HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use EMCITATE® safely and effectively. See full prescribing information for EMCITATE.

EMCITATE (tiratricol) tablets for oral suspension
Initial U.S. Approval: 2026

WARNING: NOT FOR TREATMENT OF OBESITY OR FOR WEIGHT LOSS
See full prescribing information for complete boxed warning.

- **Thyroid hormones, including EMCITATE, either alone or with other therapeutic agents, should not be used for the treatment of obesity or for weight loss. (5.2)**

----------INDICATIONS AND USAGE----------
EMCITATE is a thyroid hormone receptor agonist indicated for the treatment of peripheral thyrotoxicosis in adults and pediatric patients with monocarboxylate transporter 8 (MCT8) deficiency (Allan-Herndon-Dudley syndrome).

Limitation of Use
EMCITATE is not recommended for the treatment of primary hypothyroidism.

----------DOSAGE AND ADMINISTRATION----------
- Individualize dosage based on weight, total T3 levels, and signs and symptoms of thyrotoxicosis. (2.1, 2.2, 2.3, 2.4)
- Assess total T3 levels by liquid chromatography tandem mass spectrometry. (2.3)
- EMCITATE tablets for oral suspension must be dispersed in room temperature drinking water and administered orally or by enteral feeding tube. Do not swallow tablets whole. Do not chew or crush tablets. (2.7, 2.8)
- Refer to the Full Prescribing Information for detailed dosage and administration instructions. (2)

----------DOSAGE FORMS AND STRENGTHS----------
Tablets for oral suspension: 350 mcg (functional scoring) (3)

----------CONTRAINDICATIONS----------
Primary hyperthyroidism. (4)

----------WARNINGS AND PRECAUTIONS----------
- Thyrotoxicosis: Signs and symptoms of thyrotoxicosis (e.g., increased heart rate, elevated blood pressure, diarrhea, hyperhidrosis, irritability, insomnia, nightmares) have occurred with EMCITATE during treatment initiation and dose titration. Monitor and adjust the EMCITATE dose as indicated. (5.1)
- Laboratory Test Interference for T3 Measurement: Tiratricol can cross-react with immunoassays for T3 leading to unreliable T3 results and cause an overestimation of T3. (5.3)

----------ADVERSE REACTIONS----------
Most common adverse reactions (≥ 5%): diarrhea, vomiting, rash, and hyperhidrosis. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Egetis Therapeutics US Inc. at 1-844-4EGETIS (1-844-434-3847) or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

----------DRUG INTERACTIONS----------
- Not recommended with other thyroid medications (7.1)
- See full prescribing information for drugs that may interact with EMCITATE and alter the therapeutic response (7.2-7.4).

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

Revised: 09/2026

FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

WARNING: NOT FOR TREATMENT OF OBESITY OR FOR WEIGHT LOSS

Thyroid hormones, including EMCITATE, either alone or with other therapeutic agents, should not be used for the treatment of obesity or for weight loss *[see Warnings and Precautions (5.2)].*

1 INDICATIONS AND USAGE

EMCITATE is indicated for the treatment of peripheral thyrotoxicosis in adults and pediatric patients with monocarboxylate transporter 8 (MCT8) deficiency (Allan-Herndon-Dudley syndrome).

Limitation of Use

EMCITATE is not recommended for the treatment of primary hypothyroidism.

2 DOSAGE AND ADMINISTRATION

2.1 Overview

- EMCITATE dosage is individualized based on weight, total T3 levels, and signs and symptoms of thyrotoxicosis *[see Dosage and Administration (2.2, 2.3, 2.4) and Warnings and Precautions (5.1)]*.
- Assess total T3 levels by a liquid chromatography tandem mass spectrometry (LC-MS/MS) method *[see Dosage and Administration (2.3)]*.
- EMCITATE tablets for oral suspension must be dispersed in room temperature drinking water and administered orally or by enteral feeding tube. Do not swallow tablets whole. Do not chew or crush tablets *[see Dosage and Administration (2.7, 2.8)]*.
- Refer to the Instructions for Use (IFU) for detailed instructions on the proper preparation and administration of EMCITATE *[see Dosage and Administration (2.7, 2.8)]*.
- For pediatric patients less than 8 years of age, consider periodic vision assessment during treatment with EMCITATE to rule out lens abnormalities (e.g., cataract formation) *[see Nonclinical Toxicology (13.2)]*.

2.2 Recommended Dosage

- Administer the EMCITATE total daily dosage orally or by enteral feeding tube once daily or in two to three divided doses spread throughout the day.
- The recommended starting dosage for patients weighing:
  - 10 kg or less: 175 mcg/day
  - Greater than 10 kg: 350 mcg/day
- Titrate dosages based on total T3 levels *[see Dosage and Administration (2.3)]*.
- The maximum recommended dosage (mcg/kg) for patients weighing:
  - Less than 10 kg: 100 mcg/kg/day
  - 10 kg to less than 40 kg: 80 mcg/kg/day
  - 40 kg to less than 60 kg: 60 mcg/kg/day
  - 60 kg and above: 50 mcg/kg/day

2.3 Dose Titration

- Measure individual total T3 levels using an LC-MS/MS method. Tiratricol cross-reacts with T3 when assessed by immunoassay, which may cause unreliable test results. An FDA-authorized LC-MS/MS test for the measurement of total T3 is not currently available. Currently available LC-MS/MS tests used to measure total T3 may vary in accuracy *[see Warnings and Precautions (5.3)]*.
- Based on total T3 levels, increase the dosage approximately every two weeks in the following increments for patients weighing:
  - 10 kg or less: 175 mcg/day.
  - Greater than 10 kg: 350 mcg/day.
- Increase the dosage until a total T3 level below the midpoint of the normal range for age has been achieved (the maintenance dose) or until the maximum recommended dosage based on weight is achieved *[see Dosage and Administration (2.2)]*.
- If total T3 is within the normal range, the dosage may be further adjusted up to the maximum recommended dosage based on the patient's heart rate and blood pressure. Monitor total T3 levels approximately two weeks after these further increases in dosage and assess clinically for new or worsening thyrotoxicosis *[see Dosage and Administration (2.4), Warnings and Precautions (5.1)]*.
- Once on a stable dose of EMCITATE, reassess total T3 levels once every 6 months and modify the dosage as clinically required.

2.4 Dosage Reduction for New or Worsening Thyrotoxicosis

- If signs or symptoms of thyrotoxicosis either occur for the first time or worsen, and do not resolve within two weeks, reduce the EMCITATE dosage by 175 mcg for patients with a body weight equal to or less than 10 kg or by 350 mcg for patients with a body weight greater than 10 kg *[see Warnings and Precautions (5.1)]*. Continue to reduce the dosage by these amounts every two weeks, if needed, until the signs or symptoms of thyrotoxicosis have resolved.
- Following the resolution of thyrotoxicosis-related adverse reactions, titrate EMCITATE dosage to achieve target total T3 levels *[see Dosage and Administration (2.3)]*.

2.5 Missed Dose or Vomiting

- If a dose is missed and there are more than 4 hours to the next scheduled dose, the missed dose should be taken as soon as possible. If a dose is missed and the next dose is scheduled within 4 hours, the dose should be skipped and the next dose taken according to the regular schedule. Doses should not be doubled.
- If vomiting occurs within 30 minutes after administration, administer a new dose. Instruct patients or caregivers to contact their healthcare provider if vomiting occurs a second time.

2.6 Discontinuation

- Do not abruptly stop EMCITATE treatment in order to avoid occurrence or worsening of symptoms of thyrotoxicosis *[see Warnings and Precautions (5.1)]*. If discontinuing EMCITATE, reduce the dosage approximately every two weeks as follows:
  - For patients weighing 10 kg or less, reduce EMCITATE by 175 mcg/day once every two weeks.
  - For patients weighing greater than 10 kg, reduce EMCITATE by 350 mcg/day once every two weeks.

2.7 Preparation Instructions

- Advise patients and caregivers to read the FDA-approved Instructions for Use to properly prepare EMCITATE suspension.
- Do not swallow, chew, or crush the tablets.
- EMCITATE tablets for oral suspension must be dispersed in room temperature drinking water directly in a 10-12 mL syringe and given as a suspension only. Do not prepare with other liquids, food vehicles or enteral nutrition formulas.
- The suspension is intended for oral administration or administration via an enteral feeding tube directly into the stomach.
- If more than 3 tablets are needed for a single dose, divide the dose into multiple, separate preparations not to exceed 3 tablets per preparation.
- For enteral feeding tube administration, prepare the oral suspension based on tube size.
- Prepared suspension will be cloudy white with visible small, dispersed particles.
- Discard the suspension 30 minutes after preparation if not used.
- EMCITATE tablets for oral suspension have a functional score line and can be split into equal halves. If dosing requires half a tablet, store the unused half in the original blister pack and outer carton (or in the light-protective packaging from the pharmacy) to protect from light and refrigerate at 2°C to 8°C (36°F to 46°F).

2.8 Administration Instructions

- Advise patients and caregivers to read the FDA-approved Instructions for Use to properly administer EMCITATE suspension.
- The prepared EMCITATE suspension may be administered with or without food *[see Clinical Pharmacology (12.3)]*.

Oral Administration:

- If particles have settled in the prepared syringe, gently swirl the syringe for at least 30 seconds before administration.
- Ensure that the patient is sitting upright. Remove the tip cover of the oral syringe, and slowly and gently push down the plunger to gently squirt the suspension into the inside of the cheek of the patient.

Enteral Feeding Tube Administration:

- If particles have settled in the prepared syringe, gently swirl the syringe for at least 30 seconds before administration.
- Prepared EMCITATE suspension can be administered through an enteral feeding tube directly into the stomach. Either nasogastric (NG) tubes (6 French and above) or gastrostomy (G) tubes (12 French and above) can be used.
- Ensure that the patient is sitting upright. Ensure that the enteral feeding tube is free from obstruction before administration and follow the instructions for the selected enteral feeding tube regarding flushing and administration procedures.

3 DOSAGE FORMS AND STRENGTHS

Tablets for oral suspension: 350 mcg. White oblong tablet with functional scoring on both sides. Debossed with “E” on one side of the tablet, mirrored on both halves.

4 CONTRAINDICATIONS

EMCITATE is contraindicated in patients with primary hyperthyroidism *[see Warnings and Precautions (5.1)]*.

5 WARNINGS AND PRECAUTIONS

5.1 New Onset or Worsening of Thyrotoxicosis

Signs and symptoms of thyrotoxicosis, such as increased heart rate, elevated blood pressure, diarrhea, hyperhidrosis, irritability, insomnia, and nightmares, have occurred in patients receiving EMCITATE *[see Adverse Drug Reactions (6.1)]*. These symptoms may occur if the EMCITATE dose is further increased despite T3 normalization, due to a drug-induced thyromimetic effect *[see Dosage and Administration (2)]*. Signs and symptoms of thyrotoxicosis may also occur during the dose titration period due to a combined thyromimetic effect from endogenous T3 levels that have not yet declined and EMCITATE.

If signs and symptoms of thyrotoxicosis occur despite T3 level normalization, decrease the EMCITATE dose according to the dose titration schedule *[see Dosage and Administration (2.4)]*.

If signs and symptoms of thyrotoxicosis do not resolve within 2 weeks after dose down-titration, the dose should be further reduced *[see Dosage and Administration (2.3, 2.4)]*.

5.2 Not for Treatment of Obesity or Weight Loss

EMCITATE should not be taken for weight reduction as it may cause symptoms of thyrotoxicosis that could be serious or life-threatening.

5.3 Laboratory Test Interference for T3 Measurement

Tiratricol can cross-react with T3 immunoassays leading to unreliable T3 results. When present, such cross-reactivity causes an overestimation of T3. Cross-reactivity of tiratricol is not expected to impact measurement of T3 by LC-MS/MS. An FDA-authorized LC-MS/MS test for the measurement of total T3 is not currently available.

6 ADVERSE REACTIONS

6.1 Clinical Trials 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 EMCITATE in patients with MCT8 deficiency was evaluated in two studies. Study 1 (NCT05579327) was a 3-period, multicenter study with an up to 16-week, open-label, titration period followed by a 30-day randomized double-blind, placebo-controlled withdrawal period, then a 6-week open-label treatment period. Study 1 enrolled 20 male patients with MCT8 deficiency. Study 2 (NCT02060474) was an open-label, single-arm, multicenter study of 12 months duration that enrolled 46 male patients with MCT8 deficiency *[see Clinical Studies (14)]*. Adverse reactions reported in $\geq$ 5% of patients treated with EMCITATE are summarized in Table 1.

Table 1. Adverse Drug Reactions in ≥ 5% of Patients in Study 1 and Study 2

Adverse Reactions	Study 1 EMCITATE N = 20 n (%)	Study 2 EMCITATE N = 46 n (%)
Diarrhea	0	6 (13)
Vomiting	2 (10)	5 (11)
Rash	2 (10)	4 (9)
Hyperhidrosis	1 (5)	3 (7)

Signs and symptoms of thyrotoxicosis

In Study 2, transient increases in heart rate (≥ 10 bpm) and systolic blood pressure (≥ 5 mmHg) were observed in 35% and 26% of participants, respectively, during the titration period. In addition, 30% of participants experienced at least one adverse reaction potentially related to thyrotoxicosis during the trial (diarrhea, hyperhidrosis, irritability, insomnia, nightmares), with most of these adverse reactions occurring during the titration period *[see Warnings and Precautions (5.1)]*.

7 DRUG INTERACTIONS

7.1 Not Recommended with Other Thyroid Medications

Taking EMCITATE in combination with thyromimetic products or products used to treat thyroid conditions (e.g., levothyroxine, propylthiouracil, and carbimazole) may increase the risk of thyrotoxicosis or hypothyroidism and should be avoided.

7.2 Drugs that may Affect Thyroid Hormone Pharmacokinetics

Many drugs can exert effects on thyroid hormone pharmacokinetics and may alter the therapeutic response. No clinical drug interaction studies have been conducted with EMCITATE. Tables 2 to 4 provide a summary of expected potential clinically significant drug interactions with EMCITATE.

Table 2. Drugs that May Affect Tiratricol Absorption

Potential impact: Concurrent use may affect the efficacy of EMCITATE by binding and altering absorption.		
Drug or Drug Class	**Effect**	**Clinical Recommendation**
Bile acid sequestrants Ion exchange resins Iron and calcium supplements	Bile acid sequestrants and ion exchange resins decrease thyroid hormone exposure by binding and delaying or preventing absorption. Concurrent use may reduce the efficacy of EMCITATE. Iron and calcium may interfere with the absorption of tiratricol.	Avoid concomitant use of bile acid sequestrants and ion exchange resins with EMCITATE. Iron and calcium supplements can reduce tiratricol exposure. If concomitant use of iron or calcium supplements is necessary, administer iron or calcium supplements consistently at the same time each day relative to EMCITATE dosing.

Proton pump inhibitors (PPIs)	Changes in gastric pH associated with PPI therapy may increase the absorption of tiratricol.	Serum concentrations of T3 should be monitored and dose adjustments of EMCITATE considered when initiating, modifying or discontinuing PPI treatment.

Table 3. Drugs that May Alter Plasma Binding of Triiodothyronine (T3)

Potential Impact: Changes in serum plasma protein levels can alter concentrations of thyroid hormones (total T3 levels).		
Drug or Drug Class	**Effect**	**Clinical Recommendation**
Oral estrogen containing products	These drugs may increase serum thyroxine-binding globulin (TBG) concentration and increase total T3 serum levels.	Monitor clinical symptoms and evaluate free T3 levels**.**
Anabolic steroids and glucocorticoids	These drugs may decrease serum TBG concentration and decrease total T3 serum levels.	
Salicylates (> 2 g/day)	Salicylates inhibit binding of T3 to TBG and transthyretin and may inhibit binding of tiratricol to transthyretin.	

Table 4. Drugs that May Alter Hepatic Metabolism of Tiratricol and Thyroid Hormones

Potential impact: Stimulation of hepatic drug-metabolizing enzyme activity may cause increased hepatic degradation of tiratricol and thyroid hormones, resulting in an increased EMCITATE dose requirement.		
Drug or Drug Class	**Effect**	**Clinical Recommendation**
Drugs that may increase hepatic metabolism of tiratricol	Administration of drugs that increase hepatic drug-metabolizing enzyme activity may increase the hepatic degradation of thyroid hormones and tiratricol.	Serum concentrations of thyroid hormones should be monitored and dose adjustments of EMCITATE considered when initiating, titrating or discontinuing treatment with enzyme inducing agents.

7.3 Oral Anticoagulants
EMCITATE may increase the response to oral anticoagulant therapy, which may increase the risk of hemorrhage. Therefore, a reduction in the dose of anticoagulant may be warranted if administered concomitantly with EMCITATE. Closely monitor coagulation tests to permit appropriate and timely dosage adjustments of the anticoagulant.

7.4 Psychostimulants
Administration of psychostimulants (e.g., caffeine, norepinephrine–dopamine reuptake inhibitors (NDRIs), and amphetamines) in combination with high doses of EMCITATE may lead to increased heart rate and blood pressure. Concomitant use of psychostimulants and EMCITATE is not recommended.

7.5 Drug-Laboratory Interference
An LC-MS/MS method should be used for total T3 measurement due to interference of EMCITATE with T3 immunoassays. An FDA-authorized LC-MS/MS test for the measurement of total T3 is not currently available. Currently available LC-MS/MS tests used to measure total T3 may vary in accuracy *[see Warnings and Precautions (5.3)]*.

8 USE IN SPECIFIC POPULATIONS
8.1 Pregnancy
There are no available data on the use of tiratricol for the treatment of MCT8 deficiency during pregnancy to inform a drug-related risk of major birth defects, miscarriage, or other adverse maternal or fetal outcomes. Animal reproduction studies have not been conducted with tiratricol.

The background risk of major birth defects and miscarriage for the indicated population is unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. 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.

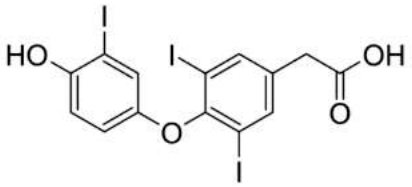
8.2 Lactation
There are no data regarding the presence of tiratricol in human or animal milk, the effects on the breastfed infant, or the effects on milk production. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for EMCITATE and any potential adverse effects on the breastfed infant from EMCITATE or the underlying maternal condition.

8.4 Pediatric Use
The safety and effectiveness of EMCITATE for the treatment of peripheral thyrotoxicosis have been established in pediatric patients with MCT8 deficiency. Use of EMCITATE in pediatric patients is supported by a single-arm trial and a double-blind, placebo-controlled, randomized withdrawal trial that included pediatric patients with MCT8 deficiency ages 10 months to less than 2 years (n=5), ages 2 years to less than 12 years (n=38), and ages 12 years to less than 17 years (n=12) *[see Clinical Studies (14)]*.

8.5 Geriatric Use
MCT8 deficiency is largely a disease of children and young adults; therefore, there are insufficient data on the use of EMCITATE in patients aged 65 years and older to determine whether they respond differently from younger patients.

11 DESCRIPTION

EMCITATE tablets for oral suspension contain tiratricol, a thyroid hormone receptor agonist.
The chemical name for tiratricol is 2-[4-(4-hydroxy-3-iodophenoxy)-3,5-diiodophenyl]acetic acid.
The molecular formula of tiratricol is $C_{14}H_9I_3O_4$, its molecular weight is 621.93 g/mol and its chemical structure is depicted below.



Tiratricol is a white to off-white solid powder, with a pH-dependent solubility in water.
EMCITATE tablets for oral suspension are supplied as 350 mcg strength to be administered as a suspension orally or via an enteral feeding tube directly into the stomach. Each tablet contains tiratricol as the active ingredient and the following inactive ingredients: anhydrous dibasic calcium phosphate, corn starch, lactose monohydrate, and magnesium stearate.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Tiratricol is a thyroid hormone receptor (THR) agonist which, unlike triiodothyronine (T3) and thyroxine (T4), can enter cells independent of the transmembrane transporter protein MCT8. In patients with MCT8 deficiency, X-linked loss-of-function mutations in the *SLC16A2* gene encoding MCT8 impair T3 entry into target tissues. This results in insufficient T3 activity in the brain concurrent with persistent peripheral thyrotoxicosis from accumulation of circulating T3. Intracellular tiratricol activity at THR-β, independent of MCT8-mediated membrane transport, can modulate hypothalamic-pituitary-thyroid axis signaling and reduce circulating T3 in patients with MCT8 deficiency.

12.2 Pharmacodynamics

Tiratricol reduces elevated T3 concentrations in patients with MCT8 deficiency in a concentration-dependent manner, with greater T3-lowering effect at higher tiratricol exposures; however, this effect plateaus at or above mean tiratricol concentrations of approximately 746 ng/dL in patients 5 years and older. Following discontinuation of EMCITATE, total T3 concentrations increased toward pretreatment levels within one week.

Cardiac Electrophysiology

There is insufficient information to characterize the effect of tiratricol on the QTc interval.

12.3 Pharmacokinetics

The area under the plasma concentration-time curve (AUC) and maximal plasma concentration (Cmax) of tiratricol increased dose proportionally over the dose range studied (175 mcg to 1050 mcg) after oral administration. Administration of EMCITATE via an enteral tube compared to standard oral administration did not affect tiratricol pharmacokinetics.

Absorption

The absorption of tiratricol is rapid with a median time to maximum plasma concentration (T_{max}) of 0.5 hours (range 0.25 to 1 hour).

Effect of Food
Administration of EMCITATE in healthy volunteers at doses of 175 mcg and 1050 mcg with a high-fat high-calorie meal (956 kcal energy, 35 g protein, 65 g carbohydrate and 61 g fat (with 57% energy from fat)) resulted in a delayed T_{max} (1 hour), reduced C_{max} (67%-70%), and unchanged AUC, compared to fasted conditions. These changes are not clinically significant *[see Dosage and Administration (2.8)]*.

Distribution
Tiratricol plasma protein binding is 99%. The apparent volume of distribution is 364 L for a 70 kg patient and 130 L for a 25 kg patient.

Elimination
The apparent clearance of tiratricol is 21 L/hr for a 70 kg patient and 10 L/hr for a 25 kg patient. The steady state half-life is approximately 12 hours for a 70 kg patient and 9.4 hours for a 25 kg patient.

Metabolism
Tiratricol is metabolized by stepwise deiodination, sulfation and glucuronidation, mainly in the liver.

Excretion
Tiratricol and its metabolites are predominantly eliminated in urine as inorganic iodine and in bile.

Specific Populations
No clinical studies have been performed in subjects with renal and hepatic impairment.

Pediatric Patients
Pediatric patients (5 to 16 years of age) with a lower body weight had a lower clearance and volume of distribution as compared to adult patients.

Drug Interaction Studies
No clinical drug-drug interaction studies have been performed with tiratricol.

In vitro studies
CYP450 Enzymes: Tiratricol is unlikely to inhibit or induce CYP1A2, CYP2B6, CYP2C8, CYP2C9, CYP2C19, CYP2D6 and CYP3A4 at clinically relevant doses.
UGT Enzymes: Tiratricol is unlikely to inhibit UGT1A1, UGT1A3, UGT1A4, UGT1A6, UGT1A9, UGT2B7, UGT2B15 and UGT2B17 at clinically relevant doses.
Transporters: Tiratricol is not a substrate for P-gp, BCRP, OAT1, OAT3, OCT1, OCT2, OATP1B1, OATP1B3, MATE1 or MATE2-K.
Tiratricol is unlikely to inhibit BCRP, OAT1, OAT3, OATP1B1 transporters at clinically relevant doses.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenesis
Tiratricol was not carcinogenic in Tg-RasH2 mouse carcinogenicity studies up to the highest tolerable dose tested of 15 mg/kg/day.

Mutagenesis
Tiratricol was not genotoxic in a bacterial reverse mutation assay, an in vitro micronucleus assay in human lymphoblastoid cells, and in an in vivo rat bone marrow micronucleus assay.

Impairment of Fertility
Dedicated fertility studies have not been conducted with tiratricol.

13.2 Ophthalmologic Findings
Beagle dogs treated orally for 13 weeks with 0, 0.15, 0.5, or 5 mg/kg/day tiratricol had lens opacities and lens fiber degeneration in all animals treated at the highest dose (approximately 24-fold clinical exposures based on AUC estimates). There were no adverse ophthalmologic findings in dogs treated with ≤0.5 mg/kg/day tiratricol (approximately 3- to 7-fold higher than clinical exposures based on AUC and C_{max}, respectively). The risk of ocular toxicity from tiratricol use in humans is unknown, but is considered low based on the absence of findings in dogs at clinically relevant exposures.

14 CLINICAL STUDIES
The efficacy of EMCITATE in patients with MCT8 deficiency was evaluated in two studies; Study 1 (NCT05579327) and Study 2 (NCT02060474).

Study 1
The efficacy of EMCITATE in patients with MCT8 deficiency was evaluated in an international, multicenter study (Study 1; NCT05579327) that consisted of three study periods as follows:

- Screening Period (Run-in/Titration period): 6-week run-in period for participants already treated with EMCITATE (Cohort A) and a 16-week dose-titration period for participants newly started on EMCITATE (Cohort B).
- Randomized Treatment Period (RTP): 30-day double-blind, placebo-controlled, randomized withdrawal period, which provided data for the primary efficacy endpoints.
- Follow-up Period: 6-week open-label treatment period.

Screening Period:
Twenty participants with MCT8 deficiency were enrolled during the Screening Period: 10 participants in Cohort A, who were already receiving EMCITATE treatment, and 10 participants in Cohort B, who were started on EMCITATE 350 mcg daily. The EMCITATE dose was titrated by 350 mcg daily every 2 weeks based on serum total T3 to achieve the stable dose criterion. The stable dose criterion was defined as at least 4 weeks of treatment with a fixed daily dose of EMCITATE and at least 2 consecutive serum total T3 results within the target range (between 80% of the lower limit of normal and no higher than the 75th percentile of the normal range). The mean duration of treatment with EMCITATE during this period was 86 days in Cohort A and 77 days in Cohort B.

The median age of the 20 participants enrolled in the study was 11 years, ranging from 5 to 31 years. All subjects were male. There were 65% White, 15% Black or African Americans, 5% Asian, 5% American Indian or Alaska Native and 10% other races.

Randomized Treatment Period:
Fifteen participants (8 participants from Cohort A and 7 participants from Cohort B) achieved the stable dose criterion and were randomized (1:1) to receive placebo or continue EMCITATE treatment for 30 days or until the rescue criterion, defined as the serum total T3 above the upper limit of normal (ULN), was met. Serum total T3 was measured weekly during this period. If the rescue criterion was met, the subject stopped the blinded study treatment and re-initiated EMCITATE at the pre-randomization dose.

Follow-up Period:
After completion of the RTP, 14 participants entered a 6-week follow-up period and received EMCITATE at the stable maintenance dose received prior to randomization.

Efficacy Assessment and Results
The two primary efficacy endpoints were: 1) Rate of change from baseline in serum total T3 during the 30-day Randomized Treatment Period; 2) Proportion of participants who met the rescue criterion during the 30-day Randomized Treatment Period.

The results for primary efficacy endpoint 1 are presented in Table 5.

Table 5. Total T3 Rate of Change During Randomized Treatment Period (Full Analysis Set)

Treatment	N	T3 rate of change [95% CI]	Ratio of T3 rate of change Placebo/Tiratricol [95% CI]
Placebo	8	1.6 [1.2; 2.1]	1.5 [1.0; 2.2] (p-value=0.034)
Tiratricol	7	1.1 [0.8; 1.3]	

Note: Estimates from random effects model
Abbreviations: CI = confidence interval; T3 = triiodothyronine

The mean (SD) change from baseline to the end of the Randomized Treatment Period in total T3 levels was 64.6 (12.7) ng/dL from a baseline of 109.1 ng/dL in the placebo arm and -0.2 (12.5) ng/dL from a baseline of 100.5 ng/dL in the tiratricol arm. The treatment difference (95% CI) in total T3 change from baseline at the end of randomized treatment period was 64.8 ng/dL (44.7, 84.8) for placebo versus tiratricol arm.

The results for primary efficacy endpoint 2 (proportion of participants meeting the rescue criterion during the Randomized Treatment Period) are provided in Table 6.

Table 6. Proportion of Subjects Who Met the Rescue Criterion (Serum Total T3 > ULN) During the 30-day Double-Blind Randomized Treatment Period (Full Analysis Set)

	Tiratricol N=7	Placebo N=8
Rescue criterion not met, n (%)	6 (85.7)	4 (50.0)
Rescue criterion met, n (%)	1* (14.3)	4 (50.0)
Difference in Proportions (Placebo-Tiratricol)	0.36	
95% CI	-0.16, 0.77	

Note:* One participant who discontinued prematurely during the Randomized Treatment Period was considered to have met the rescue criterion.
Abbreviations: CI, confidence interval; N, total number of subjects; FAS, Full analysis set; RW, randomized withdrawal; ULN, upper limit of normal

After withdrawal of EMCITATE, all 8 participants randomized to placebo had an increase in serum total T3 during the randomized treatment period (range: 31.9 to 135.4 ng/dL) that was larger than what was seen in the 7 patients randomized to continue EMCITATE (range: -15.6 to 26.0 ng/dL).

Secondary efficacy endpoints assessing mean changes in heart rate and systolic blood pressure from screening until pre-randomization and from screening until end of study showed a trend towards numerical improvements in participants in Cohort B (treatment-naïve), while heart rate and blood pressure remained stable in participants in Cohort A (previously-treated).

Study 2

The efficacy of EMCITATE was evaluated in a multicenter, single-arm, open-label study of 12 months duration that enrolled 46 male participants with MCT8 deficiency (Study 2; NCT02060474). The starting dose of EMCITATE was 350 mcg daily in participants with a body weight of ≥ 10 kg and 175 mcg daily in participants with a body weight of < 10 kg. The EMCITATE dose was titrated in 350 mcg daily (175 mcg daily for participants < 10 kg) increments every 2 weeks to achieve serum total T3 levels within the normal range for adults of 91 ng/dL to 163 ng/dL. Once the target dose was achieved, the participant was continued on that dose until Month 12 unless dose adjustments were needed. The EMCITATE dose could be down-titrated for safety reasons.

The median age of participants was 7.1 years (range: 10 months to 66.8 years). The majority (96%) of participants were White, 2% were Asian and 2% were other races. The mean maintenance dose of EMCITATE was 741 mcg.

Efficacy Assessment and Results

The primary efficacy endpoint was the change from baseline to end of study in mean serum total T3 concentration. The effect of EMCITATE treatment on serum total T3 is shown in Table 7.

Table 7. Serum Total T3 (ng/dL) - Mean Change from Baseline to Month 12 (Intent-to-Treat Population)

Variable	N	Baseline Mean (SD)	Month 12 Mean (SD)	Difference Mean [95% CI]
T3 (ng/dL)	45	323.4 (100.8)	118.3 (44.6)	-205.2 [-235.7; -174.6]

Data were imputed as Last Observation Carried Forward for patients who discontinued treatment prior to Month 12 visit.

Secondary efficacy endpoints evaluated the effect of EMCITATE on signs that could reflect thyrotoxicosis, such as systolic blood pressure, heart rate and body weight. At Month 12, there was a mean (95% confidence interval) change of: -4.1 (-8.1, -0.1) mmHg from a baseline of 107.1 mmHg in systolic blood pressure (N = 35 participants); -8.9 (-15.6, -2.3) beats per minute (bpm) from a baseline of 112.4 bpm in heart rate (N = 34 participants), 0.22 (-0.01, 0.45) from a baseline of -2.85 in body weight-for-age Z-score (N = 45 participants) and 0.51 (0.25, 0.76) from a baseline of 0.46 in body weight-for-age Z-score in an untreated MCT8 patient population (N = 36 participants).

16 HOW SUPPLIED/STORAGE AND HANDLING

How Supplied

EMCITATE (tiratricol) tablets for oral suspension, 350 mcg, are white, oblong tablets (size: 10 mm long, 5 mm wide) with functional score lines on both sides of the tablet and debossed with “E” on one side of the tablet, mirrored on both halves.

They are supplied as follows:

NDC 87216-0100-1: PVC/Aluminum blisters, 60 tablets for oral suspension. Each outer carton contains 6 blister cards of 10 tablets each.

Storage and Handling

Store refrigerated at 2°C to 8°C (36°F to 46°F), and keep protected from light.

17 PATIENT COUNSELING INFORMATION

Advise patients and caregivers to read the FDA-approved Instructions for Use.

Dosing

- Advise patients and caregivers to read and carefully follow the instructions for dose titration and adjustment *[see Dosage and Administration (2.2, 2.3, 2.4, 2.5, 2.6)].*
- If a dose is missed and there are more than 4 hours to the next scheduled dose, inform patients and caregivers to take the missed dose as soon as possible. If a dose is missed and the next dose is scheduled within 4 hours, inform patients and caregivers to skip the dose and take the next dose according to the regular schedule. Doses should not be doubled.
- Inform patients and caregivers to administer a new dose if a patient vomits within 30 minutes after administration and to contact their healthcare provider if vomiting recurs *[see Dosage and Administration (2.5)]*.

Preparation and Administration

- Advise patients and caregivers that tablets should not be swallowed whole, chewed, crushed or mixed with any other vehicle than water.
- Advise patients and caregivers to read and carefully follow the FDA-approved Instructions for Use for proper preparation and administration of EMCITATE *[see Instructions for Use]*.
- Inform patients and/or caregivers not to stop taking EMCITATE abruptly or without first checking with their healthcare providers as there will be a need for gradual dose reductions to decrease the risk of thyrotoxic symptoms and signs.

Drug Interactions

Inform patients and caregivers that EMCITATE may interact with many drugs *[see Contraindications (4), Warnings and Precautions (5.1), Drug Interactions (7)]*. Advise patients and their caregivers to report the patient's use of all prescription and nonprescription medications, including nutritional supplements and vitamins.

Signs and Symptoms of Thyrotoxicosis

Advise patients to report signs and symptoms of thyrotoxicosis (such as hyperhidrosis, irritability, insomnia, nightmares, increases in heart rate and elevations in systolic blood pressure, or diarrhea) that occur for the first time or worsen during treatment, and inform them that their dose may be adjusted until signs and symptoms resolve *[see Dosage and Administration (2.4)].*

Manufactured for:
Rare Thyroid Therapeutics International AB
Klara Norra Kyrkogata 26
Stockholm, Sweden 111 22

Distributed by Egetis Therapeutics US Inc., Cambridge, MA 02142, USA.

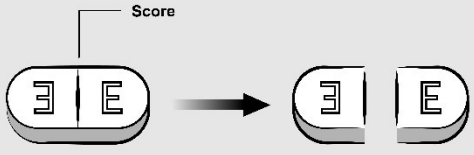
INSTRUCTIONS FOR USE
EMCITATE® (EM-si-tayt)
(tiratricol)
tablets for oral suspension

This Instructions for Use contains information on how to give EMCITATE tablets for oral mixture (suspension). Read this Instructions for Use before you start giving EMCITATE and each time you get a refill. There may be new information. This information does not take the place of talking to your healthcare provider about the medical condition or treatment of your child or the person for whom you are caring.

Important Information You Need to Know Before Giving EMCITATE

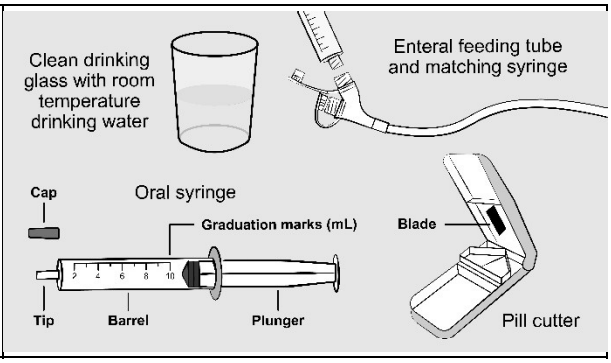
- Only give EMCITATE as a suspension by mouth or through a feeding tube, as directed by your healthcare provider.
- **Do not** swallow whole, chew or crush tablet.
- Your healthcare provider will tell you the number of tablets to give for each dose and how often to give the medication throughout the day. Give exactly as your healthcare provider tells you.
- **Do not** give less EMCITATE, immediately stop giving EMCITATE or give more EMCITATE than prescribed by your healthcare provider.
- Prepare the dose only when you are ready to give it.
- Prepare no more than 3 tablets in the syringe at a time.
- **Mix EMCITATE in room temperature drinking water before giving**.
  - the tablet will not fully dissolve.
  - **the suspension will look white and cloudy with small particles**, this is normal.
- **Do not** mix EMCITATE with any foods, liquids or feeding formulas other than room temperature drinking water.
- EMCITATE can be given before or after food.
- Throw away (dispose of) any unused suspension 30 minutes after preparing it. See "**Disposing of EMCITATE Tablets or Oral Suspension**".
- If you are not sure how to prepare or give a dose, contact your healthcare provider or pharmacist.
- Missed dose or vomiting:
  - If you miss a dose:
    - If there are more than 4 hours before the next dose, give the missed dose as soon as possible.
    - If there are less than 4 hours before the next dose, skip the missed dose and continue with the regular schedule. **Do not** double the dose.
  - If vomiting happens within 30 minutes of giving a dose, give the dose again.
  - If vomiting happens a second time, do not give another dose. Contact your healthcare provider.

Supplies You Will Need

Supplies included: • Prescribed number of EMCITATE tablets for each dose	 Whole tablet Two half tablets

Supplies not included:

- A clean drinking glass with room temperature drinking water
- A 10 to 12 mL oral syringe with a cap (provided by your healthcare provider or pharmacist)
- An enteral feeding tube and matching 10 to 12 mL syringe for enteral feeding (if needed)
- A pill cutter (if needed)



Preparing a Dose of EMCITATE Suspension

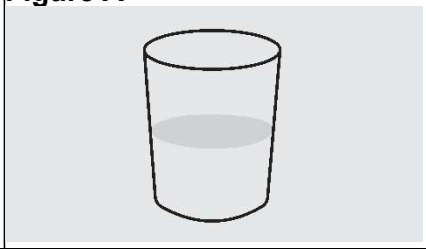
If more than 3 tablets are needed for your single dose, divide the dose into multiple separate preparations not to exceed 3 tablets per preparation and repeat Steps 1 through 5 for each preparation.

Step 1: Wash and dry your hands.

Step 2: Fill about half a clean glass with room temperature drinking water (see **Figure A**).

Only use room temperature drinking water to prepare the dose.

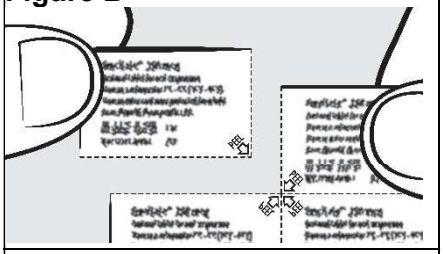
Figure A



Step 3: Remove the number of tablets needed for your dose from the blister pack**.** If your single dose is more than 3 tablets, divide it into multiple separate preparations to give right away.

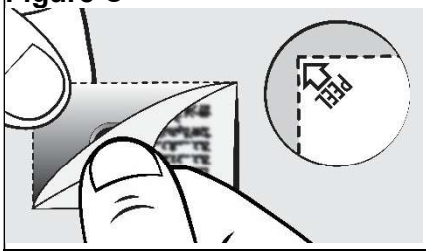
- Tear along the dotted line to separate each pill (blister) unit (see **Figure B**).

Figure B



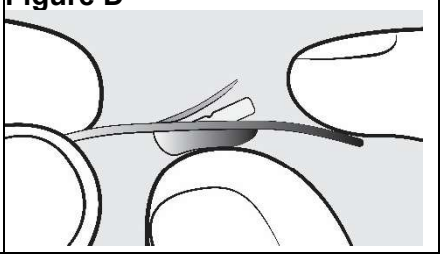
- Peel back the paper layer starting from the corner with the arrow (see **Figure C**).

Figure C



- Push the tablet out through the foil (see **Figure D**).

Figure D



- If the prescribed dose requires using a half tablet:
  - break the tablet in half along the line in the middle (score). You can do this by hand (see **Figure E**) or with a pill cutter (see **Figure F**).
  - put the unused half tablet back into the original blister pack and outer carton (or the light-protective packaging from the pharmacy). See "**Storing EMCITATE**".

Figure E

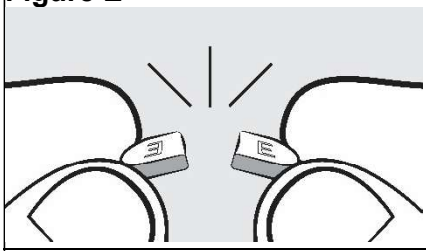
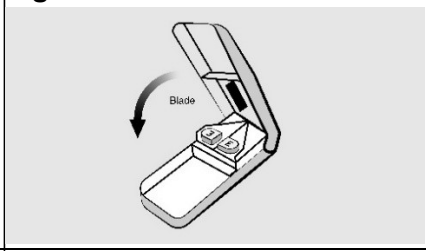


Figure F



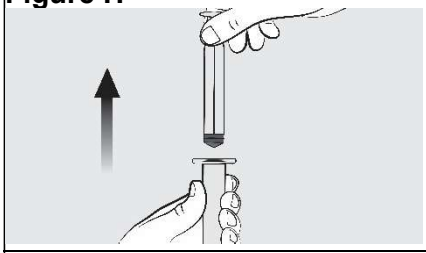
Step 4: Load the tablets into the oral or enteral syringe.

- Remove the cap from the tip of the syringe (see **Figure G**).

Figure G

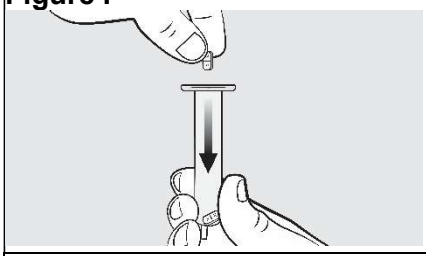
- Pull out the plunger from the back of the syringe (see **Figure H**).

Figure H



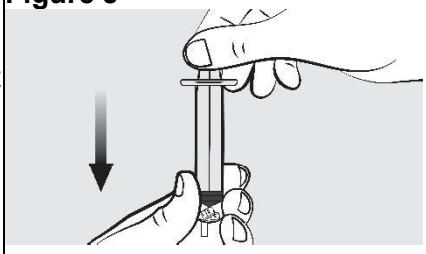
- Put the correct number of EMCITATE tablets into the barrel (see **Figure I**).

Figure I



- Carefully push the plunger back into the syringe, until it comes in contact with the tablets (see **Figure J**).

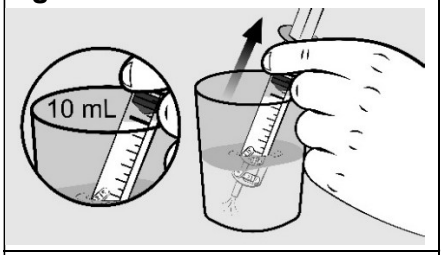
Figure J



Step 5: Draw up water into the syringe.

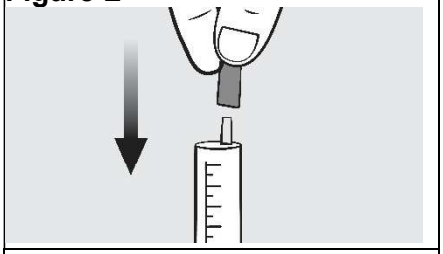
- Place the syringe, tip down, into the glass of water below the water line.
- Pull back on the plunger to draw water from the glass into the syringe until it reaches the 10 mL mark shown on the side of the syringe (see **Figure K**).

Figure K



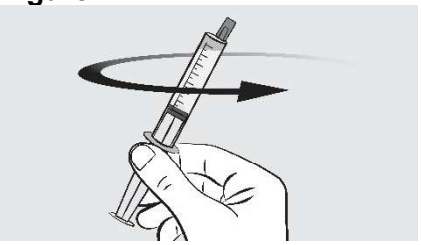
- Immediately turn the syringe upside down (so that the syringe tip is pointing upwards) and put the cap of the syringe back on (see **Figure L**).

Figure L



- Swirl the syringe for about 30 seconds until the tablets are mixed in (see **Figure M**).
- The tablet will not fully dissolve - **the suspension will look white and cloudy with small particles**. This is normal.

Figure M



Giving EMCITATE Suspension by Mouth

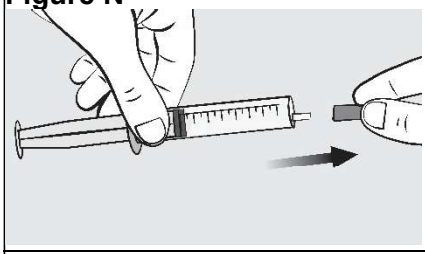
If you are giving EMCITATE suspension through a feeding tube skip to Step 10 below.

Step 6: If particles have settled in the syringe, swirl the syringe again for about 30 seconds before giving EMCITATE suspension.

Step 7: Give your prescribed dose.

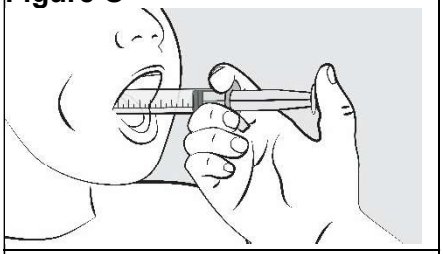
- **Make sure your child or the person receiving the EMCITATE suspension is sitting upright.**
- **Remove the oral syringe cap** (see **Figure N**).

Figure N



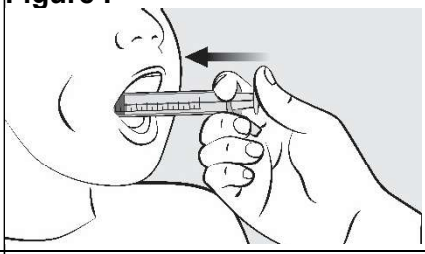
- Place the tip of the oral syringe inside their mouth pointing toward the inside of either cheek (see **Figure O**).

Figure O



- **Slowly push the plunger all the way down** to give the full dose (see **Figure P**).
- Stay upright and allow enough time for all the medicine to be swallowed.

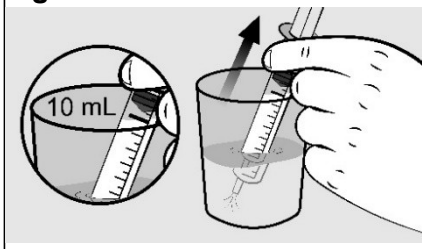
Figure P



Step 8: Rinse the oral syringe and give the rinse water.

- Draw up 10 mL of room temperature drinking water from the glass into the same oral syringe used to give the suspension (see **Figure Q**) and give the oral syringe a quick swirl to rinse the inside of the syringe.
- Give the rinse water the same way as the medicine in Step 7.
  This rinsing step helps make sure the full dose is given by rinsing out any medicine that may be left inside the oral syringe.

Figure Q



Step 9: Clean the oral syringe.

- Pull out the plunger from the back of the oral syringe.
- Rinse the barrel, plunger and cap with clean water (see **Figure R**). Allow to air dry.
- Wash your hands when you are finished.
- Do not worry if some water is left in the glass after preparing the dose. This is normal. Pour out any water left in the glass.

Figure R

Giving EMCITATE Suspension Through a Feeding Tube

If you are giving EMCITATE suspension by mouth, refer to Steps 6 through 9.

Important Information:

- Before giving the EMCITATE suspension, make sure the feeding tube is not blocked. Follow the instructions provided with your feeding tube for flushing and giving the suspension through the tube.
- **Do not** mix the EMCITATE suspension with feeding formulas or put it in feeding bags.

Use a syringe compatible with the enteral feeding tube.

Feeding tubes smaller than 6 French must not be used.

For feeding tubes of 6-7 French a maximum of 1 tablet per dose can be used.

For feeding tubes of 8-11 French a maximum of 2.5 tablets per dose can be used.

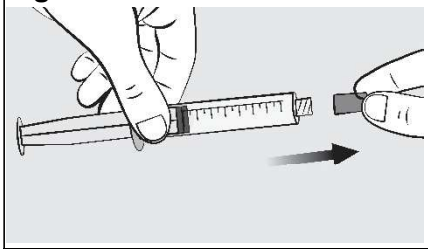
For feeding tubes of 12 French and above a maximum of 3 tablets per dose can be used.

Step 10: If the particles have settled in the syringe, swirl the syringe again for about 30 seconds before giving the dose.

Step 11: Give the dose.

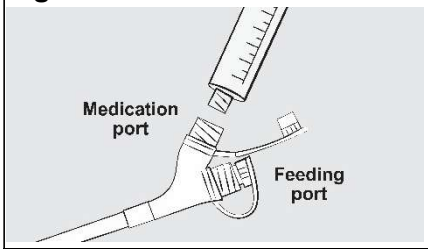
- **Make sure your child or the person receiving the EMCITATE suspension is sitting upright.**
- **Remove the enteral syringe cap** (see **Figure S**).

Figure S



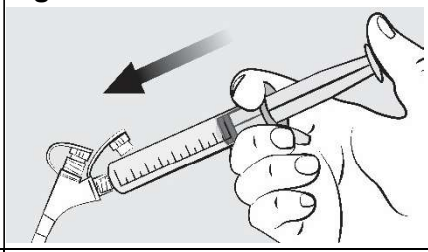
- Remove any air from the enteral syringe before connecting it to the feeding tube.
- Connect the enteral syringe to the medication port of the feeding tube (see **Figure T**).

Figure T



- Slowly and steadily push the plunger all the way down to give the full dose (see **Figure U**).
- Disconnect the enteral syringe from the medication port after the dose is given.

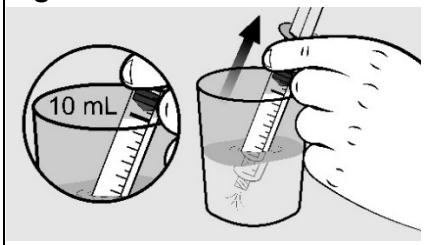
Figure U

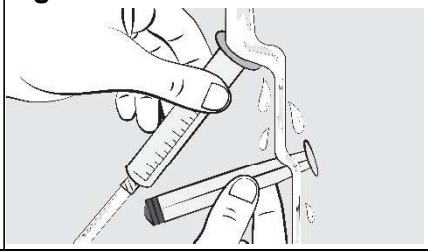


Step 12: Rinse the syringe and give the rinse water.

- Draw up 10 mL of room temperature drinking water from the glass into the same enteral syringe used to give the EMCITATE suspension (see **Figure V**). Give the enteral syringe a quick swirl to rinse the inside of the syringe.
- Reconnect the enteral syringe to the medication port and slowly give the rinse water the same way you gave the EMCITATE suspension in Step 11.
- This rinsing step helps make sure the full dose is given by rinsing out any EMCITATE residue that may be left inside the enteral syringe.

Figure V



<table>
<tr><td colspan="2">Step 13: Flush the feeding tube (if required).
Follow your healthcare provider’s instructions or the directions for your feeding tube.</td></tr>
<tr><td>Step 14: Clean the enteral syringe.
Pull out the plunger from the back of the enteral syringe.
Rinse the barrel, plunger and cap with clean water (see Figure W). Allow to air dry.
Wash your hands when you are finished.
Do not worry if some water is left in the glass after preparing the dose. This is normal. Pour out any water left in the glass.</td><td>Figure W
  </td></tr>
<tr><td>Step 15: Check the equipment.
Regularly check the feeding tube and other items used to give EMCITATE suspension to make sure they are working properly and are not breaking down.</td><td></td></tr>
</table>

Storing EMCITATE

- **Keep EMCITATE tablets in their original blister pack inside the outer carton** (or the light-protective packaging provided by the pharmacy) to **protect them from light**.
- **Keep EMCITATE tablets in the refrigerator** at 36°F to 46°F (2°C to 8°C).
  - When traveling, use insulated containers or coolers with cool packs to maintain the medicine's temperature.
  - **Do not** allow the medicine or cold packs to freeze, and avoid exposing them to direct sunlight, high heat, or extreme cold.
- If the dose includes a **half tablet,** place the unused half tablet back into the original blister pack. Put the blister pack back inside the outer carton (or the light-protective packaging from the pharmacy) to protect it from light. Place in the refrigerator.
- **Do not** keep any unused oral suspension (see “**Disposing of EMCITATE Tablets or Oral Suspension**”).
- Keep EMCITATE and all medicines out of the reach of children.

Disposing of EMCITATE Tablets or Oral Suspension

- Immediately dispose of any unused oral suspension.
- Throw away unused or expired EMCITATE tablets or prepared suspension **according to your local pharmacy or community guidelines for medication disposal.**
- **Do not** throw EMCITATE tablets in the trash, flush down the toilet or pour down the drain.
- If EMCITATE oral suspension is accidentally spilled:
  - use paper towels or similar material to soak up and clean the entire spill.
  - dispose of all contaminated materials according to the disposal instructions above.
  - wash your hands thoroughly with soap and water after cleaning up the spill.

For further information call 1-844-4EGETIS (1-844-434-3847) or go to www.EMCITATE.com

Manufactured for Rare Thyroid Therapeutics International AB and distributed by Egetis Therapeutics US Inc., Cambridge, MA 02142, USA.