseline) = Ln(VAT Baseline) + treatment group

Table 3: Changes from Baseline to Week 26 in IGF-1, IGFBP-3, Weight, and Waist Circumference by Treatment Group (Intent-To-Treat Population with Last Observation Carried Forward)

MAIN PHASE (Baseline-Week 26)					
		Study 1		Study 2	
		2 mg EGRIFTA (1 mg/vial) (N=273)	Placebo (N=137)	2 mg EGRIFTA (1 mg/vial) (N=270)	Placebo (N=126)
IGF-1 (ng/mL)	Baseline	161 (59)	168 (75)	146 (66)	149 (59)
	Change	107	-15	108	3
	Mean treatment difference (95% CI)	122 (101, 141)		105 (85, 126)	
IGFBP-3 (mg/L)	Baseline	3 (1)	3 (1)	3 (1)	3 (1)
	Change	0.4	-0.2	0.8	-0.0
	Mean treatment difference (95% CI)	0.6 (0.5, 0.8)		0.8 (0.5, 1.0)	
Weight (kg)	Baseline	90 (14)	90 (14)	89 (14)	87 (16)
	Change	-0.4	0.0	0.5	0.3
	Mean treatment difference (95% CI)	-0.4 (-1.3, 0.5)		0.2 (-0.7, 1.3)	
Waist circumference (cm)	Baseline	104 (10)	105 (9)	105 (9)	105 (9)
	Change	-3 (5)	-1 (4)	-2 (5)	-1 (5)
	Mean treatment difference (95% CI)	-2 (-2.8, -0.9)		-1 (-2.5, -0.3)	

Baseline data are expressed as mean (SD); Change refers to least-squares mean (LSM); CI: confidence interval.

At Week 26, treatment with a 2 mg dose of EGRIFTA (1 mg/vial formulation) resulted in a reduction from baseline in mean trunk 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 patients receiving placebo). Treatment with EGRIFTA 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 patients receiving placebo).

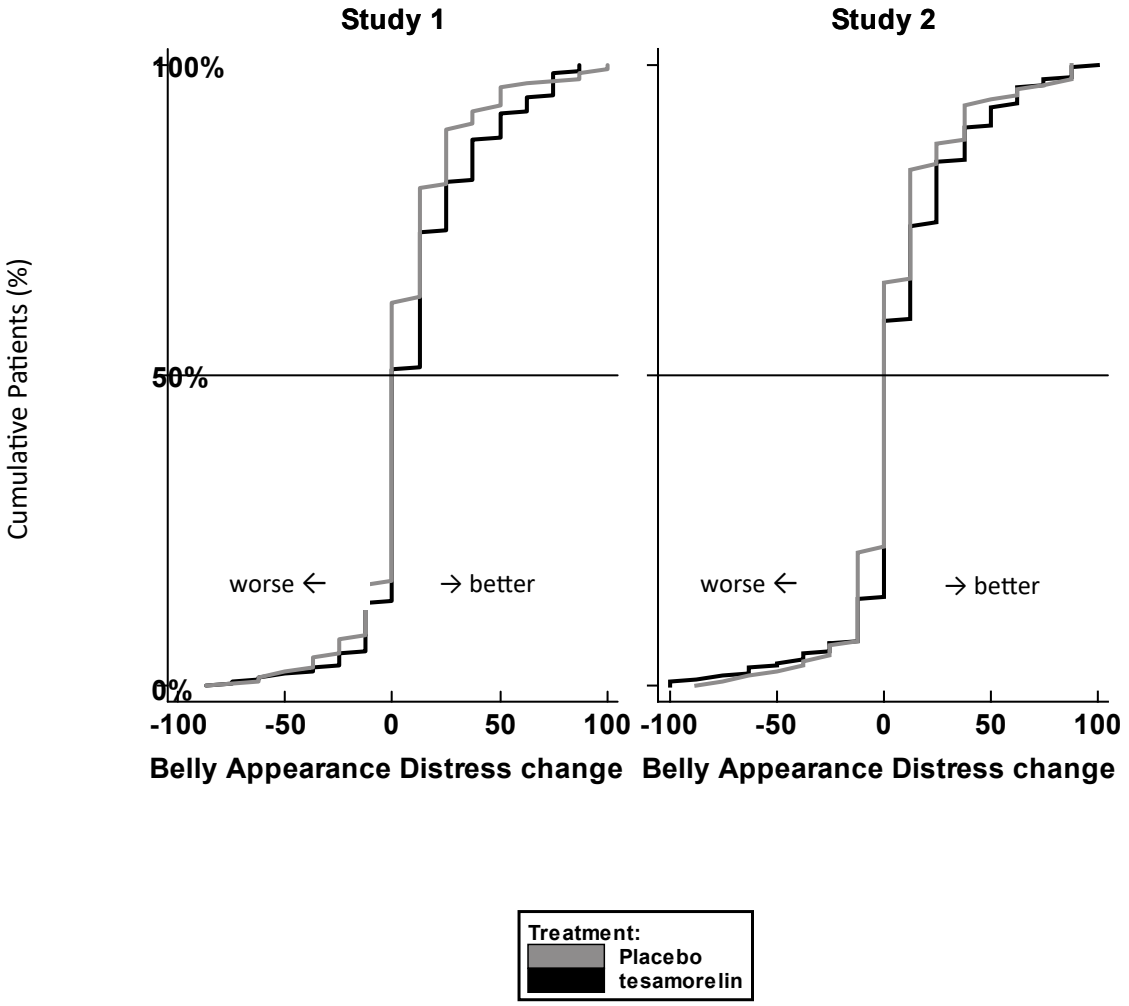
Patient Reported Outcomes

Patients rated the degree of distress associated with their belly appearance on a 9-point rating scale that was then transformed to a score from 0 (extremely upsetting and distressing) to 100 (extremely encouraging). A score of 50 indicated neutral (no feeling either way). A positive change from baseline score indicated improvement, i.e., less distress.

The cumulative distribution of response (change from baseline to 26 weeks) is shown in Figure 1 for both treatment groups. A curve shifted to the right on this scale indicates a greater percentage of patients reporting improvement.

Reference ID: 5557578

Figure 1. Cumulative Distribution of Response for Belly Appearance Distress



Reference ID: 5557578

Extension Phase (Weeks 26-52):

In the double-blind Extension Phase, patients on a 2 mg dose of EGRIFTA (1 mg/vial formulation) completing the 26-week Main Phase were re-randomized to receive a 2 mg dose of EGRIFTA (1 mg/ vial formulation) or placebo.

Study 1 (NCT 00123253)
This study re-randomized 207 HIV-infected patients with lipodystrophy who completed a 2 mg dose of EGRIFTA (1 mg/vial formulation) treatment in the Main Phase to receive either EGRIFTA (N=154) or placebo (N=50) for an additional 26-week duration (3:1 randomization ratio). At baseline (Week 26) for the two groups combined, mean age was 48 years; 88% were male; 78% were white, 12% were Black/African American, and 8% were Hispanic; mean weight was 90 kg; mean BMI was 29 kg/m^2; mean waist circumference was 102 cm; mean hip circumference was 100 cm; mean VAT was 145 cm^2; mean CD4 cell count was 639 cells/mm^3; 68% had undetectable viral load (<50 copies/mL); and for those EGRIFTA-treated patients completing the 26-week treatment period that were re-randomized to EGRIFTA (T-T group) or re-randomized to placebo, 37% and 32%, respectively, had impaired glucose tolerance, while 2% re-randomized to EGRIFTA and 6% re-randomized to placebo had diet-controlled type 2 diabetes mellitus. The completion rate for patients randomized into the extension phase of Study 1 was 83%.

Study 2 (NCT 00435136)
This study re-randomized 177 HIV-infected patients with lipodystrophy who completed EGRIFTA treatment in the Main Phase to receive either a 2 mg dose of EGRIFTA (1 mg/vial formulation) (N=92) or placebo (N=85) for an additional 26-week duration (1:1 randomization ratio). At baseline (Week 26) for the two groups combined, mean age was 48 years; 90% were male; 84% were white, 9% were Black/African American, and 7% were Hispanic; mean weight was 89 kg; mean BMI was 28 kg/m^2; mean waist circumference was 105 cm; mean hip circumference was 100 cm; mean VAT was 172 cm^2; mean CD4 cell count was 579 cells/mm^3; 82% had undetectable viral load (<50 copies/mL); and for those EGRIFTA-treated patients completing the 26-week treatment period that were re-randomized to EGRIFTA (T-T group) or re-randomized to placebo, 49% and 51%, respectively, had impaired glucose tolerance, while 4% re-randomized to EGRIFTA and 13% re-randomized to placebo had diet-controlled diabetes mellitus. The completion rate for patients randomized into the extension phase of Study 2 was 81%.

Results for the Extension Phases of Studies 1 and 2 are presented in Tables 4 and 5.

Table 4: Changes from Week 26 Baseline to Week 52 in Visceral Adipose Tissue (cm^2) by Treatment Group (Intent-To-Treat Population with Last Observation Carried Forward)

EXTENSION PHASE (Week 26-52)				
	Study 1		Study 2	
	T-T[1] (Week 26-52) (N=154)	T-P[2] (Week 26-52) (N=50)	T-T[1] (Week 26-52) (N=92)	T-P[2] (Week 26-52) (N=85)
Week 26 (cm^2)	145 (72)	144 (72)	166 (89)	177 (88)
Change (cm^2)	3	25	-11	24
Mean treatment difference (95% CI)	-22 (-34, -10)		-35 (-48, -22)	
Mean change (%)[3]	0	22	-5	16

Reference ID: 5557578

Mean treatment difference (95% CI)[3]	-17 (-24, -10)	-18 (-24, -11)

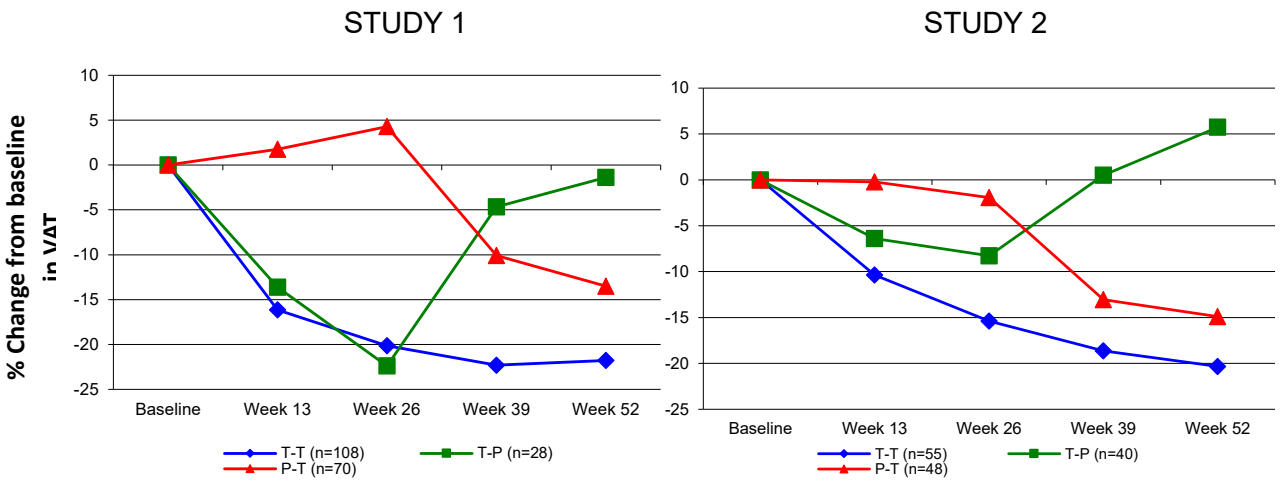
Week 26 baseline data are expressed as mean (SD). Change refers to least-squares mean (LSM); CI: confidence interval.

[1]T-T = tesamorelin for Weeks 0-26 and tesamorelin for Weeks 26-52
[2]T-P = tesamorelin for Weeks 0-26 and placebo for Weeks 26-52
[3]Results derived from the statistical model: Ln(VAT Week 52/Week 26) = Ln(Week 26 VAT) + treatment group

Reference ID: 5557578

Figure 2 shows the percent change in VAT from baseline (Week 0) over time until 52 weeks in completer patients.

Figure 2. Percent Change from Baseline in VAT over Time



Data in Figure 2 are expressed as mean values. T-T (tesamorelin to tesamorelin) refers to the group of patients who received tesamorelin for Weeks 0-26 and were re-randomized to tesamorelin for Weeks 26-52. T-P (tesamorelin to placebo) refers to the group of patients who received tesamorelin for Weeks 0-26 and were re-randomized to placebo for Weeks 26-52. P-T (placebo to tesamorelin) refers to the group of patients who received placebo for Weeks 0-26 and were switched to tesamorelin (treated open label) for Weeks 26-52.

Reference ID: 5557578

Table 5: Changes from Week 26 Baseline to Week 52 in IGF-1, IGFBP-3, Weight, and Waist Circumference by Treatment Group (Intent-To-Treat Population with Last Observation Carried Forward)

EXTENSION PHASE (Weeks 26-52)					
		Study 1		Study 2	
		T-T[1] (Week 26-52) (N=154)	T-P[2] (Week 26-52) (N=50)	T-T[1] (Week 26-52) (N=92)	T-P[2] (Week 26-52) (N=85)
IGF-1 (ng/mL)	Week 26	291 (124)	281 (105)	280 (134)	269 (110)
	Change	-59	-137	-25	-135
	Mean treatment difference (95% CI)	78 (50, 106)		110 (87, 134)	
IGFBP-3 (mg/L)	Week 26	3 (1)	3 (1)	3 (1)	3 (1)
	Change	-0.2	-0.5	-0.3	-0.9
	Mean treatment difference (95% CI)	0.3 (-0.0, 0.6)		0.6 (0.3, 0.9)	
Weight (kg)	Week 26	89 (14)	92 (17)	89 (13)	90 (14)
	Change	0.2	0.6	-0.5	0.1
	Mean treatment difference (95% CI)	-0.4 (-2, 1)		-0.6 (-2, 1)	
Waist circumference (cm)	Week 26	101 (10)	102 (12)	101 (9)	103 (11)
	Change	-0.2	2.4	-1.1	0.2
	Mean treatment difference (95% CI)	-2.6 (-4, -1)		-1.3 (-2, 0)	

Week 26 baseline data are expressed as mean (SD); Change refers to least-squares mean (LSM); CI: confidence interval.

[1]T-T = tesamorelin for Week 0-26 and tesamorelin for Week 26-52

[2]T-P = tesamorelin for Week 0-26 and placebo for Week 26-52

Patients treated with a 2 mg dose of EGRIFTA (1 mg/formulation) for 52 weeks (T-T group) showed no change between Weeks 26 and 52 in mean trunk fat (increase of 0.1 kg in Study 1 and decrease of 0.5 kg in Study 2, respectively, compared with an increase of 1.4 kg in patients in the T-P group in Study 1 and an increase of 1.09 kg in Study 2, respectively) nor was there a change from Week 26 baseline in mean lean body mass (decrease of 0.1 kg in Study 1 and increase of 0.1 kg in Study 2, respectively, compared with a decrease of 1.8 kg in patients in the T-P group in Study 1 and a decrease of 1.7 kg in Study 2, respectively).

16 HOW SUPPLIED/STORAGE AND HANDLING

How Supplied

EGRIFTA WR (tesamorelin) for injection is supplied as a white to off-white lyophilized powder in a 11.6

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mg single-patient-use vial with a 30 mL multiple-dose bottle of Bacteriostatic Water for Injection, USP, as diluent.

EGRIFTA WR (NDC 62064-381-04) is available in a package comprised of two boxes, containing 4 (four) 11.6 mg single-patient-use vials of EGRIFTA WR in the Medication Box and 1 (one) multiple-dose 30 mL bottles of Bacteriostatic Water for Injection, USP, diluent with a 28-day supply of disposable syringes, needles and alcohol swabs in the Injection Box.

Storage and Handling
Store EGRIFTA WR 11.6 mg vial at room temperature at 20°C to 25°C (68°F to 77°F) in the original box to protect from light; excursions permitted to 15°C to 30°C (59°F to 86°F) [See USP Controlled Room Temperature]. Store the Injection box (containing Bacteriostatic Water for Injection, syringes, needles and alcohol swabs) at room temperature at 20°C to 25°C (68°F to 77°F). Do not freeze.

17 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Patient Information and Instructions for Use).

Increased Risk of Malignancy
Inform patients about the increased background risk of malignancies in HIV-positive patients and for patients with a history of neoplasms, inform them about the risk of malignancy reoccurrence *[see Warnings and Precautions (5.1)]*.

Elevated IGF-1 Levels
Inform patients that treatment with EGRIFTA WR increases IGF-1 levels and that they will need periodic monitoring of their IGF-1 levels *[see Warnings and Precautions (5.2)]*.

Fluid Retention
Inform patients that treatment with EGRIFTA WR may cause fluid retention, resulting in adverse reactions including edema, arthralgia, and carpal tunnel syndrome *[see Warnings and Precautions (5.3)]*.

Glucose Intolerance or Diabetes Mellitus
Inform patients that treatment with EGRIFTA WR may result in glucose intolerance or diabetes mellitus. Advise patients that they will need to be monitored to see if impaired glucose tolerance or diabetes mellitus develops, and that if they have pre-existing diabetes mellitus, they may need adjustments to their anti-diabetic medications *[see Warnings and Precautions (5.4)]*.

Hypersensitivity Reactions
Inform patients that hypersensitivity reactions (e.g., rash, urticaria) may occur during treatment with EGRIFTA WR. Advise patients to seek prompt medical attention and to immediately discontinue treatment with EGRIFTA WR if a reaction occurs *[see Warnings and Precautions (5.5)]*.

Injection Site Reactions

Inform patients that injection site reactions may occur with EGRIFTA WR, including injection site erythema, pruritus, pain, irritation, and bruising. Advise patients to rotate the site of injection to reduce the risk of injection site reactions *[see Warnings and Precautions (5.6)]*.

Pregnancy

Advise women to discontinue EGRIFTA WR if pregnancy occurs, as the drug offers no known benefit to pregnant women and could result in fetal harm *[see Contraindications (4) and Use in Specific Populations (8.1)]*.

Lactation

Because of both the potential for HIV-1 infection transmission and serious adverse reactions in nursing infants, mothers receiving EGRIFTA WR should be instructed not to breastfeed *[see Use in Specific Populations (8.2)]*.

Administration

Counsel patients that they should never share an EGRIFTA WR syringe with another person, even if the needle is changed. Sharing of syringes or needles between patients may pose a risk of transmission of infection.

EGRIFTA WR is a trademark of Theratechnologies Inc.

Manufactured by Theratechnologies Inc., 2015 Peel Street, Suite 1100, Montréal, Québec, Canada H3A 1T8

US License No. 2091 for Theratechnologies Inc.

PATIENT INFORMATION

EGRIFTA WR™

(tesamorelin) for injection

for subcutaneous use

11.6 mg/vial

Read the Patient Information that comes with EGRIFTA WR before you start to take EGRIFTA WR and each time you get a refill. There may be new information. This leaflet does not take the place of talking to your healthcare provider about your medical condition or your treatment.

What is EGRIFTA WR?

EGRIFTA WR is a prescription medicine used to reduce the excess stomach-area (abdominal) fat in HIV-infected adult patients with lipodystrophy. EGRIFTA WR is a growth hormone-releasing factor (GHRF).

The long-term safety of EGRIFTA WR on the heart and blood vessels (cardiovascular) is not known.

EGRIFTA WR is not for weight loss management.

It is not known whether taking EGRIFTA WR helps improve how well you take (compliance with) antiretroviral medicines.

It is not known if EGRIFTA WR is safe and effective in children.

EGRIFTA WR is not recommended to be used in children with open or closed bone growth plates (epiphyses).

Who should not use EGRIFTA WR?

Do not use EGRIFTA WR if you:

- have a pituitary gland tumor, have had pituitary gland surgery, have other problems related to your pituitary gland, or have had radiation treatment to your head or a head injury.
- have active cancer. Any previous cancer should be inactive, and any previous cancer treatment should be complete before starting EGRIFTA WR.
- are allergic to tesamorelin or any of the ingredients in EGRIFTA WR. See the end of this leaflet for a complete list of ingredients in EGRIFTA WR.
- are pregnant or plan to become pregnant. EGRIFTA WR can harm your unborn baby. If you become pregnant, stop using EGRIFTA WR and talk with your healthcare provider.

What should I tell my healthcare provider before using EGRIFTA WR?

Before using EGRIFTA WR, tell your healthcare provider about all of your medical conditions, including if you:

- have or have had cancer.
- have problems with your blood sugar or diabetes. Some people with diabetes who use EGRIFTA WR may develop or may have worsening eye problems.
- have scheduled heart or stomach surgery.
- have breathing problems.
- are breastfeeding or plan to breastfeed. It is not known if EGRIFTA WR passes into your breast milk. The Centers for Disease Control and Prevention (CDC) recommends that HIV-infected mothers **not** breastfeed to avoid the risk of passing HIV infection to your baby. Talk with your healthcare provider about the best way to feed your baby if you are using EGRIFTA WR.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

How should I use EGRIFTA WR?

- Read the detailed Instructions for Use that comes with EGRIFTA WR before you start using it. Your healthcare provider will show you how to inject EGRIFTA WR.
- Use EGRIFTA WR exactly as your healthcare provider tells you to use it.
- Inject EGRIFTA WR under the skin (subcutaneously) of your stomach-area (abdomen).
- Change (rotate) the injection site on your stomach-area with each dose. Do not inject EGRIFTA WR into scar tissue, bruises or your belly button. There are two EGRIFTA formulations (EGRIFTA WR and EGRIFTA SV) with different recommended dosages. **EGRIFTA WR and EGRIFTA SV are not substitutable.**
- **Do not share your EGRIFTA WR syringe or needles with other people, even if the needle has been changed. You may give other people a serious infection or get a serious infection from them.**

What are the possible side effects of EGRIFTA WR?

EGRIFTA WR may cause serious side effects, including:

- **increase risk of new cancer in HIV positive patients or your cancer coming back (reactivation).** Stop using EGRIFTA WR if any cancer symptoms come back.
- **increased levels of your insulin-like growth factor-1 (IGF-1).** Your healthcare provider will do blood tests to check your IGF-1 levels while you are taking EGRIFTA WR.
- **swelling (fluid retention).** EGRIFTA WR can cause swelling in some parts of your body. Call your healthcare provider if you have swelling, an increase in joint pain or pain or numbness in your hands or wrist (carpal tunnel syndrome). Joint pain and swelling of your arms, hands, legs and feet are common side effects of EGRIFTA WR but may sometimes be serious.
- **increase in blood sugar (glucose) or diabetes.** Your healthcare provider will check your blood sugar before you start taking EGRIFTA WR and during your treatment with EGRIFTA WR.

- **serious allergic reaction.** Some people using EGRIFTA WR may have an allergic reaction. **Stop using EGRIFTA WR and get emergency medical help right away if you have any of the following symptoms:**
  - a rash over your body
  - shortness of breath or trouble breathing
  - hives
  - fast heartbeat
  - itching
  - swelling of your face or throat
  - feeling of faintness or fainting
  - reddening or flushing of the skin
- **injection site reactions.** Injection site reactions are a common side effect of EGRIFTA WR but may sometimes be serious. Change (rotate) your injection site to help lower your risk for injection site reactions. Call your healthcare provider for medical advice if you have any of the following symptoms around the area of the injection site:
  - redness
  - irritation
  - swelling
  - itching
  - bruising or bleeding
  - pain
  - rash
- **increased risk of death in people who have critical illnesses because of heart or stomach surgery, trauma or serious breathing (respiratory) problems** has happened when taking certain amounts of growth hormone.

The most common side effects of EGRIFTA WR include:

- pain in legs and arms
- muscle pain

These are not all the possible side effects of EGRIFTA WR. For more information, ask your healthcare provider or pharmacist.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

You may also report side effects to THERA patient support toll-free at 1-833-23THERA (1-833-238-4372).

How should I store EGRIFTA WR 11.6 mg vials, Bacteriostatic Water for Injection, syringes, needles and alcohol swabs?

- You will be given two boxes (Medication Box and Injection Box) from the pharmacy when you get your prescription of EGRIFTA WR:
  - Store the 11.6 mg EGRIFTA WR vials in the Medication Box they come in, at room temperature between 68°F to 77°F (20°C to 25°C).
  - Store the Bacteriostatic Water for Injection, syringes, needles and alcohol swabs that come in the Injection Box at room temperature between 68°F to 77°F (20°C to 25°C).
- Keep EGRIFTA WR vials out of the light. Do not freeze.
- After mixing and injecting on the first day, keep the EGRIFTA WR vial in your Medication Box, at room temperature at 20°C to 25°C (68°F to 77°F).
  - Throw away (discard) any unused EGRIFTA WR vial **7 days after mixing**.
  - Throw away (discard) any Bacteriostatic Water for Injection left in the bottle **28 days after first use**.
- **Do not use** EGRIFTA WR after the expiration date (EXP) printed on the carton and vial labels.

Keep EGRIFTA WR and all medicines out of the reach of children.

General information about the safe and effective use of EGRIFTA WR.

Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. Do not use EGRIFTA WR for a condition for which it was not prescribed. Do not give EGRIFTA WR to other people, even if they have the same symptoms you have. It may harm them.

You can ask your healthcare provider or pharmacist for information about EGRIFTA WR that is written for health professionals.

What are the ingredients in EGRIFTA WR?

Active ingredient: tesamorelin (as an acetate salt)

Inactive ingredients: hydrochloric acid, hydroxypropyl betadex, mannitol, sodium hydroxide

EGRIFTA WR does not contain any preservative. Bacteriostatic Water for Injection contains benzyl alcohol as preservative.

Manufactured by Theratechnologies Inc., 2015 Peel Street, Suite 1100, Montréal, Québec, Canada H3A 1T8 US License No. 2091 for Theratechnologies Inc.

For more information about EGRIFTA WR, go to www.EGRIFTASV.com or call toll-free at 1-833-23THERA (1-833-238-4372).

This Patient Information has been approved by the U.S. Food and Drug Administration Revised: 3/2025

INSTRUCTIONS FOR USE

EGRIFTA WR™
(tesamorelin)
for injection
for subcutaneous use

Note: This Instructions for Use contains information on how to mix and inject the **EGRIFTA WR 11.6 mg vial.**

Read and follow the steps for weekly mixing and daily injection of EGRIFTA WR 11.6 mg vial.

• Your healthcare provider should show you how to mix and inject 11.6 mg vial before you inject it for the first time. Ask your healthcare provider if you have any questions.

Important Information You Need to Know Before Injecting EGRIFTA WR 11.6 mg vial

• **For subcutaneous injection only** (inject directly under the skin).

• There are two EGRIFTA formulations (EGRIFTA WR and EGRIFTA SV) with different recommended dosages. **EGRIFTA WR and EGRIFTA SV are not substitutable.**
• The recommended **daily dose of EGRIFTA WR is 1.28 mg (0.16 mL).**

• **One (1) EGRIFTA WR 11.6 mg vial must be mixed with 1.3 mL of the Bacteriostatic Water for Injection** to prepare for 7 doses [for **7 consecutive daily injections (Day 1 to Day 7)** of treatment].

• **Do not share your syringe or needles with other people. You may give other people a serious infection or get a serious infection from them**.

• **Do not use a syringe or needle more than 1 time**.

• If supplies are missing, damaged, or expired; or if you have any questions at any time during the mixing or the injection of EGRIFTA WR, call your pharmacist or THERA patient support® toll-free at 1-833-23THERA (1-833-238-4372).

Storing EGRIFTA WR

- Store the Medication Box at room temperature between 68°F to 77°F (20°C to 25°C) and keep the EGRIFTA WR vials out of the light.
- Store the Injection Box at room temperature between 68°F to 77°F (20°C to 25°C).

- **Do not freeze or refrigerate EGRIFTA WR after it has been mixed with the Bacteriostatic Water for Injection.**
- **Keep EGRIFTA WR and all medicines out of the reach of children.**

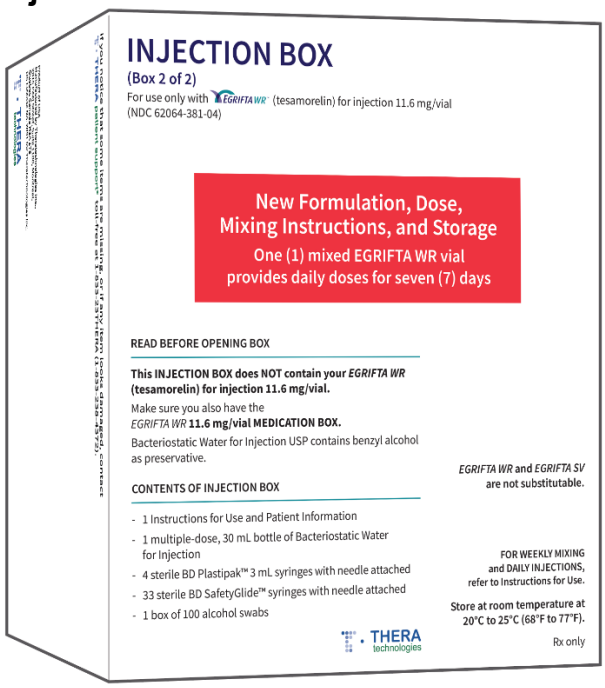
Box Content

Medication Box

Supplies for 28 days:

• 4 single-patient use EGRIFTA WR 11.6 mg vials (**mix only 1 vial per week as per weekly mixing**)

Injection Box



Supplies for 28 days:

• 1 multiple-dose, 30 mL bottle of Bacteriostatic Water for Injection (**to be used for weekly mixing**)

• 4 sterile BD Plastipak™ 3 mL Syringes with needle attached (clear cap), for **weekly mixing**

• 33 sterile BD SafetyGlide™ syringes with needle attached (orange cap), for **daily injection**

• 1 box of 100 alcohol swabs

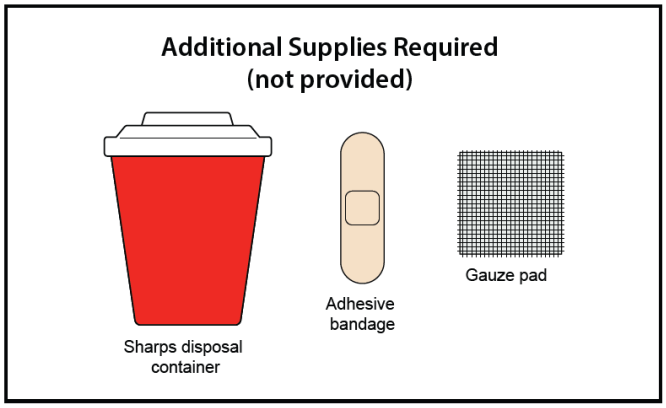


Figure A

Weekly Mixing (Day 1)

Getting Started

For Weekly Mixing of EGRIFTA WR, follow steps 1 through 23.

For Daily Injection (Day 1 to Day 7), follow steps 24 through 49.

Step 1: Use a well-lit, clean, and flat surface as a working area.

Step 2: Take out the following: (See **Figure B**)
- One (1) vial of EGRIFTA WR11.6 mg
- One (1) 30 mL bottle of Bacteriostatic Water for Injection
- One (1) BD Plastipak™ 3 mL Syringe with needle attached (clear cap) for **Weekly Mixing**
- One (1) alcohol swab
- Sharps disposal container

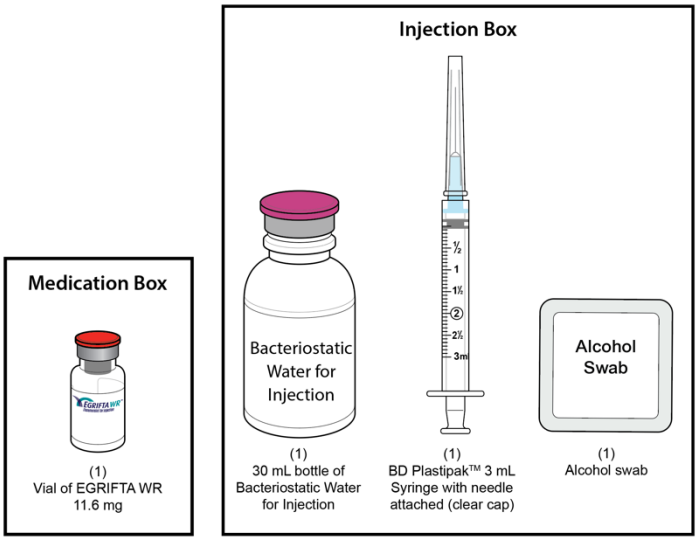


Figure B

Step 3: Wash and dry your hands well. (See **Figure C**)

Figure C

Step 4: Inspect the compact powder in the EGRIFTA WR vial. It should be white to off-white. (See **Figure D)**

• **Do not** use the vial if the powder is discolored or has particles in it. Get a new vial, and call your healthcare provider, pharmacist, or contact THERA patient support® toll free at 1-833-23THERA (1-833-238-4372).

Figure D

Step 5: Check the **expiration dates (EXP) on the:** (See **Figure E**)

1) EGRIFTA WR **vial** label
2) Bacteriostatic Water for Injection **bottle**

• **Do not** use if expired.

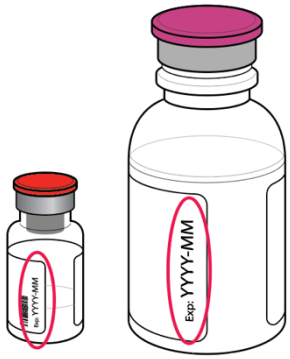


Figure E

Step 6: Remove the plastic caps from the **vial** and the **bottle**. (See **Figure F**)

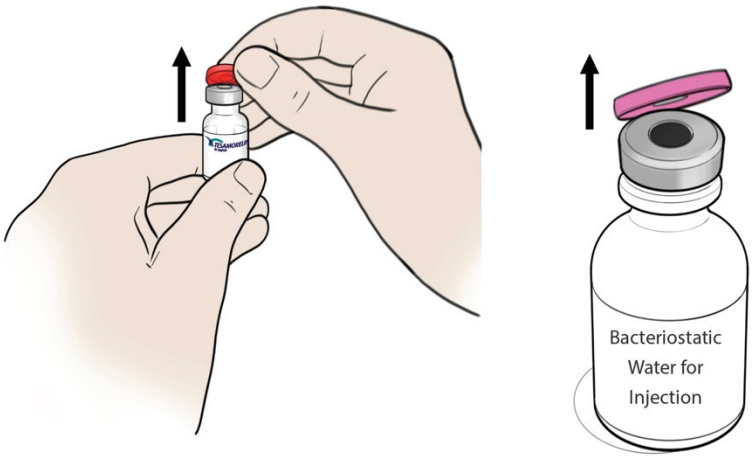


Figure F

Step 7: Clean the top of **both** the vial and the bottle with an alcohol swab (See **Figure G**). Throw away (discard) the alcohol swab after use.

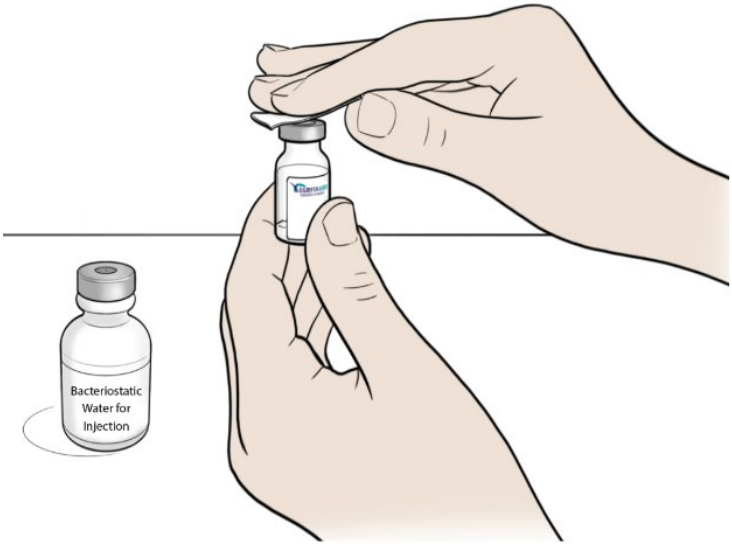


Figure G

Preparing to Mix EGRIFTA WR

Step 8: Take a BD Plastipak™ 3 mL Syringe with needle attached (clear cap) out of its packaging. (See **Figure H**)

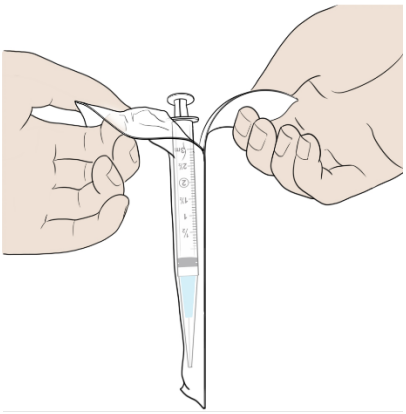


Figure H

Step 9: Pull the protective clear needle cap straight off and throw it away (discard) (See **Figure I**). Make sure the needle is tightly screwed to the syringe.

- **Do not** twist the needle cap.

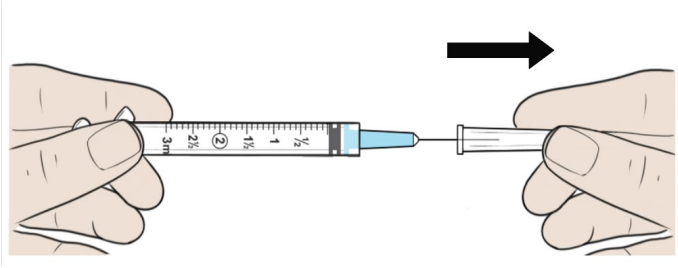


Figure I

Step 10: Pull down the plunger to reach the **1½ mark (1.5 mL)** on the syringe to fill it with air. (See **Figure J**)

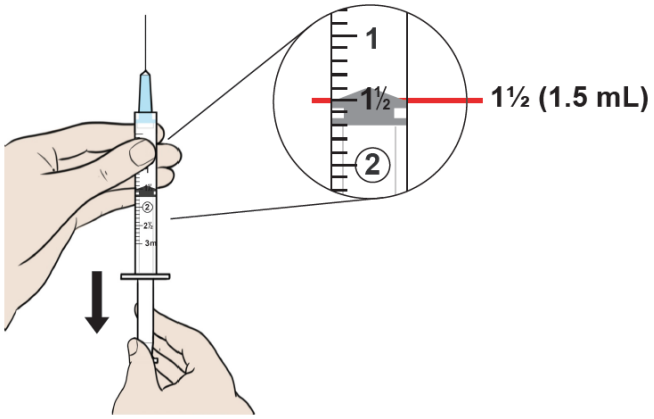


Figure J

Step 11: Insert the needle straight into the top of the Bacteriostatic Water for Injection bottle. (See **Figure K**)

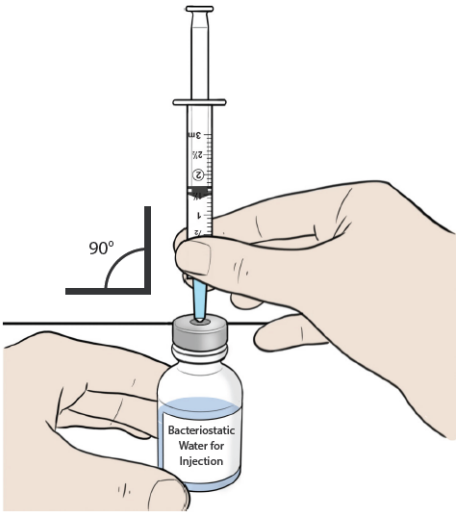


Figure K

Step 12: Turn the bottle and syringe upside down. (See **Figure L**)

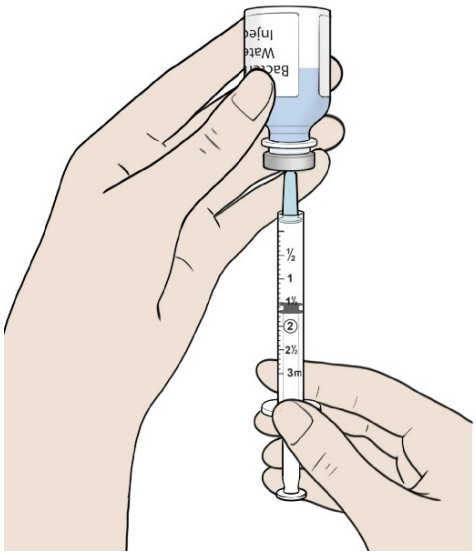


Figure L

Step 13: Push the plunger all the way up (See **Figure M**). Some resistance may be felt.

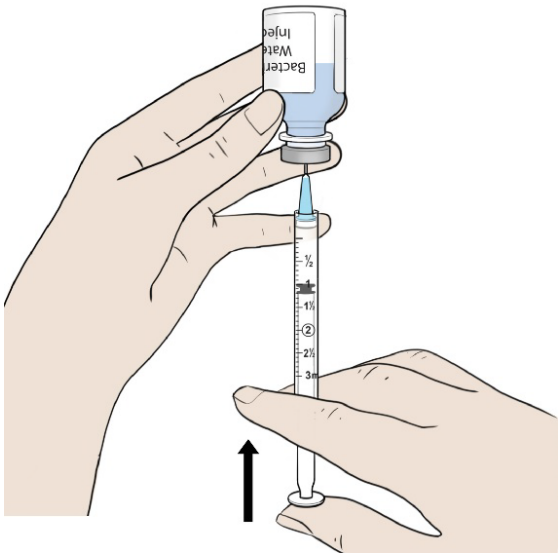


Figure M

Step 14: Pull down the plunger **slowly** to reach the **1½ mark (1.5 mL)** on the syringe. A visible air pocket and tiny air bubbles in the syringe are normal. (See **Figure N**)

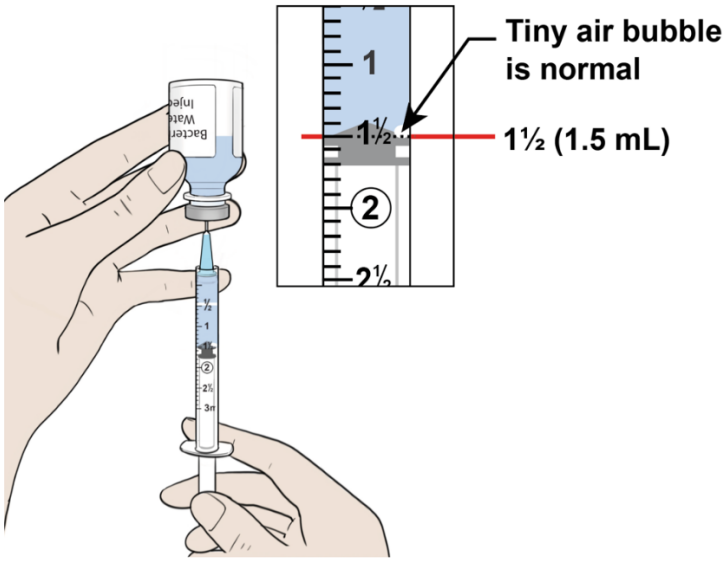


Figure N

Step 15: Turn the bottle right side up and remove the needle. (See **Figure O**)

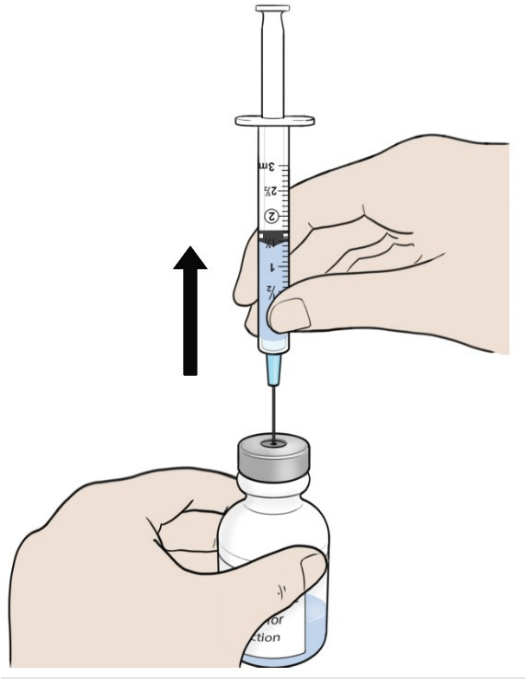


Figure O

Step 16: Place the syringe upright and tap it with your finger to force any large air bubbles to rise to the top. (See **Figure P**)

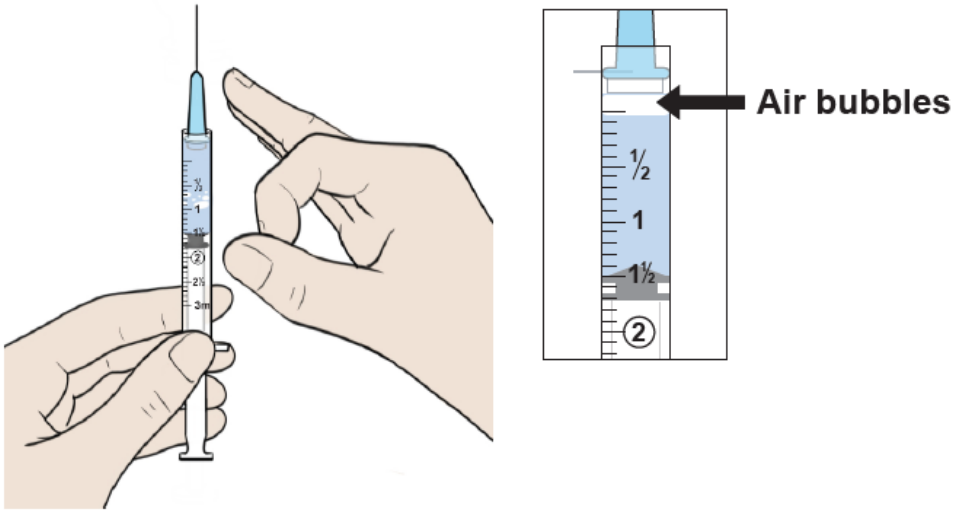


Figure P

Step 17: Push the plunger up **slowly** to remove 0.2 mL of excess water and air out of the syringe and align the **top rim of the plunger** to the **1.3 mL** mark. Some water should come out of the needle. (See **Figure Q**)

- If you have **less than 1.3 mL**, **repeat step 10 to step 17** until 1.3 mL of water is in the syringe.

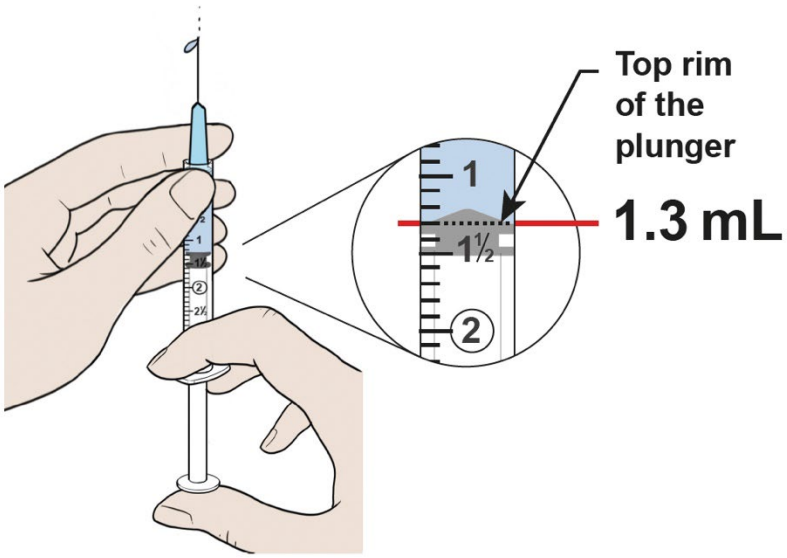


Figure Q

Step 18: Put the Bacteriostatic Water for Injection bottle back in the Injection box **for the next Weekly Mixing.** (See **Figure R**)

- Throw away (discard) the Bacteriostatic Water for Injection bottle **after 28 days of use**. Record the date of first use of the Bacteriostatic Water for Injection bottle as indicated on the back side of the Injection Box. The mixing and injection tracker provided inside the injection box can also be used to record this information.

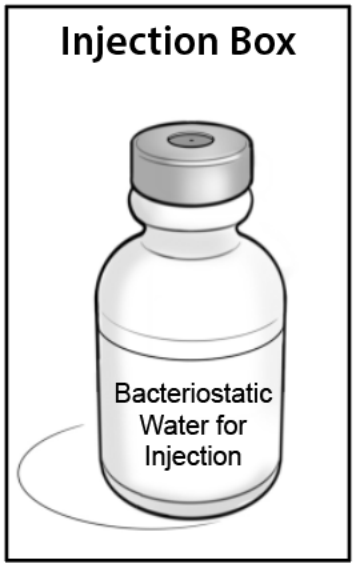


Figure R

Mixing EGRIFTA WR

Step 19: Insert the needle straight into the top of the EGRIFTA WR **vial**. (See **Figure S**)

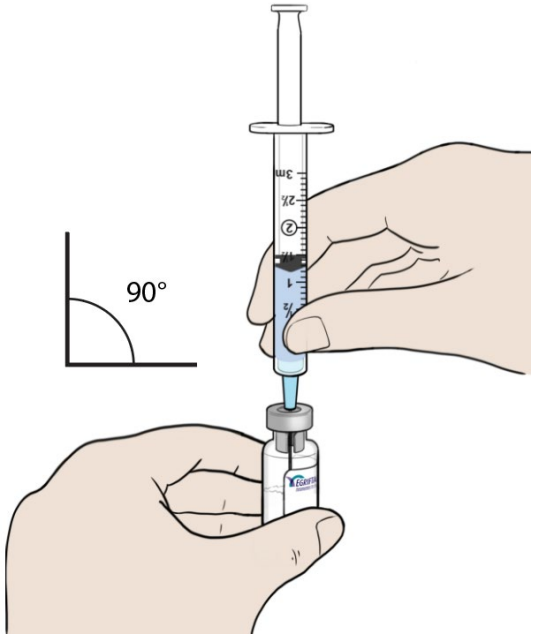


Figure S

Step 20: Push the plunger down until the syringe is completely empty. While keeping the plunger down, remove the needle from the vial. (See **Figure T**)

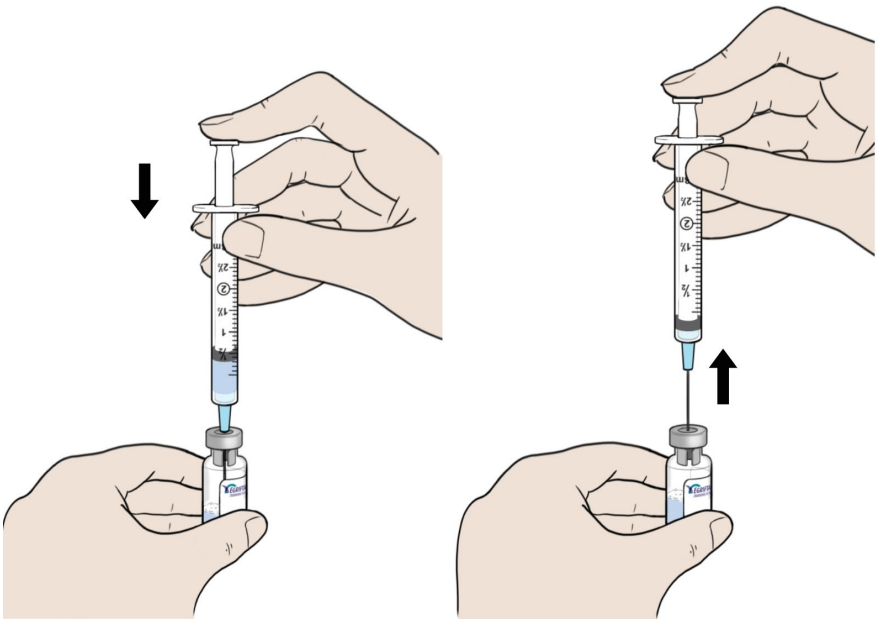


Figure T

Step 21: Throw away (discard) the syringe and needle in the sharps container. (See **Figure U)**

Figure U

Step 22: Move the vial in a circle (swirl) to mix all the powder and liquid. (See **Figure V**)

- **Do not** shake the vial.

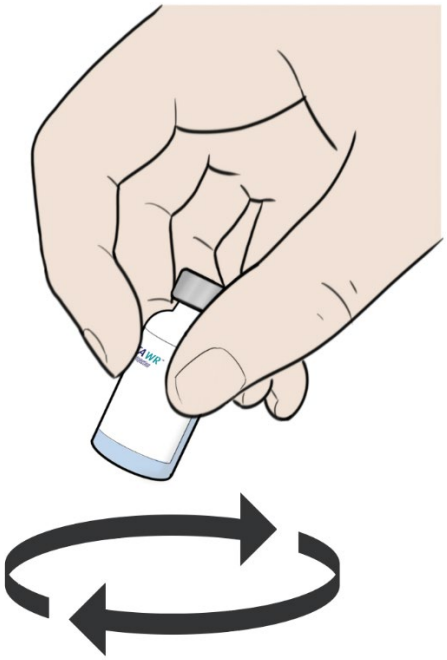


Figure V

Step 23: Let the vial rest for a few seconds until the layer of foam separates and the solution becomes clear and colorless, with no particles in it. (See **Figure W**)

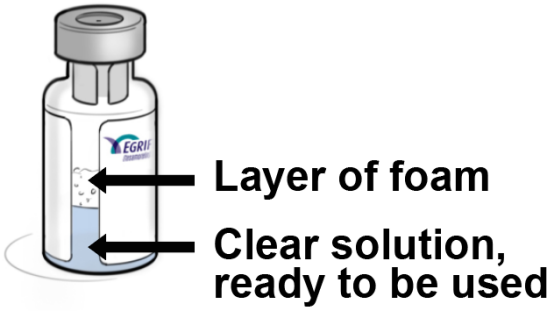


Figure W

• **Do not** use the vial if after a few seconds the solution looks cloudy, is discolored, or has particles in it. Get another vial, and call your healthcare provider, pharmacist, or contact THERA patient support® toll free at 1-833-23THERA (1-833-238-4372).

Daily Injection (DAY 1 TO DAY 7)

Preparing to Inject EGRIFTA WR

Step 24: For daily injection of EGRIFTA WR (step 24 through step 49), you will need: (See **Figure X**)

- One (1) **mixed and clear solution** of EGRIFTA WR **(prepared during the Weekly Mixing)**
- One (1) BD SafetyGlide™ syringe with needle attached (orange cap) for injection
- Two (2) alcohol swabs
- One (1) sterile gauze pad
- One (1) adhesive bandage
- Sharps disposal container

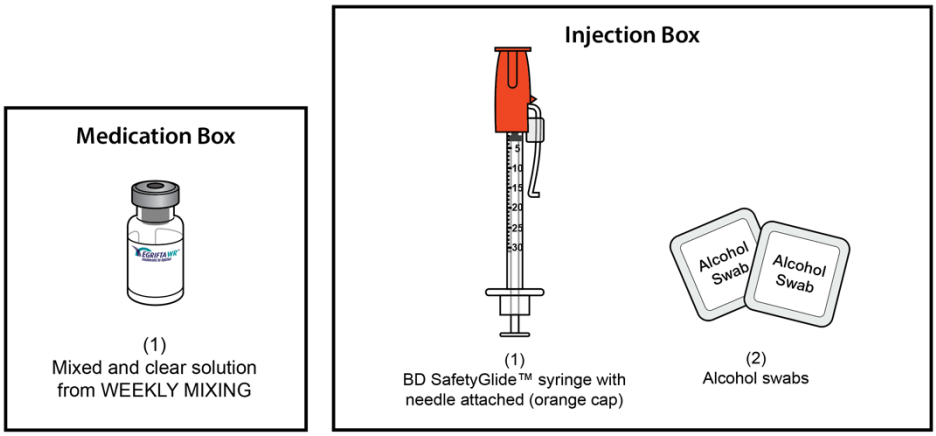


Figure X

Step 25: Wash and dry your hands well. (See **Figure Y**)

Figure Y

Step 26: Clean the top of the EGRIFTA WR vial with an alcohol swab (See **Figure Z**). Throw away (discard) the alcohol swab after use.

Figure Z

Step 27: Take a BD SafetyGlide™ syringe with needle attached (orange cap) out of its packaging. (See **Figure AA**)

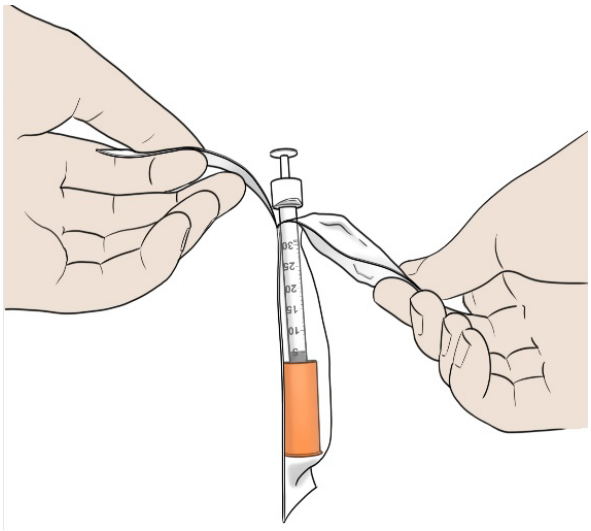


Figure AA

Step 28: Twist the orange needle cap to clearly see the graduated markings on the syringe, if needed. (See **Figure AB**)

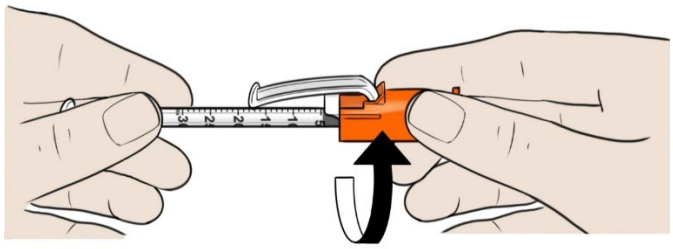


Figure AB

Step 29: Pull the orange needle cap straight off and keep it aside. (See **Figure AC**)

• **Do not** touch the needle.

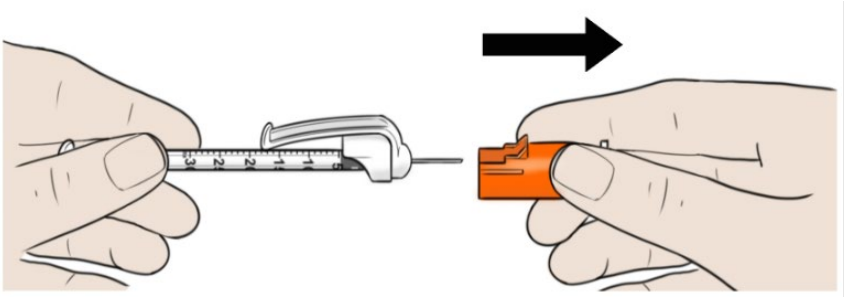


Figure AC

Step 30: Insert the needle carefully and **straight** into the top of the vial to avoid bending the needle. (See **Figure AD**)

- If you bend the needle, use a new syringe.

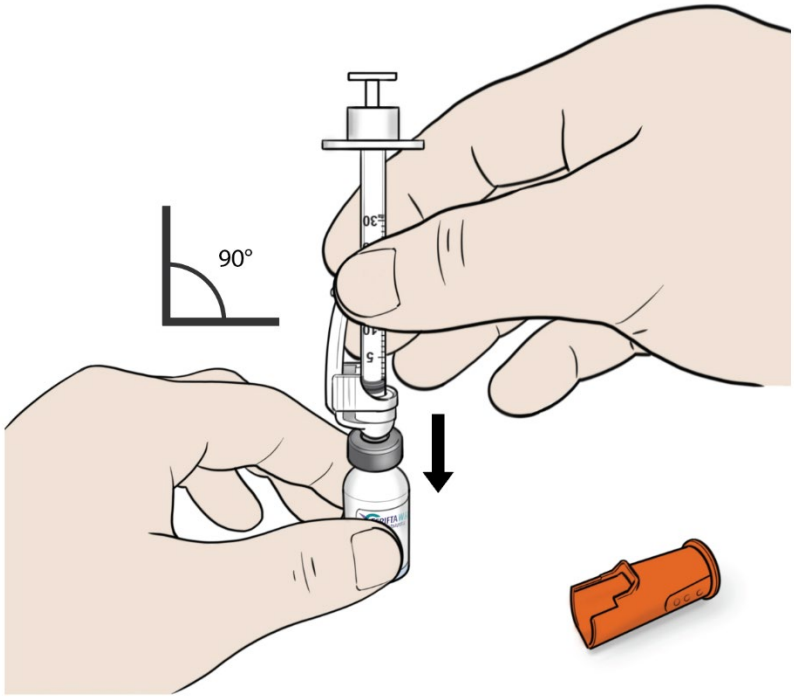


Figure AD

Step 31: Turn the vial and syringe upside down. (See **Figure AE**)

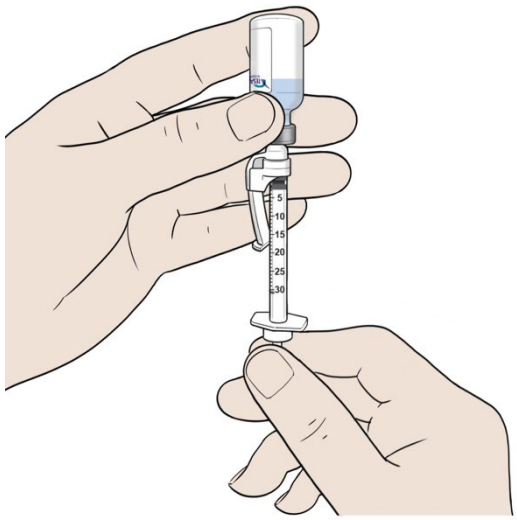


Figure AE

Step 32: Pull down the plunger **slowly** to reach the **18 mark (0.18 mL)**. (See **Figure AF**)

- If you do not have enough liquid in the syringe, **repeat step 30 and step 31**.

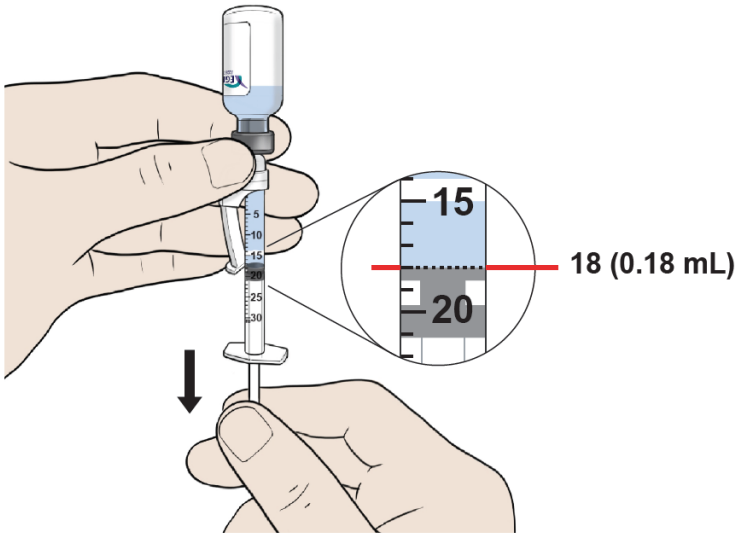


Figure AF

Step 33: Turn the vial right side up and remove the needle. (See **Figure AG**)

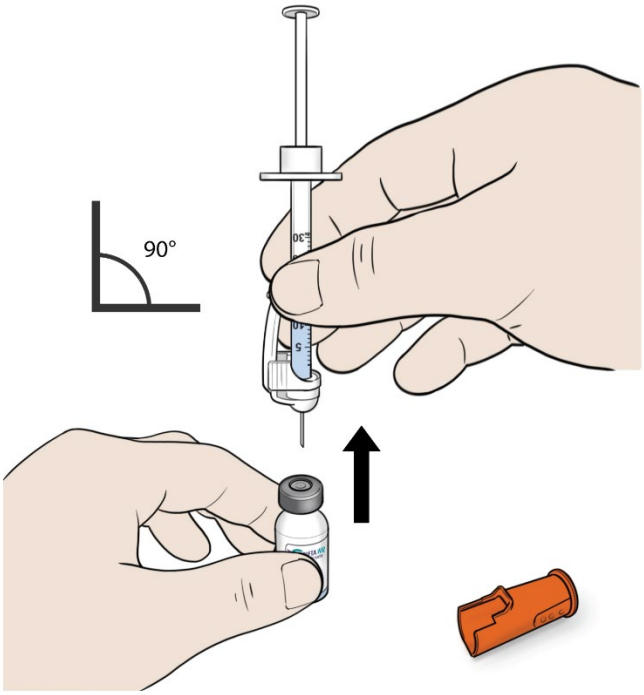


Figure AG

Step 34: Place the syringe upright and tap it with your finger to force any air bubbles to rise to the top. (See **Figure AH)**

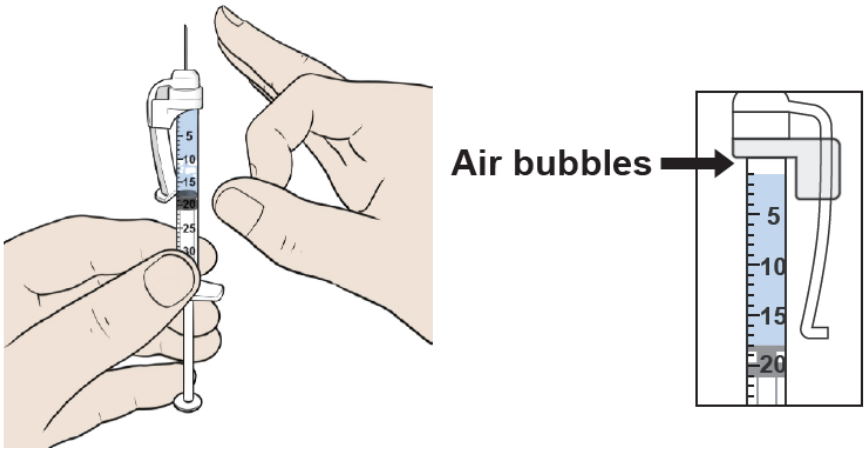


Figure AH

Step 35: Hold the plunger rod half-way to carefully adjust the volume in **step 36**. (See **Figure AI)**

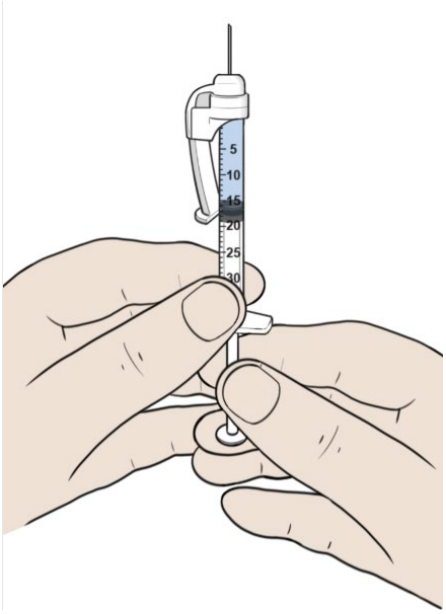


Figure AI

Step 36: Adjust the plunger to reach exactly the **16 mark (0.16 mL)** by slowly pushing the plunger up to remove air and excess liquid from the syringe (See **Figure AJ**). Some resistance may be felt when pushing the plunger.

- No air pockets should be left.

Note: This is your recommended daily dose of EGRIFTA WR: 1.28 mg (0.16 mL).

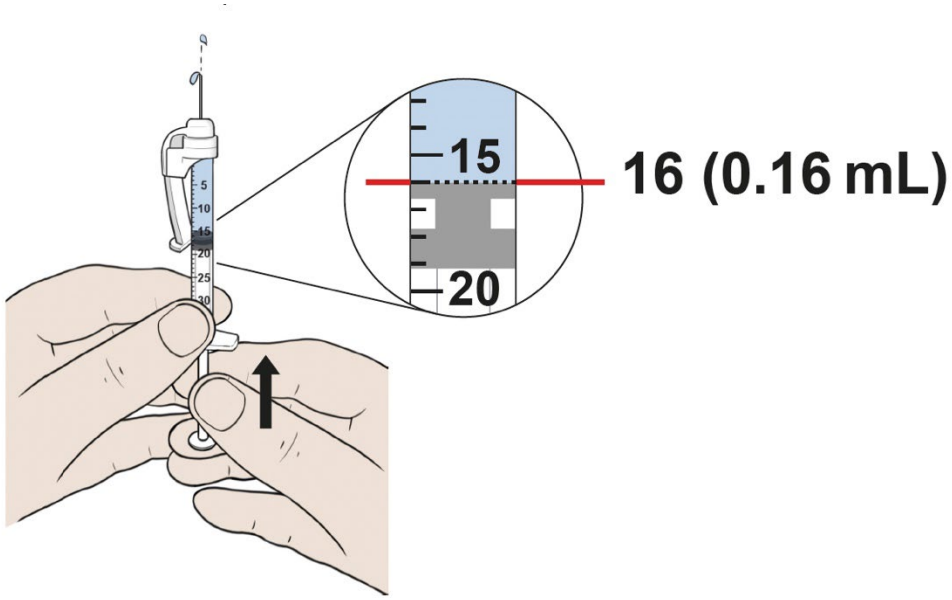


Figure AJ

Step 37: Safely place the orange needle cap on the needle. (See **Figure AK**)

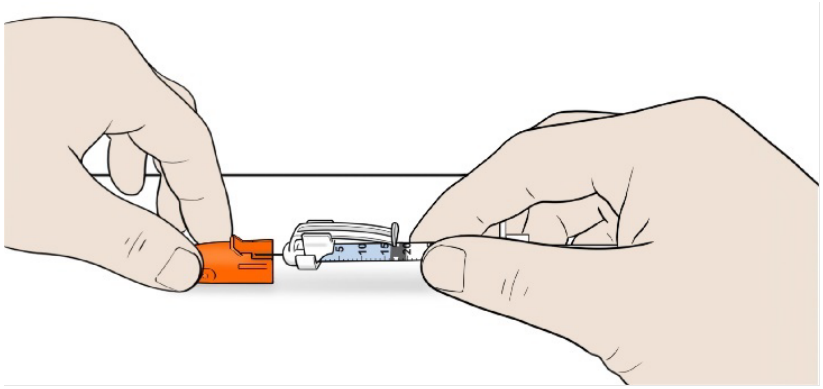


Figure AK

Step 38: Keep the mixed EGRIFTA WR **vial for the next Daily Injections in the Medication Box** at room temperature up to 77°F (25°C)**.** (See **Figure AL**)

Figure AL

Injecting EGRIFTA WR

Step 39: Choose an **injection site** on the stomach area (abdomen) that is **at least 2 inches (5 cm) away from your belly button**. (See the green area in **Figure AM**)

- **Do not** inject into your belly button, nor on areas with scar tissue, bruises or on any hard bumps from previous injections.
- Rotate the site for each injection. This may help prevent bruising or irritation.

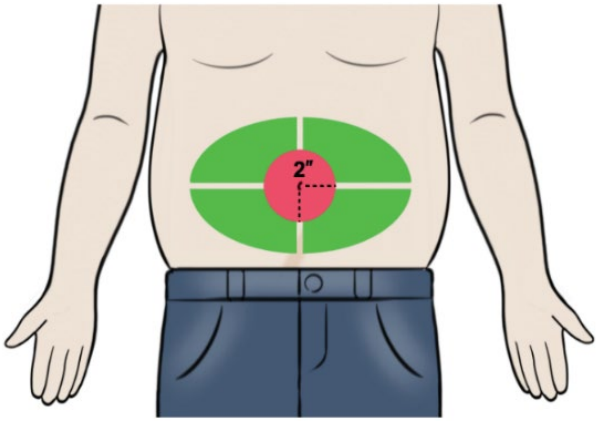


Figure AM

Step 40: Clean the injection site with a **new** alcohol swab and let it dry. (See **Figure AN**)

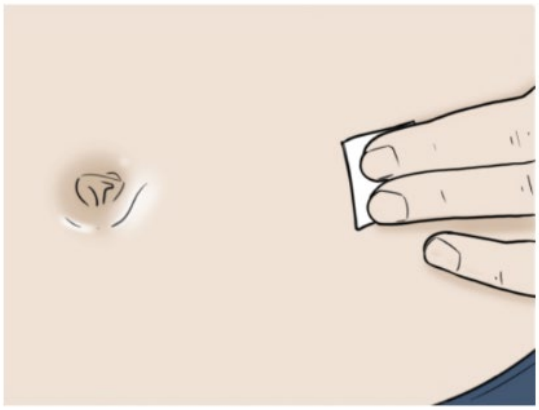


Figure AN

Step 41: Remove the orange needle cap and throw it away (discard). (See **Figure AO**)

- **Do not** touch the needle.
- **Do not** move the plunger.

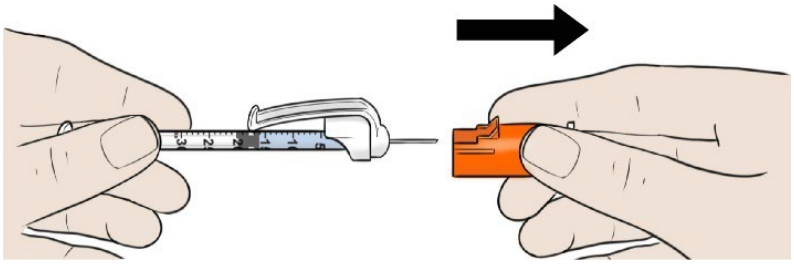


Figure AO

Step 42: Pinch a fold of skin at your cleaned injection site between your thumb and fingers. (See **Figure AP**)

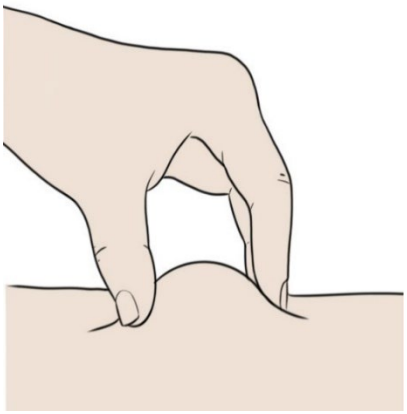


Figure AP

Step 43: Insert the needle straight into the skin. (See **Figure AQ**)

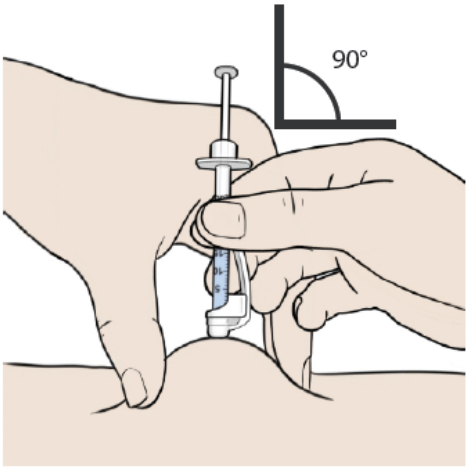


Figure AQ

Step 44: Remove your hand from the pinched area of skin, while keeping the needle in the skin. (See **Figure AR**)

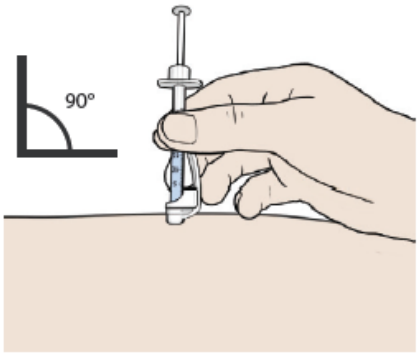


Figure AR

Step 45: Push the plunger all the way down until **all the medicine** in the syringe has been injected under the skin. (See **Figure AS**)

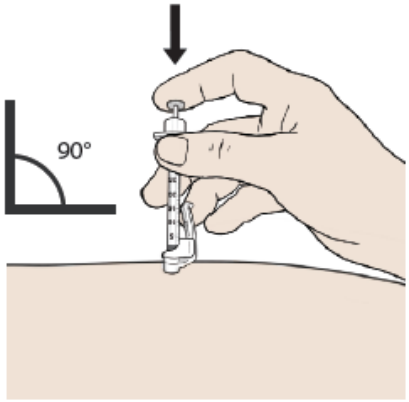


Figure AS

Step 46: Pull the needle out. (See **Figure AT**)

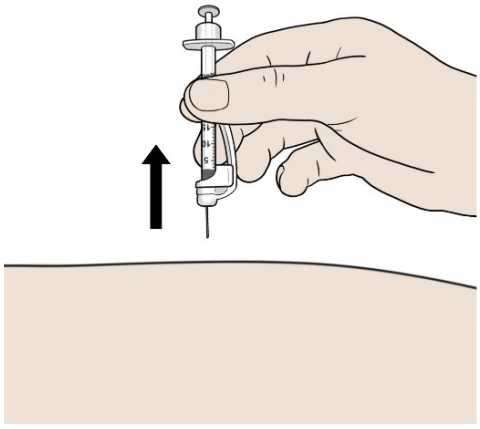


Figure AT

Step 47: Hold the syringe and carefully slide up the white safety needle shield along the needle until you hear a “click”. (See **Figure AU**)

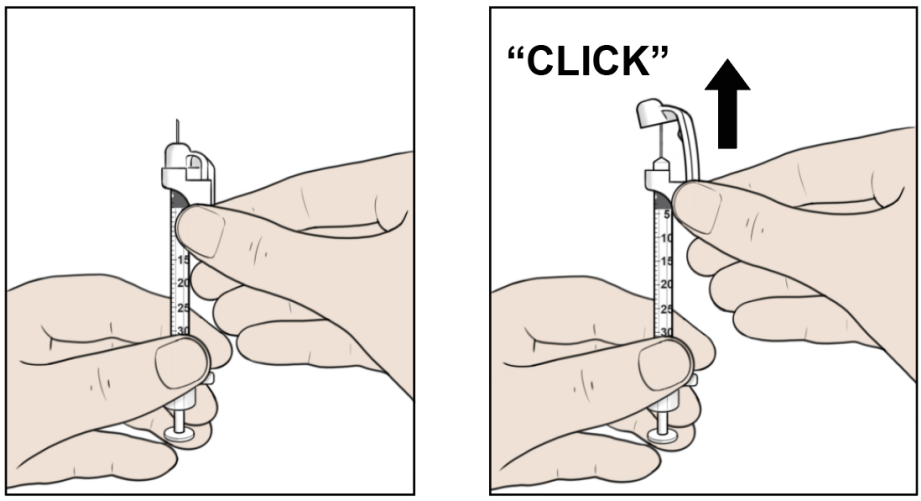


Figure AU

Step 48: Throw away (discard) the syringe with the needle attached into the sharps container. (See **Figure AV**)

Figure AV

Step 49: If there is bleeding at the injection site, use gauze to apply pressure and apply an adhesive bandage if necessary.

For the next Daily Injection (Day 2 to Day 7) go directly to step 24 of this Instructions for Use.

Throw away (discard) the EGRIFTA WR vial after it has been used for 7 Daily Injections (Day 1 TO Day 7).

Disposing of EGRIFTA WR

- **Do not recap the needle with the needle cap after you inject EGRIFTA WR.**
- Throw away (discard) the EGRIFTA WR vial after it has been used for **7 Daily Injections (Day 1 TO Day 7)**.
- Throw away (discard) the Bacteriostatic Water for Injection bottle **after 28 days of use**.
- Put your used EGRIFTA WR needles and syringes in an FDA-cleared sharps disposal container right away after use.
- **Do not throw away (dispose of) loose needles and syringes in your household trash**.
- If you do not have an FDA-cleared sharps disposal container, you may use a household container that is:
  - made of a heavy-duty plastic,
  - can be closed with a tight-fitting, puncture-resistant lid, without sharps being able to come out,
  - upright and stable during use,
  - leak-resistant, and
  - properly labeled to warn of hazardous waste inside the container.
- When your sharps disposal container is almost full, you will need to follow your community guidelines for the right way to dispose of your sharps disposal container. There may be state or local laws about how you should throw away used needles and syringes. For more information about safe sharps disposal, and for specific information about sharps disposal in the state that you live in, go to the FDA's website at: https://www.fda.gov/safesharpsdisposal.
- **Do not throw away** (dispose of) your used sharps disposal container in your household trash unless your community guidelines permit this.
- **Do not recycle** your used sharps disposal container.
- If another person receives a needle stick with a used needle, that person should be told to contact a healthcare provider right away.
- Keep the sharps container away from children and pets.
- **If you have any questions**, call your healthcare provider, or you can call THERA patient support® toll free at 1-833-23THERA (1-833-238-4372) for more information.

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