ENCELTO- revakinagene taroretcel-lwey implant
Neurotech Pharmaceuticals, Inc.

HIGHLIGHTS OF PRESCRIBING INFORMATION

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

ENCELTO (revakinagene taroretcel-lwey) implant, for intravitreal use
Initial U.S. Approval: 2025

INDICATIONS AND USAGE

ENCELTO is an allogeneic encapsulated cell-based gene therapy indicated for the treatment of adults with idiopathic macular telangiectasia type 2 (MacTel). (1)

DOSAGE AND ADMINISTRATION

For intravitreal implantation only.

- ENCELTO is intended for surgical intravitreal implantation under aseptic conditions by a qualified ophthalmologist. (2.1)
- The recommended dose is one ENCELTO implant per affected eye containing 200,000 to 440,000 allogeneic retinal pigment epithelial cells expressing recombinant human ciliary neurotrophic factor (rhCNTF). (2.1)
- Carefully inspect ENCELTO prior to use and refer to the Instructions for Use when preparing for and performing surgical placement or removal of ENCELTO. (2.2, 2.3)

DOSAGE FORMS AND STRENGTHS

One single-dose implant containing 200,000 to 440,000 allogeneic retinal pigment epithelial cells expressing rhCNTF. (3)

CONTRAINDICATIONS

- Ocular or periocular infections. (4)
- Known hypersensitivity to Endothelial Serum Free Media (Endo-SFM). (4)

WARNINGS AND PRECAUTIONS

- ENCELTO implantation has been associated with severe vision loss, infectious endophthalmitis, retinal tears and/or detachment, vitreous hemorrhage, implant extrusion, cataract formation, suture related complications, and delayed dark adaptation. Patients should be instructed to report signs or symptoms that could be associated with these events without delay. Additional surgical and/or medical management may be required. (5.1, 5.2, 5.3, 5.4, 5.5, 5.6, 5.7, 5.8)

- Vitreous Hemorrhage: Temporarily discontinue antithrombotic medication prior to ENCELTO insertion surgery to reduce the risk of implantation related vitreous hemorrhage. Vitreous hemorrhages occurring greater than one year from implantation could be a sign of ENCELTO extrusion. The surgical site should be examined closely and the ENCELTO should be surgically repositioned if indicated. (5.4)

ADVERSE REACTIONS

The most common adverse reactions (incidence ≥2%) were conjunctival hemorrhage, delayed dark adaptation, foreign body sensation, eye pain, suture related complications, miosis, conjunctival hyperemia, eye pruritus, ocular discomfort, vitreous hemorrhage, blurred vision, headache, dry eye, eye irritation, cataract progression or formation, vitreous floaters, severe vision loss, eye discharge, anterior chamber cell, iridocyclitis. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Neurotech at 1-833-963-9275 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.
See 17 for FDA-approved patient labeling.

Revised: 3/2025

FULL PRESCRIBING INFORMATION: CONTENTS*

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

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

ENCELTO is indicated for the treatment of adults with idiopathic macular telangiectasia type 2 (MacTel).

2 DOSAGE AND ADMINISTRATION

2.1 Recommended Dose

For intravitreal implantation only

• ENCELTO is administered by a single surgical intravitreal procedure performed by a qualified ophthalmologist.

• The recommended dose is one ENCELTO implant per affected eye. Each ENCELTO implant contains 200,000 to 440,000 allogeneic retinal pigment epithelial cells expressing recombinant human ciliary neurotrophic factor (rhCNTF) (NTC-201-6A cell line), a neurotrophic factor.

2.2 ENCELTO Surgical Placement

The ENCELTO implant insertion is a surgical procedure performed in an operating room under aseptic conditions by a qualified ophthalmologist.

Pre-Surgical Preparation

1. Inspect the ENCELTO packaging for any signs of damage or leakage.
2. Verify the use-by date.
3. Confirm that the disposable temperature recording device displays a checkmark at the top of the screen.
4. Ensure the liquid medium is at the correct pH using the provided pH color guide reference card.

Prepare the surgical field properly.

Surgical Steps

1. Preparing the Surgical Site

a. Create a 7x7 mm peritomy of the conjunctiva and Tenon's capsule at the selected implantation site.

b. Place a corneal-limbal traction suture in the selected surgical quadrant (either inferotemporal or inferonasal) (Figure 1).

c. Maintain hemostasis of the underlying sclera and conjunctiva (Figure 1).

d. Using an MVR and 15-degree blade, create a 3.0 mm full-thickness sclerotomy 3.75 mm posterior and parallel to the limbus (Figure 2). Do not insert ENCELTO outside of the pars plana.

e. Confirm:

- The incision is full thickness.
- There is adequate hemostasis.
- There is no spanning uveal tissue.

Figure 1

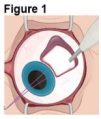
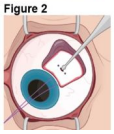


Figure 2



2. Preparing the ENCELTO Implant

a. Open the inner container and expose the upper compartment and luer lock cap (Figure 3).

b. Unlock the luer lock cap by turning it counterclockwise once.

c. Lift the luer lock cap vertically to remove ENCELTO (attached to the gripper).

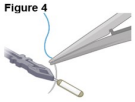
d. Rinse ENCELTO with at least 5 mL of sterile Balanced Saline Solution (BSS).

e. Keep ENCELTO moist by applying BSS every 10 minutes until insertion.

f. While holding the luer lock cap, pass a double-armed 9-0 polypropylene

Figure 3

Figure 4



suture needle through ENCELTO’s fixation loop (Figure 4).

3. Implantation of ENCELTO

a. Gently open the sclerotomy incision and insert ENCELTO perpendicularly into the eye (Figure 5).

b. Ensure only the fixation loop is exposed.

c. Release ENCELTO from the gripper by squeezing the indicated region with forceps or a fine needle holder (Figure 6).

Figure 5

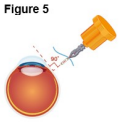
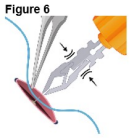


Figure 6



4. Securing the Implant

a. Secure ENCELTO by creating a 3-1-1 anchor knot with the polypropylene suture at the apex of the fixation loop (Figure 7).

b. Confirm ENCELTO is centered in the incision.

c. Pass each suture arm centrally through either side of the wound at 90-99% scleral depth (Figure 8).

d. Pull up the suture ends and confirm that the fixation loop is at the proper depth (90-99%).

e. Tie down the suture to the sclera with a 3-1-1 knot, ensuring the knot is placed away from the incision.

f. If a suture breaks, leave the tail as long as possible and lay it flat.

g. Take a 2.0 mm scleral bite at 50-75% depth beyond the sclerotomy on each side (Figure 9).

Figure 7

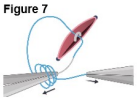


Figure 8

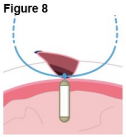
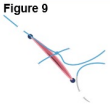


Figure 9



5. Closing the Incision

a. Close the scleral incision with 9-0 nylon sutures (Figure 10), ensuring:

- The polypropylene suture is captured to prevent irritation and erosion.
- All nylon suture knots are rotated into the sclera.
- The closure is watertight.

b. Pull the polypropylene suture end taut and cut it flush to the sclera.

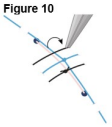
c. Close the conjunctiva and Tenon’s capsule using 6-0 plain gut or chromic suture, or 7-0 Vicryl suture or similar.

d. Ensure Tenon’s capsule covers the insertion site and use 3-point fixation and scleral bites.

e. Administer sub-conjunctival steroid injection: dexamethasone, 2 mg/0.5 ml (4 mg/ml) or equivalent. If the case is complicated and inflammation is anticipated, a higher dose of dexamethasone (0.5 cc of 10 mg/ml) or equivalent may be used, at the surgeon’s discretion.

f. Perform indirect ophthalmoscopy to confirm placement of ENCELTO in the vitreous and that there are no intraocular complications. Failure to perform indirect ophthalmoscopy can lead to unidentified malpositioning of ENCELTO and intraocular complications.

Figure 10



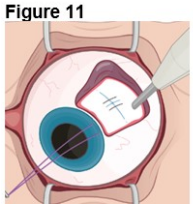
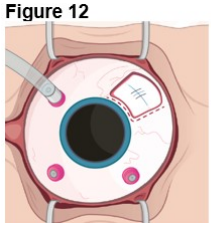
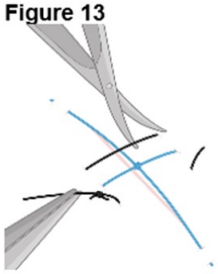
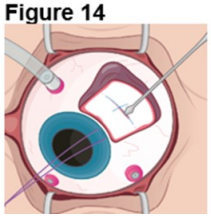
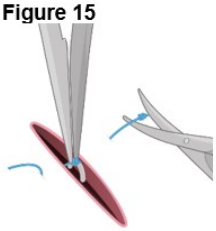
Post-Operative Wound Care

- The patient is to use:
  - A topical antibiotic solution at a frequency of 1 drop four times a day for 7 days.
  - A steroid drop taper of prednisolone acetate 1% (or equivalent) starting the day after surgery with the following taper:
    - 1 drop four times a day for the first 7 days;
    - 1 drop three times a day for the next 7 days;
    - 1 drop two times a day for the next 7 days;
    - 1 drop once a day for the last 7 days.

Refer to ENCELTO Instructions for Use for detailed guidance on implantation procedure.

2.3 ENCELTO Removal Procedure

Removal of ENCELTO is a surgical procedure performed in an operating room under aseptic conditions by a qualified ophthalmologist. Remove ENCELTO implant, if vitrectomy with a complete gas fill or silicone oil fill is required or if infectious endophthalmitis occurs.

Surgical Steps	
1. Preparing the Surgical Site (Figure 11) a. Create a 7x7 mm peritomy of the conjunctiva and Tenon's capsule to expose the insertion site. b. Place a corneal-limbal traction suture in the quadrant where ENCELTO is located. c. Maintain hemostasis of the sclera and surrounding conjunctiva.	Figure 11 
2. Establishing Infusion & Vitrectomy (Figure 12) a. Place an infusion cannula in the inferior quadrant (opposite ENCELTO). b. Confirm the infusion line is positioned within the vitreous cavity before opening the infusion. c. Insert two superior cannulas following normal pars plana vitrectomy protocol. d. Perform a thorough vitrectomy to remove vitreous surrounding ENCELTO without disrupting the hollow fiber membrane.	Figure 12 
3. Reopening the Sclerotomy a. Locate the ENCELTO incision and remove the two nylon sutures while leaving the polypropylene suture intact (Figure 13). b. Using an MVR blade, carefully dissect open the original scleral incision down to the ENCELTO cap at the base of the fixation loop (Figure 14). c. Extend the incision along the entire 3.0 mm length to full thickness. d. Cut the polypropylene anchor suture on the anterior side of the knot. e. Turn off or lower infusion pressure.	Figure 13  Figure 14 
4. Removing ENCELTO (Figure 15) a. Fully open the pars plana sclerotomy and confirm there is no spanning uveal tissue. b. Identify and grasp the fixation loop. c. Cut off the remaining polypropylene knot. d. Remove ENCELTO from the eye. e. Inspect the ENCELTO capsule for any damage or penetration. f. Do not discard or dispose of the ENCELTO implant. Call and report to 1-833-963-9275. The appropriate action will be taken to initiate the	Figure 15 

return of ENCELTO and possible replacement.	
5. Closing the Incision a. Remove any prolapsed vitreous. b. Close the sclerotomy with interrupted 7-0 Vicryl sutures for a watertight closure. c. Remove the infusion line and additional cannulas. d. Close the conjunctiva with 6-0 plain gut sutures or equivalent.	
Post-Operative Wound Care • The patient is to use: ◦ A topical antibiotic solution at a frequency of 1 drop four times a day for 7 days. ◦ A steroid drop taper of prednisolone acetate 1% (or equivalent) starting the day after surgery with the following taper: ▪ 1 drop four times a day for the first 7 days; ▪ 1 drop three times a day for the next 7 days; ▪ 1 drop two times a day for the next 7 days; ▪ 1 drop once a day for the last 7 days.	

Refer to ENCELTO Instructions for Use for detailed guidance on removal procedure.

3 DOSAGE FORMS AND STRENGTHS

ENCELTO is a single-dose implant that contains 200,000 to 440,000 allogeneic retinal pigment epithelial cells expressing recombinant human ciliary neurotrophic factor (rhCNTF) (NTC-201-6A cell line) for intravitreal surgical placement. ENCELTO is an opaque semi-permeable capsule that is white to off-white, capped on both ends, and has a titanium loop on one end. The ENCELTO width is 1.2 ± 0.1 mm, its length is 6.1 ± 0.4 mm, and its internal diameter is 0.88 ± 0.02 mm (Figure 17).

4 CONTRAINDICATIONS

ENCELTO is contraindicated in patients with:

- Active or suspected ocular or periocular infections.
- Known hypersensitivity to Endothelial Serum Free Media (Endo-SFM)

5 WARNINGS AND PRECAUTIONS

5.1 Severe Vision Loss

Severe vision loss defined as three or more lines of visual acuity loss [≥15 Early Treatment Diabetic Retinopathy Study (ETDRS) letters] has occurred following ENCELTO implantation [*see Adverse Reactions (6)*]. Monitor patients for signs and symptoms of vision loss and manage as clinically indicated.

5.2 Infectious Endophthalmitis

Infectious endophthalmitis may occur following ENCELTO implantation. Signs and symptoms of infectious endophthalmitis include progressively worsening eye pain, vision loss, or scleral and conjunctival injection. To mitigate the risk of endophthalmitis, use

proper aseptic surgical technique for ENCELTO implantation [*see Dosage and Administration (2.2)*]. Monitor patients for signs or symptoms of infectious endophthalmitis. Remove ENCELTO implant if infectious endophthalmitis occurs and manage symptoms according to clinical practice.

5.3 Retinal Tear and Detachment

Retinal tears and retinal detachment may occur following ENCELTO implantation. Signs and symptoms of retinal tears include acute onset of flashing lights, floaters, and/or loss of visual acuity. Signs and symptoms of retinal detachment may include progressive visual field loss and/or loss of visual acuity. Use standard vitreoretinal surgical techniques during ENCELTO implantation to minimize the risk of retinal tears and retinal detachment. Monitor for any signs or symptoms of retinal tear and/or retinal detachment. Treat rhegmatogenous retinal detachment and retinal tears promptly. Remove ENCELTO implant, if vitrectomy with a complete gas fill or silicone oil fill is required [*see Dosage and Administration (2.3)*].

5.4 Vitreous Hemorrhage

Vitreous hemorrhage, which may result in temporary vision loss, has occurred following ENCELTO implantation [*see Adverse Reactions (6)*]. Patients receiving antithrombotic medication (e.g., oral anticoagulants, aspirin, nonsteroidal anti-inflammatory drugs) may be at increased risk of vitreous hemorrhage. To reduce the risk of vitreous hemorrhage, interrupt antithrombotic medications prior to the ENCELTO implantation. Vitrectomy surgery may be necessary to clear severe, recurrent, or non-clearing vitreous hemorrhage. If the patient has a late onset vitreous hemorrhage (greater than one year following ENCELTO implantation surgery), examine the ENCELTO implantation site for possible implant extrusion. If implant extrusion has occurred, surgically reposition ENCELTO [*see Implant Extrusion (5.5)*].

5.5 Implant Extrusion

Implant extrusion through the initial scleral wound has occurred following ENCELTO implantation [*see Adverse Reactions (6)*]. Signs and symptoms of implant extrusion include recurrent uveitis, vitreous hemorrhage, eye pain more than one year after implantation, or visibility of titanium fixation loop under the conjunctiva. To reduce the risk of implant extrusion, carefully follow the specific surgical steps for ENCELTO implantation [*see Dosage and Administration (2.2)*].

Evaluate patients after 6 months to confirm proper positioning of ENCELTO and then annually. If ENCELTO begins to extrude, surgically reposition ENCELTO to a proper scleral wound depth either in the same site or in the opposing inferior quadrant of the vitreous cavity.

5.6 Cataract Formation

Cataract formation, including cataract cortical, cataract nuclear, cataract subcapsular, cataract traumatic, and lenticular opacities, has occurred following ENCELTO implantation [*see Adverse Reactions (6)*]. To reduce the risk of ENCELTO-related cataract formation or progression, carefully follow the specific surgical steps for ENCELTO implantation [*see Dosage and Administration (2.2)*].

5.7 Suture Related Complications

Suture related complications, including conjunctival erosions due to suture tips and suture knots, have occurred following ENCELTO implantation [*see Adverse Reactions (6)*]. To mitigate the risk of suture related complications, carefully follow the specific surgical steps for ENCELTO implantation [*see Dosage and Administration (2.2)*] and manage suture-related complications as clinically indicated.

5.8 Delayed Dark Adaptation

Delayed Dark Adaptation, a delay in the ability to adjust vision from a bright lighting condition to a dim lighting, has occurred following ENCELTO administration which remained unchanged for the duration of study follow up [*see Adverse Reactions (6)*]. Advise patients to take caution while driving and navigating in the dark.

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 data described in this section reflects exposure to ENCELTO in two clinical trials, Study 1 (NTMT-03-A) and Study 2 (NTMT-03-B) and are pooled for analysis. A total of 117 patients received ENCELTO, and 111 patients underwent a sham procedure and were followed for a duration of 24 months [*see Clinical Studies (14)*].

Serious adverse reactions occurred in six patients (5%) including suture related complications (n=5) and implant extrusion (n=1).

Table 1 lists the most common adverse reactions that occurred in $\geq$2% patients and with higher frequency in ENCELTO group compared to Sham group in Study 1 and Study 2.

Table 1. Adverse Reactions occurring in ≥2% of Patients and with higher frequency in ENCELTO group compared to Sham group in ENCELTO studies*

Adverse Reactions	ENCELTO (N=117) n (%)	Sham (N=111) n (%)
Conjunctival hemorrhage	36 (31)	29 (26)
Delayed dark adaptation	27 (23.1)	1 (1)
Foreign body sensation in eyes	18 (15)	15 (13.5)
Eye pain	18 (15)	10 (9)
Suture related complication**	18 (15.4)	3 (2.7)
Miosis	18 (15.4)	0 (0.0)
Conjunctival hyperemia	13 (11)	9 (8)
Eye pruritus	10 (9)	4 (3.6)
Ocular discomfort	10 (9)	1 (1)
Vitreous hemorrhage	10 (8.5)	0 (0.0)

Vision blurred	8 (7)	4 (4)
Headache	8 (7)	1 (1)
Dry eye	7 (6)	2 (2)
Eye irritation	6 (5.1)	2 (2)
Cumulative cataract incidence	6 (5)	0 (0)
Vitreous floaters	6 (5)	0 (0.0)
Severe visual loss>15 letters***	4 (3)	0 (0)
Eye discharge	4 (3.4)	1 (0.9)
Anterior chamber cell	4 (3.4)	0 (0.0)
Iridocyclitis	3 (2.6)	0 (0)

* Pooled data from Study 1 and Study 2; Adverse reaction rates were comparable between the two studies
**Suture related complications include exposed suture, foreign body sensation, conjunctival wound dehiscence, painful sutures, suture irritation, suture granuloma, scleral wound opening, and itchy suture
*** Includes one case of visual loss due to cataract formation which remained unresolved at the end of the study

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

There are no data on the use of ENCELTO in pregnant women. Endogenous CNTF is naturally found in maternal plasma, placental cells, and umbilical cord blood. It is not known if the use of ENCELTO increases CNTF above naturally occurring levels in these tissues.

In animal reproduction studies, subcutaneous administration of rhCNTF to pregnant rats and rabbits demonstrated no evidence of teratogenic effects on the fetus. However, when administered to rabbits at a dose level of 10ug/kg/day, a decrease in implantations and live fetuses was observed. When administered to rats at a dose level of 100ug/kg/day a decrease in corpora lutea was observed.

The estimated background risk of major birth defects and miscarriage in 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 is 2% to 4% and of miscarriage is 15% to 20% of clinically recognized pregnancies.

Data

Animal Data

See *Risk Summary* for details on data.

8.2 Lactation

Risk Summary

There is no data on the presence of ENCELTO in human milk, its effects on the breastfed infant, or its impact on milk production.

The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for ENCELTO and any potential adverse effects on the breastfed infant from rhCNTF or from the underlying maternal condition.

8.4 Pediatric Use

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

8.5 Geriatric Use

There were 38 patients (32%) 65 years of age and older and two patients (1%) 75 years of age and older in Study 1 and Study 2 who received ENCELTO [*see Clinical Studies (14)*]. Clinical studies of ENCELTO did not include sufficient numbers of patients aged 65 and over to determine whether they respond differently than younger patients.

11 DESCRIPTION

ENCELTO (revakinagene taroretcel-lwey) implant, is single-dose, sterile, nonpyrogenic and retrievable.

ENCELTO is an allogeneic encapsulated cell-based gene therapy that contains 200,000 to 440,000 allogeneic retinal pigment epithelial cells expressing recombinant human ciliary neurotrophic factor (rhCNTF) (NTC-201-6A cell line) for surgical intravitreal placement.

ENCELTO consists of an opaque, semi-permeable white to off-white capsule surrounding a scaffold of polyethylene terephthalate (PET) yarn, loaded with rhCNTF secreting allogeneic retinal pigment epithelial cells (NTC-201-6A cell line). Each end of the semi-permeable capsule is sealed with medical grade methacrylate adhesive, and to one end a titanium fixation loop is attached. ENCELTO width is 1.2 ± 0.1 mm, length is 6.1 ± 0.4 mm, and its internal diameter is 0.88 ± 0.02 mm (Figure 17).

ENCELTO is packaged in a protective inner container within an orange to pink liquid hold medium referred to as Endothelial Serum Free Media (Endo-SFM), which is maintained sterile by a sealed outer container. ENCELTO is provided attached, by the fixation loop, to a gripper that both suspends ENCELTO in the Endo-SFM and facilitates intraocular insertion. The Endo-SFM within the packaging inner container may contain visible particles generally described as fiber, solid, white, or metallic in appearance.

ENCELTO is manufactured using animal and human derived reagents.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

ENCELTO secretes recombinant human ciliary neurotrophic factor (rhCNTF), which is one of several neurotrophic factors endogenously produced by neurons and supporting glial cells. Exogenous CNTF is thought to initially target Müller glia to trigger a cascade of signaling events that may promote photoreceptor survival; however, the mechanism of action for ENCELTO is not completely understood.

12.3 Pharmacokinetics

Systemic exposure of rhCNTF was measured in 2 distribution studies in rabbits and in 2 toxicology studies in minipigs. Overall, there was no evidence of systemic exposure to rhCNTF after implantation of ENCELTO in rabbits for periods up to 9 months or in minipigs for periods of up to 6 months.

Following intraocular implantation of a single ENCELTO dose in rabbits at 12 weeks, the mean C_{max} of rhCNTF in the vitreous and aqueous was 2.0 and 0.3 ng/mL, respectively, and below the level of quantitation (LLOQ) in the serum and contralateral, untreated eye. Similarly in human patients, rhCNTF levels were below the limit for LLOQ in the serum.

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 anti-drug antibodies in other studies, including those of ENCELTO or of other products.

In a six-month Study NTMT-02B in which patients received ENCELTO in a single eye, one out of 31 patients (3%) tested positive for serum antibodies against the ENCELTO secreted product protein rhCNTF and one patient (3%) tested positive to serum non-secreted intracellular protein DHFR.

Because of the low occurrence of anti-drug antibodies, the effect of serum anti-rhCNTF and anti-DHFR antibodies on the safety or efficacy of ENCELTO is unknown.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenesis and Mutagenesis

No carcinogenicity or mutagenicity studies have been conducted with rhCNTF.

Impairment of Fertility

In male rats, fertility was unaffected at subcutaneous doses of rhCNTF up to 300 µg/kg/day.

See *Pregnancy (8.1)* for data regarding effects on female fertility.

14 CLINICAL STUDIES

The efficacy of ENCELTO was evaluated in two studies, Study NTMT-03-A (NCT03316300; Study 1) and Study NTMT-03-B (NCT03319849; Study 2) as described below.

Study 1

Study 1 was a randomized, multi-center, sham-controlled study which enrolled adults with MacTel. For enrollment, the patients were required to have a photoreceptor inner

segment/outer segment (IS/OS PR) break (loss) in ellipsoid zone (EZ) between 0.16 and 2.00 mm^2 measured by spectral domain-optical coherence tomography (SD-OCT) and best corrected visual acuity (BCVA) of 54-letter score or better (20/80 or better) as measured by the Early Treatment Diabetic Retinopathy Study (ETDRS) chart at screening. Patients with neovascular MacTel were excluded. Patients were randomized to receive either ENCELTO intravitreal implant or sham procedure under standard operative procedures. Patients in ENCELTO group underwent conjunctival peritomy, implant placement in the vitreous cavity via sclerotomy and closure with sutures. Patients in the Sham group underwent conjunctival peritomy, scleral pressure, and conjunctival closure with sutures. One hundred and fifteen (96%) of 120 patients underwent the assigned procedure and were included in the analysis of efficacy.

A total of 120 patients were randomized and of these, 115 patients (ENCELTO group: 58; Sham group: 57) comprise the efficacy analysis population. The demographic characteristics of the efficacy analysis population were as follows: the mean age was 61 years (range 40 to 78 years), 79 patients (69%) were female, 98 patients (85%) were White, 5 patients (4%) were Asian, 3 patients (3%) were Black or African American, 1 patient (1%) was American Indian, and 8 patients (7%) were of “other” race. Six patients (5%) were Hispanic. The median (min, max) baseline EZ area loss was 0.35 (0.15, 1.99) mm^2 for the ENCELTO group and 0.36 (0.16, 1.7) mm^2 for the Sham group. The median (min, max) baseline aggregate sensitivity of microperimetry within the EZ break area 35.2 (0.75, 398.8) dB for the ENCELTO group and 35.5 (2, 281.3) dB for the Sham group.

The primary efficacy outcome measure was the rate of change in the area of EZ loss (IS/OS, macular PR loss) over 24 months, as measured by SD-OCT. The secondary outcome measure was the mean change in aggregate sensitivity loss of microperimetry within the EZ break area from baseline to Month 24.

The efficacy outcome results for Study 1 are summarized in Table 2.

Table 2. Efficacy Results for Study 1 (N=115)

Efficacy endpoints	ENCELTO n= 58	Sham n=57	Difference ENCELTO-Sham	P-value[c]
Rate of change in EZ area loss from baseline over 24 months[a] mm^2 (95% CI)	0.075 (0.05, 0.10)	0.166 (0.14, 0.19)	-0.091 (-0.13, -0.06)	<0.0001
Mean change in aggregate retinal sensitivity loss from baseline to 24-months[b] dB (95% CI)	25.27 (15.88, 34.67)	43.02 (31.78, 54.26)	-17.75 (-32.58, -2.91)	0.02

CI = confidence interval, EZ=ellipsoid zone

[a] Estimated by using a longitudinal mixed model including EZ area loss as the dependent variable, patient-specific random intercepts, treatment group, time (continuous), and interaction between treatment and time as covariates. The baseline and Months 12, 16, 20, and 24 visits were included.

[b] Estimated by using two-sample t-test; seven ENCELTO and four Sham patients were excluded due to missing data.

[c] Statistically significant at two-sided alpha of 0.05.

Study 2

Study 2 was a randomized, multi-center, sham-controlled study which enrolled adult with MacTel. For enrollment, the patients were required to have an IS/OS PR break in EZ between 0.16 and 2.00 mm^2 measured by SD-OCT and BCVA of 54-letter score or better (20/80 or better) as measured by the ETDRS chart at screening. Patients with neovascular MacTel were excluded.

Patients were randomized to receive either ENCELTO intravitreal implant or sham procedure under standard peri-operative procedures. Patients in ENCELTO group underwent conjunctival peritomy, implant placement in the vitreous cavity via sclerotomy and closure with sutures. Patients in the Sham group underwent conjunctival peritomy, scleral pressure, and conjunctival closure with sutures. One hundred and thirteen (95%) of the 119 patients underwent the assigned procedure and were included in efficacy evaluation.

A total of 119 patients were randomized and of these, 113 patients (ENCELTO group: 59; Sham group: 54) comprise the efficacy analysis population. The demographic characteristics of the efficacy analysis population were as follows: the mean age was 59 years (range: 40 to 75 years), 82 patients (73%) were female, 102 patients (90%) were White, 4 patients (4%) were Asian, and 7 patients (6%) were of “other” race or “unable to specify” race. Eight patients (7%) were Hispanic. The median (min, max) baseline EZ area loss was 0.48 (0.16, 1.63) mm^2 for the ENCELTO and 0.39 (0.16, 1.38) mm^2 for the Sham group. The median (min, max) baseline aggregate sensitivity of microperimetry within the EZ break area 40.07 (4.82, 291.52) dB for the ENCELTO group and 28.86 (0.33, 221.17) dB for the Sham group.

The primary efficacy outcome measure was the rate of change in the area of EZ loss (IS/OS, macular PR loss) over 24 months, as measured by SD-OCT. The secondary outcome measure was the mean change in aggregate sensitivity loss of microperimetry within the EZ break area from baseline to Month 24.

The efficacy results from Study 2 are summarized in Table 3 below.

Table 3. Efficacy Results for Study 2 (N=113)

Efficacy endpoints	ENCELTO n= 59	Sham n=54	Difference ENCELTO-Sham	P-value[c]
Rate of change in EZ area loss from baseline over 24 months[a] mm^2 (95% CI)	0.111 (0.08, 0.14)	0.160 (0.13, 0.19)	-0.049 (-0.089, -0.008)	0.0186[c]
Mean change in aggregate retinal sensitivity loss from baseline to 24-month[b] dB (95% CI)	40.02 (26.08, 53.96)	41.97 (30.34, 53.60)	-1.95 (-20.33, 16.43)	0.83

CI = confidence interval, EZ=ellipsoid zone

[a] Estimated by using a longitudinal mixed model including EZ area loss as the dependent variable, patient-specific random intercepts, treatment group, time (continuous), and interaction between treatment and time as covariates. The baseline and Months 12, 16, 20, and 24 visits were included.

[b] Estimated by using two-sample t-test; Seven ENCELTO and six Sham patients were excluded due to missing data.

[c] Statistically significant at two-sided alpha of 0.05.

16 HOW SUPPLIED/STORAGE AND HANDLING

16.1 How Supplied

ENCELTO is supplied as a sterile, single-dose, implant that contains 200,000 to 440,000 allogeneic retinal pigment epithelial cells expressing rhCNTF (NTC-201-6A cell line).

ENCELTO is packaged in a protective inner container within an Endothelial Serum Free Media (Endo-SFM), which is maintained sterile by a sealed outer container. ENCELTO is provided attached to a gripper that both suspends ENCELTO in the Endo-SFM and facilitates intraocular insertion. ENCELTO contains no preservatives.

NDC: 82958-501-01

See Table 4, (Figure 16) and ENCELTO “Instructions for Use” for additional details.

Table 4. ENCELTO Corepack Contents

Components	Description
Inner container	This is provided sterile. It is a cylindrical plastic container with a lower compartment filled with liquid medium. It has an upper compartment connected to it via a narrow channel that is secured shut with a luer lock cap.
Outer container	This is a plastic container with a foil lid hermetically sealed. It maintains the sterility of the inner container until ready to use.
Disposable temperature recording device	A disposable device that measures and records the temperature in the package. If ENCELTO has been stored within the acceptable range, a “✓” will be shown at the top of the screen. If an “X” is displayed, ENCELTO has been exposed to temperatures outside of the acceptable range and must not be used.
ENCELTO Medium pH Color Guide	A card that provides a color scale to indicate the acceptable pH range for the liquid medium.
ENCELTO Instructions for Use	A booklet that contains the full instructions and includes the ENCELTO patient card.
ENCELTO Inspection Checklist	An information sheet that contains instructions for inspection prior to use.
USPI	United States Prescribing Information.

Figure 16. ENCELTO Corepack Contents

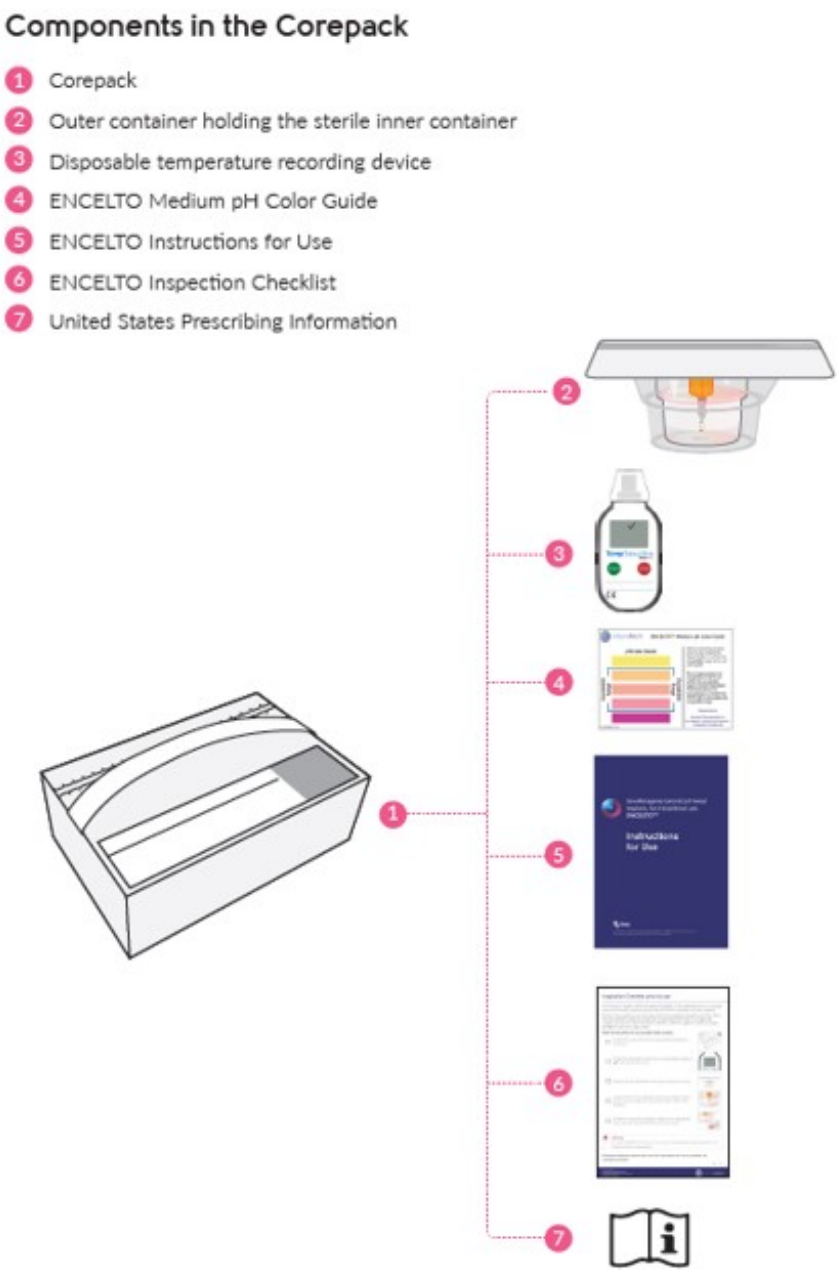


Figure 17. ENCELTO

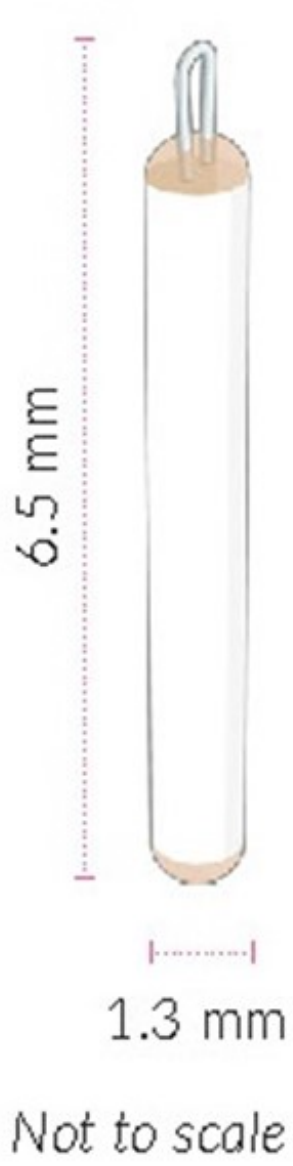


Figure 18. ENCELTO Inner Container

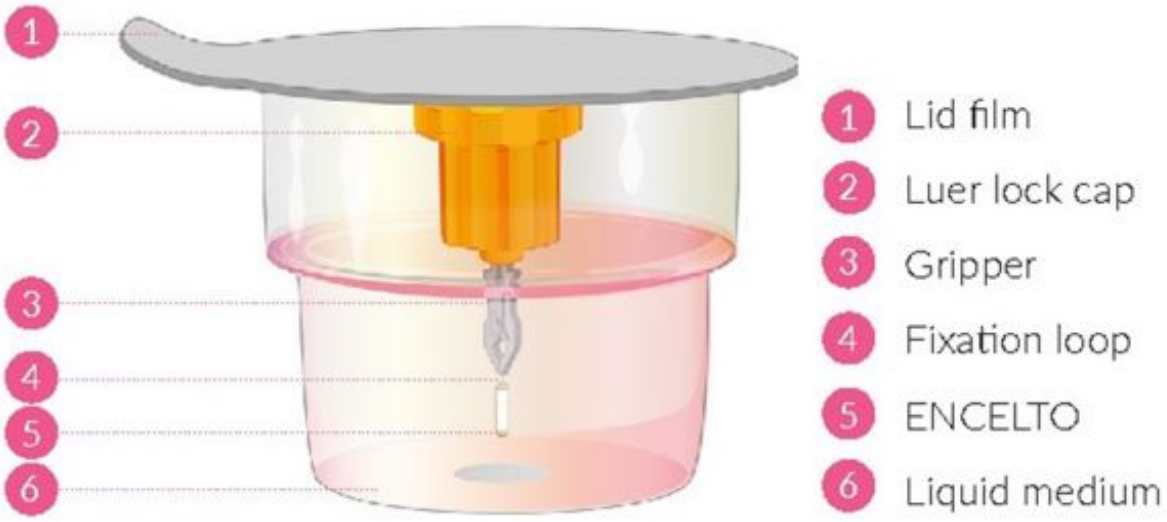
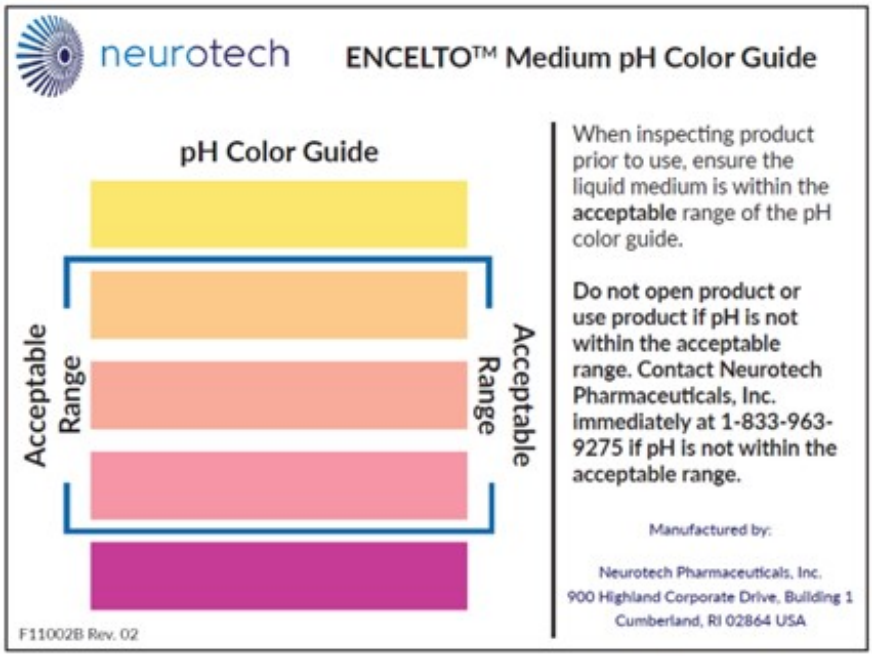


Figure 19. pH Color Guide



16.2 Storage and Handling

1. Using the handle, remove the corepack from the larger shipping box (Figure 16).

2. Store ENCELTO in the corepack at 16º to 37ºC (61º to 99ºF) until ready for use.

3. Do not freeze or refrigerate.

4. Inspect the disposable temperature recording device. If a check mark is displayed, the ENCELTO has remained within the acceptable temperature range and may be used. If a "X" is displayed, the ENCELTO was exposed to temperatures outside the acceptable range and must not be used. Contact Neurotech immediately at (833)-963-9275.

- Protect ENCELTO from light.

5. Handle inner container (Figure 18) using sterile technique.

6. Do not use beyond the "use by" date identified on the corepack label.

7. Do not use ENCELTO if the pH is not within the acceptable range (Figure 19). Contact Neurotech immediately at (833)-963-9275.

- Prior to disposal of an ENCELTO implant per local institutional protocols, call 1-833-963-9275 for assessment of ENCELTO return or replacement.

Orange to pink liquid hold medium referred to as Endothelial Serum Free Media (Endo-SFM) within packaging inner container may contain visible particles. Particle general description fiber, solid, white, or metallic in appearance.

17 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Patient Information).

Discuss the following with the patient.

Advise patients that ENCELTO implantation may be associated with infectious

endophthalmitis (eye infection), retinal tear and detachment (retina separates from the eye wall resulting in vision loss), vitreous hemorrhage (bleeding within the central cavity of the eye), implant extrusion, suture-related complications, cataract formation (clouding of the lens of the eye), severe vision loss, and delayed dark adaptation (ability of the eye to adjust from bright lighting conditions to dark lighting conditions) [*see Warnings and Precautions (5)*].

Instruct patients to seek immediate care from an ophthalmologist if they experience any signs or symptoms that could be associated with these events which may include the following:

- An increase in floaters, the appearance of “spider webs”, flashing lights, sensitivity to light, or loss of vision or visual field;
- Increasing eye pain, progressive redness in the white of the eye, a sudden sensation that something is in their eye (i.e., foreign body sensation) or eye discharge.

Advise patients that they may temporarily experience the following after ENCELTO implantation:

- Mild sensation of something in the eye (i.e., foreign body sensation)
- Eye redness, irritation, pain or discomfort, or dryness
- Blurred vision or floaters

Advise patients that delayed dark adaptation may be experienced for the length of time that ENCELTO is surgically placed [*see Warnings and Precautions (5.8)*]. Advise patients on the following safety precautions.

- Driving: delayed dark adaptation may impair one's ability to see objects, pedestrians, or road signs when moving rapidly from a brightly lit environment to a dimly lit environment (for example, entering a tunnel during the daytime).
- Navigating in the dark: Advise caution when moving from bright to dark areas, such as entering a dark room or stepping outside at dusk. Consider using flashlights, nightlights, or motion-activated lighting at home.
- Consider wearing sunglasses or tinted lenses in bright environments to reduce the impact of transitioning from light to dark.

Magnetic Resonance (MR) Conditional Information

ENCELTO is MR conditional. Advise patients that they have ENCELTO implanted in their eye and provide the patient with their implant card should they require Magnetic Resonance Imaging (MRI).

Driving and Using Machines

- Advise patients to not drive or use machinery until the eye shield has been removed and their ophthalmologist informs them that their vision has recovered to an acceptable level.

Postoperative Care

Advise patients on the following post operative care:

- Avoid heavy lifting (over 20 pounds) for one week.

- Keep water out of the eye (e.g., close eye while showering) for one week.
- Protect eyes by wearing glasses or protective eyewear during the day and using an eye shield at night for one week.
- Use a topical antibiotic solution at a frequency of 1 drop four times a day for 7 days.
- Use a steroid drop taper of prednisolone acetate 1% (or equivalent) starting the day after surgery with the following taper:
  - 1 drop four times a day for the first 7 days;
  - 1 drop three times a day for the next 7 days;
  - 1 drop two times a day for the next 7 days;
  - 1 drop once a day for the last 7 days.

Manufactured by:

Neurotech Pharmaceuticals, Inc.

Building 1, Suite 101

Cumberland, RI 02864

U.S. license number: 2321

PATIENT INFORMATION
ENCELTO (En-SEL-toh)
A surgical implant for use in the eye

What is ENCELTO?

ENCELTO is an encapsulated cell-based gene therapy. It is a small capsule, about the size of a grain of rice, that is placed inside the eye to release a protein called recombinant human ciliary neurotrophic factor (rhCNTF) that can directly reach the retina, the light sensitive part of the eye. The capsule contains living cells that have been genetically modified to continuously produce and release CNTF. This protein helps protect certain cells in your retina, supporting their health and reducing the loss of light-sensing cells known as photoreceptors.

ENCELTO is used to treat adults with idiopathic macular telangiectasia type 2 (MacTel); a retinal disease that causes progressive vision loss. Your ophthalmologist will assess your vision and review your medical history to determine if ENCELTO is the right treatment for you.

Who should not receive an ENCELTO surgical implant?

ENCELTO has not been tested in pediatric patients or pregnant women.

The outpatient surgical procedure should not be performed if you are currently experiencing an active or suspected eye infection.

You should not receive ENCELTO if you have a known hypersensitivity to Endothelial Serum Free Media (Endo-SFM)

Before receiving ENCELTO, tell your ophthalmologist about all your medical conditions, including:

- Are pregnant or plan to become pregnant. Although studies have shown that rhCNTF does not enter the bloodstream, its effects on an unborn baby have not been fully

studied.
- Are breastfeeding or plan to breastfeed. It is not known if rhCNTF passes into your breast milk.
- Any current infections
- Are currently taking or have recently taken medicines that lower the chance of blood clots forming in the body such as warfarin, low or regular doses of aspirin, or nonsteroidal anti-inflammatory drugs (NSAID)

How is ENCELTO administered?

ENCELTO is inserted into the eye as an outpatient surgical procedure performed by an ophthalmologist experienced in retinal surgery. If removal of ENCELTO is necessary, the removal surgery must also be done by an ophthalmologist experienced in vitreoretinal surgery in an operating room as an outpatient surgery.

What should I avoid after placement of ENCELTO?

Immediately post-operative:
- Avoid heavy lifting (over 20 pounds) for one week.
- Keep water out of the eye (e.g., close your eye while showering) for one week.
- Protect your eyes by wearing glasses or protective eyewear during the day and using an eye shield at night for one week.
- Do not drive or use machinery until the eye shield has been removed and your ophthalmologist informs you that your vision has recovered to an acceptable level.

Post operative care:
- Use a topical antibiotic solution at a frequency of 1 drop four times a day for 7 days.
- Use a steroid drop taper of prednisolone acetate 1% (or equivalent) starting the day after surgery with the following taper:
  - 1 drop four times a day for the first 7 days;
  - 1 drop three times a day for the next 7 days;
  - 1 drop two times a day for the next 7 days;
  - 1 drop once a day for the last 7 days.

Magnetic Resonance (MR) Conditional Information

IMPORTANT: ENCELTO is MR conditional. You will receive an implant card, which should be shown to your imaging technician if you need Magnetic Resonance Imaging (MRI) at any time while the ENCELTO implant is in your eye. The card will include details about the ENCELTO implant, the date of insertion, and on the back, instructions for the imaging technician to access important MRI safety information.

Call your ophthalmologist for medical advice about side effects. You may report side effects to the Food and Drug Administration (FDA) at 1-800-FDA-1088.

What are the possible side effects of ENCELTO?

Please follow all post-operative instructions given by your ophthalmologist and ensure you attend all follow-up visits as recommended.

Potential side effects

Please be advised that ENCELTO and the surgical insertion has related risks such as, but not limited to, endophthalmitis (eye infection), retinal tear and detachment (retina tears and potentially separates from the eye wall resulting in vision loss), vitreous hemorrhage (bleeding within the central cavity of the eye), implant extrusion (the ENCELTO begins to work it's way out of the eye), suture related issues (such as suture related eye irritation or exposure of sutures), temporary or permanent loss of vision, accelerated cataract formation (clouding of the lens of the eye), and delayed dark adaptation (the ability of the eye to adjust from bright lighting conditions to dark lighting conditions).

If delayed dark adaptation occurs, it is unknown for how long these symptoms will be experienced. Take the following safety precautions.

- Driving: delayed dark adaptation may impair one's ability to see objects, pedestrians, or road signs when moving rapidly from a brightly lit environment to a dimly lit environment (for example, entering a tunnel during the daytime).
- Navigating in the Dark: Take caution when moving from bright to dark areas, such as entering a dark room or stepping outside at dusk. Consider using flashlights, nightlights, or motion-activated lighting at home.
- Consider wearing sunglasses or tinted lenses in bright environments to reduce the impact of transitioning from light to dark

It is common to experience the following symptoms following ENCELTO surgery:

- Sensation of something in the eye (i.e., foreign body sensation)
- Eye redness
- Eye irritation
- Eye dryness
- Eye discharge
- Mild to moderate eye pain or discomfort
- Floaters (small spots or shapes that appear in your vision)
- Headache

When to Seek Ophthalmologist Advice

You are to seek immediate care from an ophthalmologist if there are sudden changes in your vision, such as an increase in floaters, the appearance of "spider webs," flashing lights, sensitivity to light, loss of vision or visual field, progressively worsening eye pain, or increasing discharge/drainage from the eye as these symptoms could be a sign of a more serious issue.

General information about the safe and effective use of ENCELTO

Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet.

You can ask your ophthalmologist for a copy of the information about ENCELTO that is written for healthcare professionals.

You should inform your ophthalmologist that you have an ENCELTO implant inserted prior to any eye examination.

What are the ingredients in ENCELTO?

Active ingredients: ENCELTO is an encapsulated cell-based therapy that contains 200,000 to 440,000 allogeneic retinal pigment epithelial cells expressing rhCNTF (NTC-201-6A cell line), a neurotrophic factor.

Inactive ingredients: ENCELTO contains excipients (Human Endothelial Serum Free Medium (SFM) that may cause sensitivity in some patients.

Manufactured for: Treatment of idiopathic macular telangiectasia type 2 (MacTel)

Manufactured by:
Neurotech Pharmaceuticals, Inc.
Building 1, Suite 101
Cumberland, Rhode Island, 02864

This Patient Information has been approved by the U.S. Food and Drug Administration.

F11002F Rev. 01

Revised: 2025/03

Instructions for Use

(revakinagene taroretcel-lwey)
implant, for intravitreal use
ENCELTO™

Instructions for Use

℞ Only

ENCELTO procedures should be performed by an ophthalmologist experienced in vitreoretinal surgery and trained in ENCELTO procedures.

Neurotech Pharmaceuticals, Inc.
900 Highland Corporate Drive
Building 1
Cumberland, RI 02864
U.S. License No. 2321

This IFU has been approved by the U.S. Food and Drug Administration.
Approved: 2025/03

F11002A Rev: 03

ENCELTO Patient Card

Following the procedure, provide the patient with a completed ENCELTO Patient Card and advise the patient to keep the card in a safe place for future reference.

The patient should be advised that this card contains important information related to ENCELTO and that the card should be shown to their current and future eye care providers.

ENCELTO™ Patient Card

Patient name _____

Physician name _____

Clinic name _____

_____

Clinic phone number _____

Date of insertion _____

LOT number _____

neurotech

MR Conditional

This person is implanted with ENCELTO and can be safely scanned with magnetic resonance imaging (MRI) only under very specific conditions.

Scanning under different conditions may result in severe patient injury or implant malfunction.

Full MRI safety information is available in the 'Magnetic Resonance Imaging (MRI)' section of the ENCELTO Instructions for Use which can be obtained at:

www.ENCELTO.com/ecp/instructions-for-use

Or telephone: 1-833-963-9275

Neurotech Pharmaceuticals, Inc.
900 Highland Corporate Drive
Building 1
Cumberland, RI 02864

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Contents

Introduction

These instructions include the procedures for using ENCELTO™. For more information on dosage, administration, warnings, and precautions, refer to the ENCELTO Prescribing Information.

Intended Use/Indications for Use

ENCELTO is indicated for the treatment of adults with idiopathic macular telangiectasia type 2 (MacTel).

Recommended Dose

For intravitreal implantation only.

- ENCELTO is administered by a single surgical intravitreal procedure performed by a qualified ophthalmologist.
- The recommended dose of ENCELTO is one implant per affected eye. Each ENCELTO implant contains 200,000 to 440,000 allogeneic retinal pigment epithelial cells expressing rhCNTF (NTC-201-6A cell line), a neurotrophic factor.

ENCELTO Description

ENCELTO (revakinagene taroretcel-lwey) is single-dose, sterile, nonpyrogenic and retrievable.

ENCELTO is an allogeneic encapsulated cell-based gene therapy product that contains 200,000 to 440,000 allogeneic retinal pigment epithelial cells expressing rhCNTF (NTC-201-6A cell line) for surgical intravitreal placement.

ENCELTO consists of an opaque, semi-permeable white to off-white capsule surrounding a scaffold of polyethylene terephthalate (PET) yarn, loaded with rhCNTF secreting allogeneic retinal pigment epithelial cells (NTC-201-6A cell line). Each end of the semi-permeable capsule is sealed with medical grade methacrylate adhesive, and to one end a titanium fixation loop is attached. ENCELTO width is 1.2 ± 0.1 mm, its length is 6.1 ± 0.4 mm, and its internal diameter is 0.88 ± 0.02 mm.

ENCELTO is packaged in a protective inner container within an orange to pink liquid hold medium referred to as Endothelial Serum Free Media (Endo-SFM), which is maintained sterile by a sealed outer container. ENCELTO is provided attached to a gripper that both suspends ENCELTO in the Endo-SFM and facilitates intraocular

insertion. The Endo-SFM within the packaging inner container may contain visible particles generally described as fiber, solid, white, or metallic in appearance.

Components

Components in the Corepack

On the day of surgery, before bringing the patient to the operating room, in a proper clean environment, remove the ENCELTO container from the corepack.

Perform the inspection as instructed within the Inspection Checklist and IFU. Verify that all conditions meet the inspection criteria before ENCELTO is cleared for surgical use. Do not open the outer container until the surgeon is ready to accept ENCELTO onto the surgical field.

A corepack contains one ENCELTO sealed within a sterile inner container.

The inner container is sealed within an outer container to facilitate sterile transfer to the surgical technician or surgeon for preparation.

The outer container is held in support foam within the corepack and provided alongside the Instructions for Use, ENCELTO Medium pH Color Guide, Inspection Checklist, a disposable temperature recording device, and the United States Prescribing Information (USPI).

Components in the Corepack

1. Corepack
2. Outer container holding the sterile inner container
3. Disposable temperature recording device
4. ENCELTO Medium pH Color Guide
5. ENCELTO Instructions for Use
6. ENCELTO Inspection Checklist
7. United States Prescribing Information

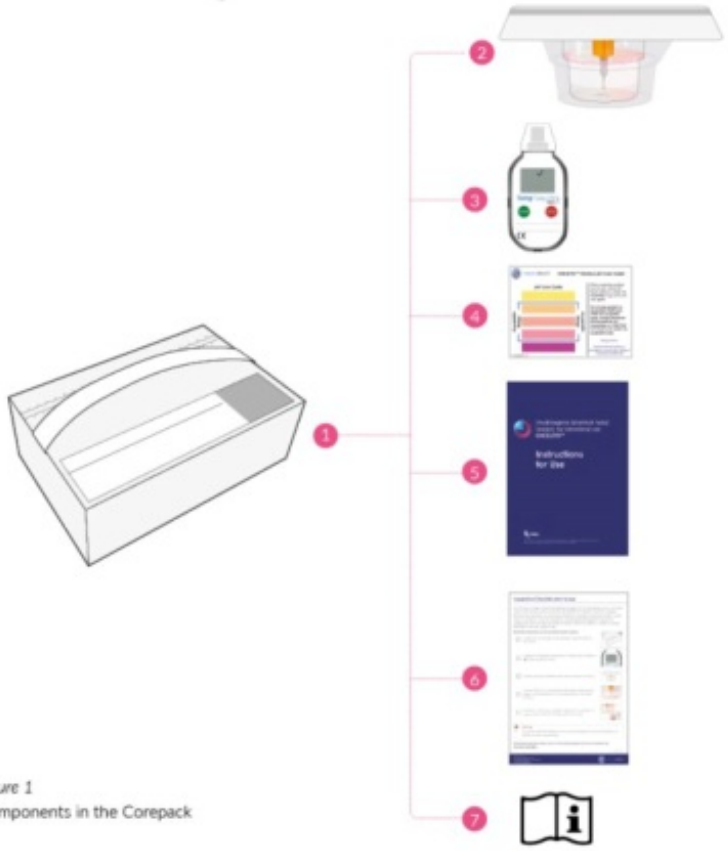

Figure 1
Components in the Corepack

Table 1 Description of Corepack components

Components	Description
Inner container	This is provided sterile. It is a cylindrical plastic container with a lower compartment filled with liquid medium. It has an upper compartment connected to it via a narrow channel that is secured shut with a luer lock cap.
Outer container	This is a plastic container with a Tyvek lid. It maintains the sterility of the inner container until ready to use.
Disposable temperature recording device	A disposable device that measures and records the temperature in the corepack. If ENCELTO has been stored within the acceptable range, a ✓ will be shown at the top of the screen. If an ✗ is displayed, ENCELTO has been exposed to temperatures outside of the acceptable range and must not be used.
ENCELTO Medium pH Color Guide	A card that provides a color scale to indicate the acceptable pH range for the liquid medium.
ENCELTO Instructions for Use	A booklet that contains the full instructions and includes the ENCELTO patient card.
ENCELTO Inspection Checklist	An information sheet that contains instructions for inspection prior to use.
USPI	United States Prescribing Information.

ENCELTO Overview

ENCELTO is packaged in a protective inner container within an Endothelial Serum Free Media (Endo-SFM), which is maintained sterile by a sealed outer container. ENCELTO is provided attached to a gripper that both suspends ENCELTO in the Endo-SFM and facilitates intraocular insertion. ENCELTO contains no preservatives.

Figure 2
ENCELTO in detail
Not to scale

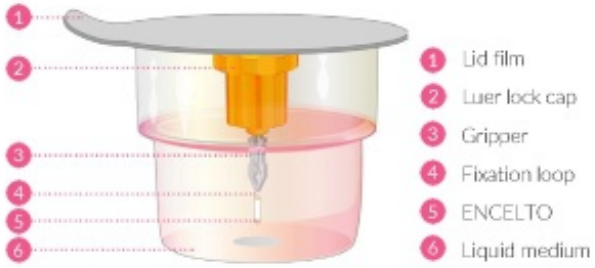

Figure 3
ENCELTO within sterile inner container

Table 2 ENCELTO component description

Components	Description
Lid film	The lid film provides a seal to maintain the sterile environment within the inner container. It should be peeled back to reveal the luer lock cap when the surgeon is ready to implant ENCELTO.
Luer lock cap	A luer lock fitting is attached to the gripper and is used to suspend ENCELTO in liquid medium within the inner packaging. It is also used to handle and manipulate ENCELTO during preparation and insertion.
Gripper	The gripper holds ENCELTO by the fixation loop. Squeezing the gripper releases ENCELTO.
Fixation loop	A titanium loop that is attached to one end of ENCELTO. It is used to suture ENCELTO to the sclera.
ENCELTO	ENCELTO is a sealed semi-permeable capsule that has a width of 1.2 ± 0.1 mm, length of 6.1 ± 0.4 mm, and internal diameter of 0.88 ± 0.02 mm.
Liquid medium	The liquid medium provides a nutrient rich environment to sustain ENCELTO during storage and transport.

Storage and Handling

Using the handle, remove the corepack from the larger shipping box.

Store ENCELTO in the corepack at 16° to 37°C (61° to 99°F) until ready for use.

Inspect the disposable temperature recording device. If a check mark is displayed, ENCELTO has remained within the acceptable temperature range and may be used. If a "X" is displayed, the ENCELTO was exposed to temperatures outside the acceptable range and must not be used. Contact Neurotech immediately at (833)-963-9275.

Protect ENCELTO from light.

Handle inner container (Figure 3) using sterile technique.

Prior to disposal of an ENCELTO implant per local institutional protocols, call 1-833-963-9275 for assessment of ENCELTO return or replacement.

Caution

- Do not use beyond the "use by" date identified on the corepack label.
- Do not freeze, refrigerate, or expose to temperatures >38°C (101°F).

ENCELTO Medium pH Color Guide

When inspecting the inner container prior to use, ensure the liquid medium is within the acceptable pH range on the ENCELTO Medium pH Color Guide.

Orange to pink liquid hold medium referred to as Endothelial Serum Free Media (Endo-SFM) within packaging inner container may contain visible particles. Particle general description fiber, solid, white, or metallic in appearance.

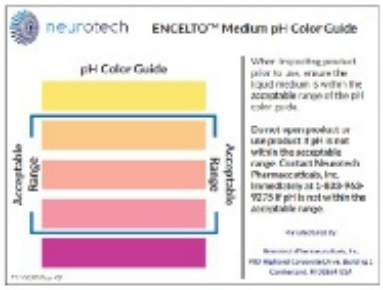

Figure 4
ENCELTO Medium pH Color Guide

Caution

- Do not use ENCELTO if the pH is not within the acceptable range. Contact Neurotech immediately at 1-833-963-9275.

Warnings

Read and follow all instructions, warnings, and cautions prior to use.

The ENCELTO Prescribing Information contains a complete list of indications, contraindications, warnings, precautions, and adverse events.

ENCELTO Insertion Procedure

1 Preparatory Procedures

- Do not use ENCELTO if there are any signs of leakage or damage to the corepack, as sterility may have been compromised. Contact Neurotech immediately at 1-833-963-9275.
- Do not use ENCELTO if there are signs of damage to the outer container and lid films. Contact Neurotech immediately at 1-833-963-9275.
- Do not use ENCELTO if there is medium in the upper portion of the inner container, as sterility may have been compromised. Contact Neurotech immediately at 1-833-963-9275.
- Do not use ENCELTO if the pH of the medium is not within the acceptable range. Contact Neurotech immediately at 1-833-963-9275.
- Do not use ENCELTO if there are any concerns following the visual inspection or if sterility has been compromised. Contact Neurotech immediately at 1-833-963-9275.

2 Surgical Site Preparation

- Do not use the superior quadrants. When ENCELTO is inserted in a superior quadrant, it may enter the patient's visual axis.
- Do not insert ENCELTO outside of the pars plana.
- Ensure the sclerotomy incision is 3.0 mm in length, parallel to the limbus, and full-thickness throughout with square corners.

3 ENCELTO Preparation

- Do not use ENCELTO if it is damaged or if sterility has been compromised. Contact Neurotech immediately at 1-833-963-9275.

4 Insertion and Closure

- Using an alternative knot to the anchor knot and not placing it at the apex of the fixation loop increases the risk of migration and extrusion of ENCELTO.
- Ensure the second and third throws of the polypropylene anchor suture are tight locking throws at the very apex of the fixation loop.
- When suturing ENCELTO to the sclera, avoid shallow placement of the polypropylene suture as this increases the risk of migration and extrusion of ENCELTO.
- Passing the polypropylene suture too wide from the incision increases the risk of hitting other ocular structures.
- Placing the polypropylene suture off-center makes wound closure more difficult and increases the risk of wound leak, ENCELTO migration, and/or endophthalmitis.
- Ensure the fixation loop is at 90-99% depth for correct wound closure to minimize the risk of migration and extrusion of ENCELTO.
- Do not tie or pull the polypropylene suture too tight when securing with the 3-1-1 knot as this could lead to migration and extrusion of the ENCELTO. This is an anchor suture and is not used for closure.
- Do not cut off the needles from the polypropylene suture as they will be needed to bury the ends of the suture. Not burying the suture ends will increase the risk of postoperative complications.
- Do not pass the polypropylene suture more anterior or posterior to the incision to avoid other structures of the eye.
- Failure to perform indirect ophthalmoscopy can lead to unidentified malpositioning of ENCELTO and intraocular complications.

5 End of Surgery

- None specified

Warnings (cont'd)

6 Postoperative Wound Care

- Failure to follow postoperative antibiotic and steroid application can lead to increased risk of injury, inflammation, or infection.

ENCELTO Removal Procedure

1 Surgical Site Preparation

- None specified

2 ENCELTO Removal and Closure

- Do not cut the center polypropylene anchor suture when removing the nylon sutures.
- Do not cut the posterior side of the polypropylene anchor suture before grasping the fixation loop.
- Failure to grasp the fixation loop may release ENCELTO into the vitreous and may require a complete vitrectomy to recover.

3 Post-operative Wound Care

- Failure to follow postoperative antibiotic and steroid application can lead to increased risk of injury, inflammation, or infection.

Precautions

- There is no data on the use of ENCELTO in pregnant women.
- There is no data on the presence of ENCELTO in human milk, the effects of ENCELTO on breastfed infant, and effects of ENCELTO on milk production.
- The safety and effectiveness of ENCELTO has not been established in pediatric patients

Contraindications

ENCELTO is contraindicated in patients with:

- Active or suspected ocular or periocular infections.
- Known hypersensitivity to Endothelial Serum Free Media (Endo-SFM)

Use with Standard Procedures

ENCELTO is compatible for use with the following standard procedures:

- A-scan ophthalmic ultrasound slit lamp examination
- Indirect ophthalmoscopy
- Tonometry
- Optical coherence tomography (OCT)
- Visual field (perimetry)
- Standard lasers for ophthalmic treatments
- Radiography (x-ray)
- Computed tomography (CT) scan
- Fluorescein/indocyanine angiography
- Fundus autofluorescence

Use caution when performing ophthalmic procedures that may cause deflection of ENCELTO and subsequent injury. For example, B-scan ophthalmic ultrasound, scleral depression, gonioscopy or intraocular surgery.

Magnetic Resonance Imaging (MRI)

A patient with ENCELTO may be safely scanned under the following conditions. Failure to follow the conditions outlined in Table 3 might result in injury to the patient.

Table 3 MRI Safety Information

Parameter	Condition of Use/Information
Static Magnetic Field Strength (B_0)	1.5T or 3.0T
Static Magnetic Field (B_0) Orientation	Horizontal, Cylindrical Bore
Maximum Spatial Field Gradient	40 T/m (4000 gauss/cm)
RF Polarization	Circularly Polarized (CP) (ie, quadrature drive)
RF Transmit Coil Type	Any Transmit RF coil may be used
RF Receive Coil Type	Any Receive RF coil may be used
RF Operating Mode	Normal Operating Mode
Scan Duration	Scan for 60 minutes of continuous RF exposure with one or more MR imaging pulse sequences (scans or series) followed by a wait time of 5 minutes before resuming scanning.
MR Image Artifact	The image artifact can extend approximately 1 mm from the ENCELTO. Imaging protocol modifications may be necessary to compensate for the MR image artifact.

(revakinagene taroretcel-lwey)
implant, for intravitreal use
ENCELTO™

Insertion Procedure

Preoperative Procedure

Prepare additional items for surgery

Standard ophthalmic instruments will be required for this procedure.

The following surgical instruments are referenced and suggested for use but are not provided.

Table 4 Surgical instruments description

Item description	Further detail
20-gauge microvitreoretinal blade	-
15-degree asymmetric blade	-
Sutures - all on spatulated needles	• 7-0 Vicryl corneal traction suture to rotate eye • 9-0 polypropylene double-armed anchor suture • 9-0 nylon wound closure suture • 6-0 plain gut or chromic suture preferred, but can use 7-Vicryl conjunctival suture
Cautery	18-gauge eraser tip and 25-gauge fine tip

Topical antibiotics and topical steroids are suggested for use but are not provided.

Prepare patient for surgery

Prepare patient for surgery using standard sterile surgical methods and standard operating room practices.

Conduct standard periocular preparation and draping. Place a lid speculum and optional corneal shield. See Figure 5.

Perform the procedure under local anesthesia using either peribulbar, retrobulbar, or subtenon's technique.

Figure 5 Prepare patient for insertion procedure

1 Preparatory Procedures

On the day of surgery, before bringing the patient to the operating room, in a proper clean environment, carefully remove the ENCELTO container from the corepack.

Perform the inspection as instructed within the Inspection Checklist and IFU. Verify that all conditions meet the inspection criteria before ENCELTO is cleared for surgical use. Do not open the outer container until the surgeon is ready to accept ENCELTO onto the surgical field.

1.1 Inspect ENCELTO prior to use

i. Inspect the corepack for damage and signs of leakage.

Warning

- Do not use ENCELTO if there are any signs of leakage or damage to the corepack, as sterility may have been compromised.

  Contact Neurotech immediately at 1-833-963-9275.

ii. Confirm the use-by date on the corepack label has not passed. See Figure 6.

Caution

- Do not use ENCELTO beyond the use-by date. See corepack label for use-by date.

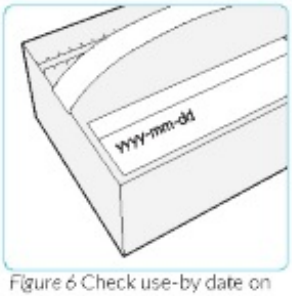

Figure 6 Check use-by date on corepack

iii. Open the corepack and confirm the disposable temperature recording device displays a ✓ at the top of the screen. See Figure 7.

Caution

If the temperature recording device displays an ✗ at the top of the screen, this indicates a temperature exposure outside of the acceptable range occurred. Contact Neurotech immediately at 1-833-963-9275 to report the issue. The appropriate action will be taken to initiate return of ENCELTO and possible replacement. Maintain the original packing material.

Figure 7 Check disposable temperature recording device

1.1 Inspect ENCELTO prior to use (cont'd)

iv. Remove the outer container from the corepack and perform an inspection of ENCELTO by confirming:

- All seals and lid films are intact.
- The liquid medium is in the lower portion of the inner container.
- ENCELTO is suspended in the liquid medium by the gripper. See Figure 8.

Figure 8 Check ENCELTO is suspended in liquid medium

ⓘ Note

ENCELTO can be visually inspected in the outer container. Do not open the outer container until ready to use.

Warning

- Do not use ENCELTO if there are signs of damage to the outer container and lid films.
- Do not use ENCELTO if there is medium in the upper portion of the inner container, as sterility may have been compromised.

Contact Neurotech immediately at 1-833-963-9275.

v. Using the ENCELTO Medium pH Color Guide, inspect the color of the liquid medium and confirm it is within the acceptable pH range. See Figure 9.

Figure 9 Inspect integrity of medium

Warning

- Do not use ENCELTO if the pH of the medium is not within the acceptable range.

Contact Neurotech immediately at 1-833-963-9275.

1.2 Transfer the inner container to the sterile field

Warning

- Do not use ENCELTO if there are any concerns following the visual inspection or if sterility has been compromised.

  Contact Neurotech immediately at 1-833-963-9275.

i. Peel back the lid film of the non-sterile outer container and hold it open for the sterile surgical technician or nurse. See Figure 10.

Figure 10 Open outer container

Maintain the sterility of the inner container while handling.

ii. Using sterile technique, remove the inner container and place it in an upright position into the sterile field. See Figure 11.

Discard the outer container after the inner container is removed.

Figure 11 Transfer inner container into sterile field

iii. Perform a second inspection of ENCELTO by confirming:

- All seals and lid films are intact.
- ENCELTO is suspended in the liquid medium by the gripper.
- The medium is in the lower portion of the inner container.
- The color is within the acceptable pH range using the ENCELTO Medium pH Color Guide. See Figure 12.

Figure 12 Perform inspection of ENCELTO

2 Surgical Site Preparation

2.1 Conduct conjunctival peritomy

i. Identify the inferior quadrant for planned ENCELTO insertion.

> **Warning**
> - Do not use the superior quadrants. When ENCELTO is inserted in a superior quadrant, it may enter the patient's visual axis.

ii. Expose the planned insertion site by creating a 7.0 mm conjunctival limbal peritomy and a 7.0mm conjunctival radial incision, or similar. See Figure 13.

> ⓘ Note
> Avoid creating buttonholes in the conjunctiva during this procedure.

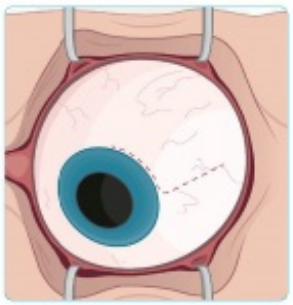

Figure 13 Create insertion site

iii. Carefully dissect the conjunctiva and Tenon's capsule from the bare sclera. See Figure 14.

iv. Maintain hemostasis using wet-field cautery.

> ⓘ Note
> Avoid blood entering the scleral wound.

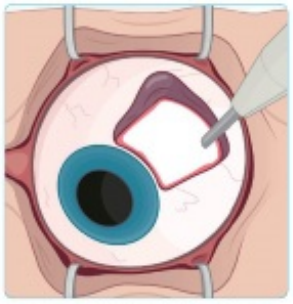

Figure 14 Dissect from sclera

v. Under microscopic visualization, place a corneal-limbal traction suture using a 7-0 Vicryl suture on a spatulated needle or similar, in the identified inferotemporal or inferonasal quadrant. See Figure 15.

ⓘ Note

Take care to avoid penetrating the anterior chamber, as this could lead to procedural complications and visual impairment.

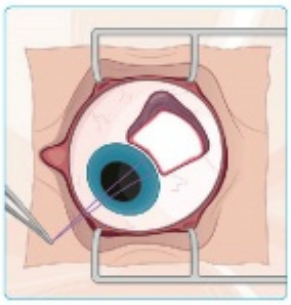

Figure 15 Place corneal-limbal traction suture in inferior quadrant

2.2 Perform a 3.0 mm sclerotomy

Warning

- Do not insert ENCELTO outside of the pars plana.

i. While keeping the sclera dry, measure and mark 3.75 mm from the limbus using an inked adjustable caliper at the selected location.

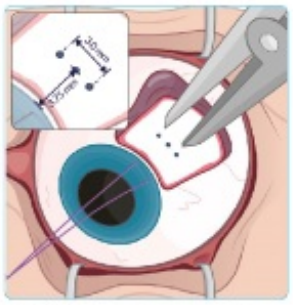

Figure 16 Measure and mark 3.0 mm incision

ii. Mark a 3.0 mm length for the scleral incision, parallel to and 3.75 mm posterior to the limbus using an inked adjustable caliper. See Figure 16.

iii. Use a 20 gauge microvitreoretinal blade or similar to enter the sclera 3.75 mm posterior to the limbus, creating a full-thickness incision of the sclera and choroid. See Figure 17.

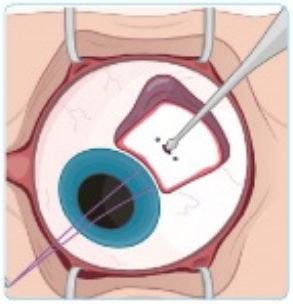

Figure 17 Enter sclera 3.75 mm posterior to limbus

iv. Enlarge the full-thickness incision of the sclera and choroid to 3.0 mm using a 15 degree asymmetric blade, or similar. See Figure 18.

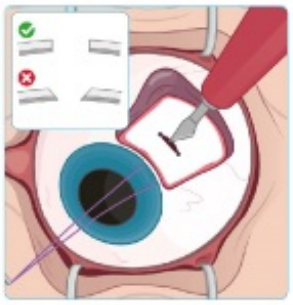

Figure 18 Enlarge the full-thickness incision to 3.0mm

Warning

- Ensure the sclerotomy incision is 3.0mm in length, parallel to the limbus, and full-thickness throughout with square corners.

v. Gently open the sclerotomy incision.

Confirm the incision is full-thickness and that hemostasis has been achieved. If there is any spanning uveal tissue, incise the wound again. If there is any active bleeding, apply further wet-field cautery. See Figure 19.

ⓘ Note

Take care to ensure the incision is full thickness to avoid potential complications such as vitreous hemorrhage, cyclodialysis or retinal detachment.

Figure 19 Confirm no spanning uveal tissue

vi. Excise any significant prolapsed vitreous with minimal traction 'Weck-Cel vitrectomy' or a standard vitrectomy cutter prior to insertion. See Figure 20.

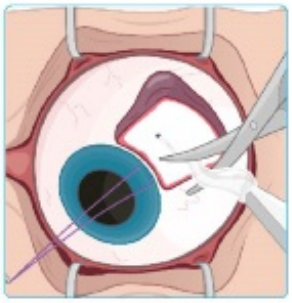

Figure 20 Excise prolapsed vitreous

3 ENCELTO Preparation

3.1 Prepare ENCELTO for insertion

Warning

- Do not use ENCELTO if it is damaged or if sterility has been compromised.

  Contact Neurotech immediately at 1-833-963-9275.

i. Peel back the lid film of the inner container exposing the upper compartment of the container and the luer lock cap. See Figure 21.

ⓘ Note

Keep the inner container in the sterile field as ENCELTO can be returned to the liquid medium if necessary.

Figure 21 Open inner container

ii. Unlock the luer lock cap with one complete counter-clockwise turn.

Lift the luer lock cap vertically to remove ENCELTO, which should be attached to the gripper. See Figure 22.

ⓘ Notes

Avoid dislodging ENCELTO from the gripper when withdrawing it from the inner container.

Ensure ENCELTO does not come into contact with anything.

Figure 22 Unlock and remove ENCELTO from inner container

iii. Rinse ENCELTO with at least 5 mL of sterile Balanced Salt Solution (BSS) prior to insertion, until no excess liquid medium is left on the surface.

BSS rinse should be applied every 10 minutes to keep ENCELTO moist and prevent dehydration. See Figure 23.

ⓘ Note

Avoid touching ENCELTO while rinsing.

Figure 23 Rinse with at least 5 mL of BSS

⚠ Caution

- Rinse all liquid medium from the surface of ENCELTO prior to insertion, to reduce the patient's exposure to excipients.
- Avoid resting ENCELTO on an absorbent surface.
- Avoid exposing ENCELTO to air for more than 10 minutes, as this could reduce the efficacy of the therapy.
- Only use BSS or other salt solutions to rinse ENCELTO.

3.1 Prepare ENCELTO for insertion (cont'd)

iv. While holding the luer lock cap, visualize the fixation loop at the end of ENCELTO under the microscope.

Pass a double-armed 9-0 polypropylene suture needle through the fixation loop and pull one fourth of the suture length through. See Figure 24.

Figure 24 Pass 9-0 polypropylene suture through fixation loop

ⓘ Notes

There is a 0.5 mm distance between the fixation loop and end of ENCELTO.

Pulling one fourth of suture length makes it easier to create a 3-1-1 knot than if pulled halfway.

⚠ Caution

- Using alternative sutures may cause post-operative complications.

4 ENCELTO Insertion and Closure

4.1 ENCELTO insertion

Warning

- Do not use ENCELTO if it is damaged or if sterility has been compromised.

  Contact Neurotech immediately at 1-833-963-9275.

i. Gently open the sclerotomy incision using toothed forceps.

ⓘ Note

Confirm complete hemostasis and that there is no blood over or around the sclerotomy site.

ii. Holding the luer lock cap, insert ENCELTO perpendicularly to the globe through the scleral incision until only the fixation loop is exposed. See Figure 25 and 26.

ⓘ Note

While inserting ENCELTO, aim towards the optic nerve and away from the lens and out of the visual axis.

Caution

- Avoid inserting ENCELTO towards the lens or deeply into the eye. Do not insert ENCELTO beyond the fixation loop.

Figure 25 Perpendicular entry of ENCELTO

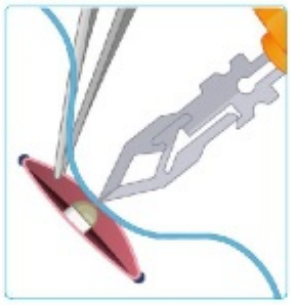

Figure 26 Insert ENCELTO

4.1 ENCELTO insertion (cont'd)

iii. Using forceps or needle holders, squeeze the gripper in the indicated region to release ENCELTO. See Figure 27.

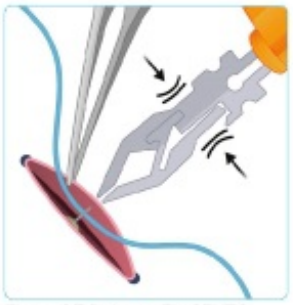

Figure 27 Release ENCELTO

ⓘ Notes

The traction suture might need to be released to allow visualization of the gripper release site.

Squeezing below the indicated region or using other methods to release ENCELTO may crush the gripper, making it difficult or impossible to release. If the release fails or is damaged in any way, ENCELTO cannot be used, and procedure must be rescheduled. Contact Neurotech immediately at 1-833-963-9275 to report the issues. The appropriate action will be taken to initiate return of ENCELTO and possible replacement.

iv. Create an anchor knot by tying the polypropylene suture in a 3-1-1 knot using large tying loops. See Figure 28.

ⓘ Note

The polypropylene suture has memory and requires careful handling. It is best to keep large tying loops and grasp the needle rather than the suture for the pull through.

⚠ Warning

- Using an alternative knot to the anchor knot and not placing it at the apex of the fixation loop increases the risk of migration and extrusion of ENCELTO.

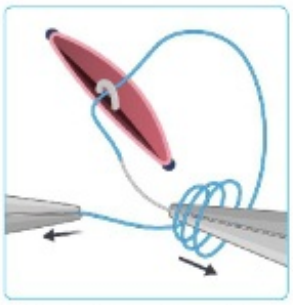

Figure 28 Create anchor knot by tying a 3-1-1 knot

v. Place the anchor knot at the apex of the fixation loop. See Figure 29.

⚠ Warning

- Ensure the second and third throws of the polypropylene anchor suture are tight locking throws at the very apex of the fixation loop.

Figure 29 Place anchor knot at apex of fixation loop

4.2 Anchoring ENCELTO to the sclera

i. Gently grasp the edge of the sclerotomy with toothed forceps to open the wound.

With ENCELTO centered in the incision, pass each arm of the polypropylene suture centrally through either side of the wound at a scleral depth of 90 - 99%. See Figure 30.

Figure 30 Pass polypropylene suture at 90-99% depth

ⓘ Note

Adjust the fixation loop as needed if it is in the way of the passing sutures.

⚠ Warning

- When suturing ENCELTO to the sclera, avoid shallow placement of the polypropylene suture as this increases the risk of migration and extrusion of ENCELTO.
- Passing the polypropylene suture too wide from the incision increases the risk of hitting other ocular structures.
- Placing the polypropylene suture off-center makes wound closure more difficult and increases the risk of wound leak, ENCELTO migration, and/or endophthalmitis.

ii. Pull up the suture ends and confirm that the anchor knot is at the apex of the fixation loop and is visible at 90 - 99% depth. See Figure 31.

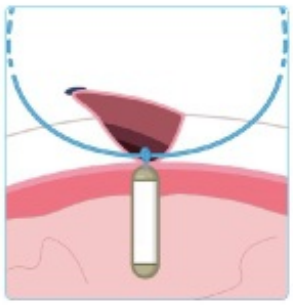

Figure 31 Confirm anchor knot is visible at 90-99% depth

⚠ Warning

- Ensure the fixation loop is at 90-99% depth for correct wound closure to minimize the risk of migration and extrusion of ENCELTO.

iii. Tie the polypropylene suture down to the sclera with a 3-1-1 knot. Placing the knot away from the incision will allow for wound healing without the knot in the wound. See Figure 32.

Leave needles attached to the polypropylene suture as they will be used for the final closure.

If a suture breaks, keep the tail as long as possible and lay it flat. Ensure a watertight closure of the sclera.

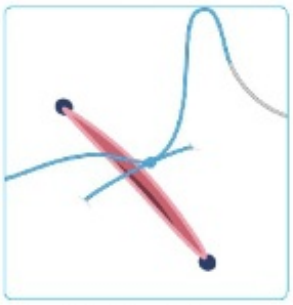

Figure 32 Tie with a 3-1-1 knot

ⓘ Note

The polypropylene suture has memory and requires careful handling. It is best to keep large tying loops and grasp the needle rather than the suture for the pull through.

⚠ Caution

- Tying the polypropylene suture with an alternative knot to a 3-1-1 knot may make wound closure more difficult.

⚠ Warning

- Do not tie or pull the polypropylene suture too tight when securing with the 3-1-1 knot as this could lead to migration and extrusion of ENCELTO. This is an anchor suture and is not used for closure.
- Do not cut off the needles from the polypropylene suture as they will be needed to bury the ends of the suture. Not burying the suture ends will increase the risk of postoperative complications.

4.2 Anchoring ENCELTO to the sclera (cont'd)

iv. With the polypropylene suture, take at least a 2.0 mm long bite of the sclera at 50-75% depth beyond the end of the sclerotomy on each side. See Figure 33.

Warning

- Do not pass the polypropylene suture more anterior or posterior to the incision to avoid other structures of the eye.
- Not burying the suture ends will increase the risk of post-operative complications.

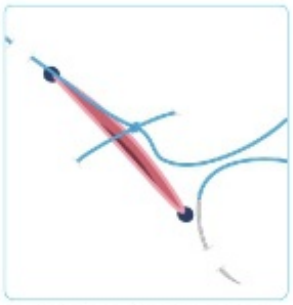

Figure 33 Create 2.0 mm bites of sclera beyond sclerotomy

4.3 Wound closure

i. Using standard surgical techniques for scleral wound closure, close the scleral incision with 9-0 nylon sutures. Recommended best practices follow in section 4.3. The nylon sutures will be used to capture the polypropylene suture to mitigate suture tip irritation and conjunctival erosion.

a. Using 9-0 nylon sutures, divide the sclerotomy into thirds. Pass each needle at a depth of 75 - 80%. See Figure 34.

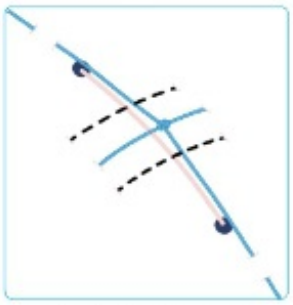

Figure 34 Location of nylon sutures

ⓘ Note

The nylon sutures will be closer to the center polypropylene suture than to the ends of the sclerotomy.

b. Using a 3-1-1 closure, ensure the locking throws are square and tight so the nylon suture knots can be rotated into the sclera. See Figure 35.

Figure 35 Ensure locking throws are square and tight

ⓘ Note

The nylon sutures must completely close the wound, leaving no wound gape anywhere, to create a watertight closure. If there is any gaping, the sutures should be replaced and closed tighter or another suture placed to close the wound.

c. Rotate the knots and suture tails of the 9-0 nylon sutures into the sclera. See Figure 36.

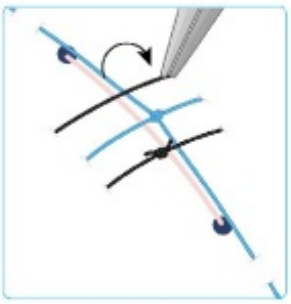

Figure 36 Rotate nylon sutures

ⓘ Note

If you are unable to rotate the nylon knot into the sclera, replace that suture with a new nylon suture and close it with a smaller 1-1-1 "Dangel" style adjustable locking knot.

4.3 Wound closure (cont'd)

ii. Pull the polypropylene suture end taut and cut the polypropylene suture flush to the sclera. See Figure 37.

⚠ Caution

- Not pulling the suture taut and not cutting the suture flush to the sclera will increase the risk of post-operative suture exposure and irritation.

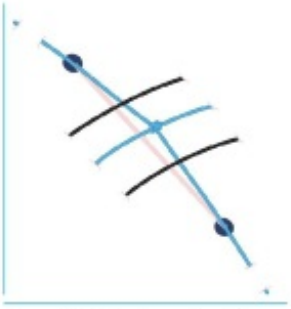

Figure 37 Cut suture flush to sclera

iii. Perform a conjunctival and Tenon's capsule closure using a 6-0 plain gut or chromic suture or a 7-0 Vicryl suture or similar suture. Ensure the Tenon's capsule covers the insertion site. Use a 3-point fixation and scleral bites as indicated in Figure 38.

ⓘ Notes

Make sure conjunctiva and Tenon's capsule are sutured to the limbus and sclera to prevent conjunctival retraction and subsequent exposure of the scleral sutures.

Buried sutures are preferable when possible.

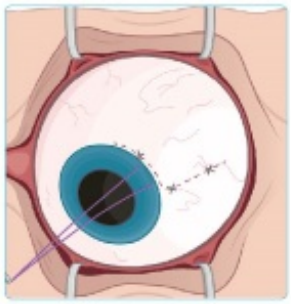

Figure 38 Perform conjunctival and Tenon's capsule closure

iv. Administer sub-conjunctival steroid injection: dexamethasone, 2 mg/0.5 ml (4 mg/ml) or equivalent.

ⓘ Note

If the case is complicated and inflammation is anticipated, a higher dose of dexamethasone (0.5 cc of 10 mg/ml) or equivalent may be used, at the surgeon's discretion.

v. Perform indirect ophthalmoscopy to confirm placement of ENCELTO in the vitreous and that there are no intraocular complications.

⚠ Warning

- Failure to perform indirect ophthalmoscopy can lead to unidentified malpositioning of ENCELTO and intraocular complications.

v. Apply topical antibiotic to the surface of the eye.

⚠ Caution

- Do not inject antibiotics into the eye.

vi. Patching the eye is optional but encouraged to prevent conjunctival wound dehiscence.

5 End of Surgery

5.1 Complete ENCELTO Patient Card

i. Provide the patient with a completed ENCELTO Patient Card (see page 3) and advise the patient to keep the card in a safe place for future reference. The patient should be advised that this card contains important information related to ENCELTO and that the card should be shown to their current and future health care providers.

5.2 Dispose of all materials

ii. Follow local institutional protocols to dispose of all ENCELTO materials and packaging after the procedure.

6 Postoperative Wound Care

6.1 Antibiotic and steroid application

Warning

- Failure to follow postoperative antibiotic and steroid application can lead to increased risk of injury, inflammation, or infection.

The patient is to use:

- A topical antibiotic solution at a frequency of 1 drop four times a day for 7 days.
- A steroid drop taper of prednisolone acetate 1% (or equivalent) starting the day after surgery with the following taper:
  - 1 drop four times a day for the first 7 days
  - 1 drop three times a day for the next 7 days
  - 1 drop two times a day for the next 7 days
  - 1 drop once a day for the last 7 days.

6.2 Complications

See Adverse Reactions Section of USPI.

(revakinagene taroretcel-lwey)
implant, for intravitreal use
ENCELTO™

Removal Procedure

Preoperative Procedure

Prepare additional items for surgery

Standard ophthalmic instruments will be required for this procedure. The following surgical instruments are referenced and suggested for use but are not provided.

Table 5 Surgical instruments description

Item description	Further details
20-gauge microvitreoretinal blade	-
15-degree asymmetric blade	-
Sutures - all on spatulated needles	• 7-0 Vicryl corneal traction suture to rotate eye and to close the scleral wound • 6-0 plain gut suture for conjunctival closure

Topical antibiotics and topical steroids are suggested for use but are not provided.

Prepare patient for surgery

Prepare patient for surgery using standard sterile surgical methods and standard operating room practices.

Conduct standard periocular preparation and draping. Place a lid speculum and corneal shield (if available). See Figure 39.

Perform the procedure under local anesthesia using either peribulbar, retrobulbar, or sub-tenon's technique.

Figure 39 Prepare patient for removal procedure

1 Surgical Site Preparation

1.1 Conduct conjunctival peritomy in the appropriate quadrant

i. Place a partial thickness corneal-limbal traction suture using a 7-0 Vicryl suture on a spatulated needle or similar in the quadrant where ENCELTO is located. See Figure 40.

ⓘ Note

Take care to avoid penetrating the anterior chamber, as this could lead to procedural complications and visual impairment.

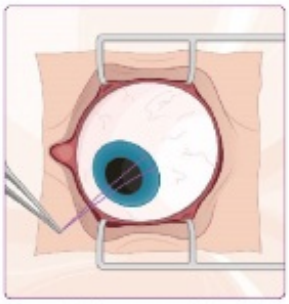

Figure 40 Place corneal-limbal traction suture

ii. Expose ENCELTO insertion site by creating a 7.0 mm conjunctival limbal peritomy and a 7.0 mm conjunctival radial incision. See Figure 41.

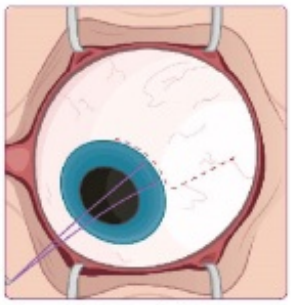

Figure 41 Create limbal peritomy and radial incision

iii. Carefully dissect the conjunctiva and Tenon's capsule to expose the underlying sclera and insertion site. See Figure 42.

iv. Use wet-field cautery to achieve hemostasis.

ⓘ Note

Avoid blood entering the scleral wound.

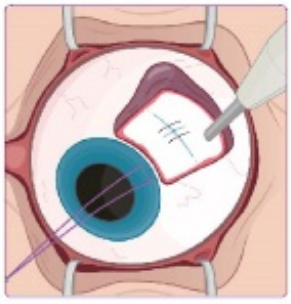

Figure 42 Expose insertion site

1.2 Conduct 3-port small gauge vitrectomy

i. Place an infusion cannula and infusion line in the inferior quadrant which is not occupied by ENCELTO. See Figure 43.

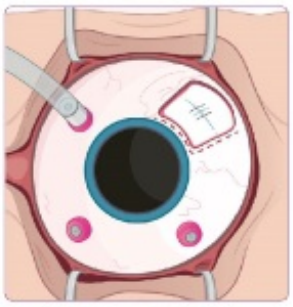

Figure 43 Place infusion cannula

ii. Visually confirm that the infusion line rests within the vitreous cavity prior to opening the infusion. See Figure 44.

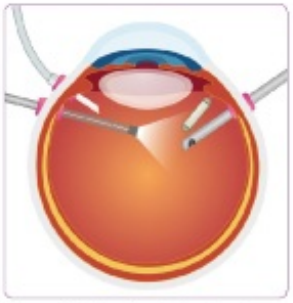

Figure 44 Confirm infusion line position

iii. Insert the other two superior cannulas as per normal routine.

iv. Perform vitrectomy to remove the vitreous surrounding ENCELTO without disrupting the integrity of the white portion of ENCELTO. See Figure 45.

ⓘ Note

Direct the cutter away from ENCELTO. The smooth part of the vitrectomy probe can gently touch the white portion of ENCELTO.

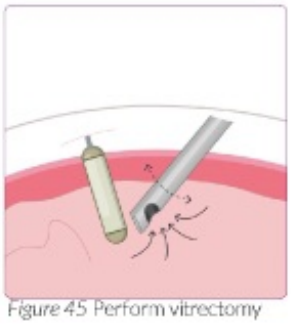

Figure 45 Perform vitrectomy

2 ENCELTO Removal and Closure

2.1 Locate and open incision

ⓘ Notes

This should be located 3.75 mm posterior to limbus.

Apply bipolar wet-field cautery as needed. Avoid applying cautery to the polypropylene anchor suture or wound lips.

i. Remove the two nylon sutures on either side of the center polypropylene anchor suture, but leave the center anchor suture in place. See Figure 46.

⚠ Warning

- Do not cut the center polypropylene anchor suture when removing the nylon sutures.

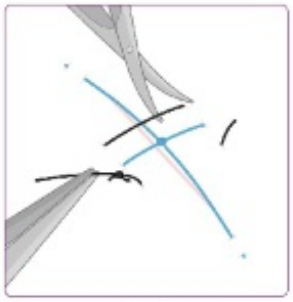

Figure 46 Remove nylon sutures

ii. Using a 20-gauge microvitreoretinal blade or similar, carefully dissect the original scleral incision on either side of polypropylene suture down to the ENCELTO cap at the base of the fixation loop. See Figure 47.

ⓘ Note

Direct blade motion away from ENCELTO to reduce risk of inadvertently cutting ENCELTO.

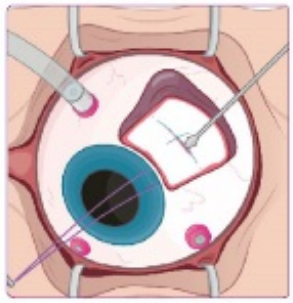

Figure 47 Dissect incision on either side of polypropylene suture to base of the fixation loop

2.1 Locate and open incision (cont'd)

iii. When the original incision is opened to full-thickness along the entire 3.0 mm length, cut the polypropylene anchor suture on the anterior side of the knot. See Figure 48.

ⓘ Note

The remaining polypropylene knot will prevent ENCELTO from dislocating into the vitreous cavity.

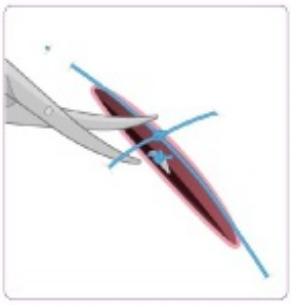

Figure 48 Cut polypropylene suture

⚠ Warning

- Do not cut the posterior side of the polypropylene anchor suture before grasping the fixation loop.

iv. Turn off or lower the infusion pressure.

Fully open the pars plana wound, confirm that there is no spanning uveal tissue and identify the fixation loop. See Figure 49.

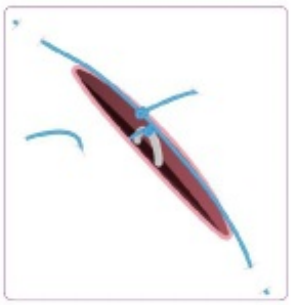

Figure 49 Identify the fixation loop

2.2 ENCELTO removal

i. Grasp the fixation loop with toothed forceps and begin to remove ENCELTO. See Figure 50.

ⓘ Note

Take care not to damage the white portion of ENCELTO during removal.

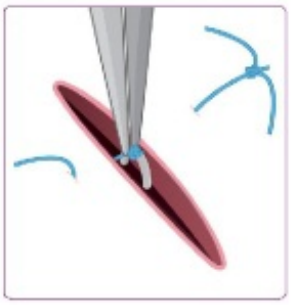

Figure 50 Grasp fixation loop

⚠ Warning

- Failure to grasp the fixation loop may release ENCELTO into the vitreous and may require a complete vitrectomy to recover.

ii. Cut off the remaining polypropylene knot and fully remove ENCELTO from the eye. See Figure 51.

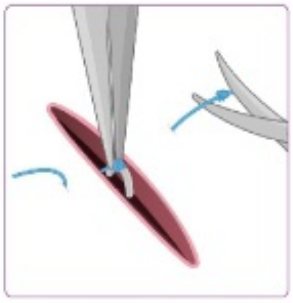

Figure 51 Cut off remaining knot and remove ENCELTO

iii. Carefully inspect ENCELTO capsule for any signs of damage or penetration.

ⓘ Note

If there is suspicion that the white portion of ENCELTO has been penetrated, perform a complete vitrectomy with extra attention to removal of vitreous that had surrounded ENCELTO prior to its removal. The goal is to remove any contents that may have been released into the vitreous when inadvertently penetrated.

Prior to disposal of an ENCELTO implant per local institutional protocols, call 1-833-963-9275 for assessment of ENCELTO return or replacement.

2.3 Removal wound closure

i. Use a vitrector to remove any prolapsed vitreous flush with the sclera. See Figure 52.

ⓘ Note

The vitrector does not need to enter the eye through the sclerotomy.

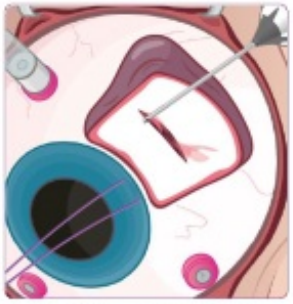

Figure 52 Remove prolapsed vitreous

ii. Close the sclerotomy with interrupted 7-0 Vicryl sutures to create a watertight closure. Remove the infusion line and the additional cannulas. See Figure 53.

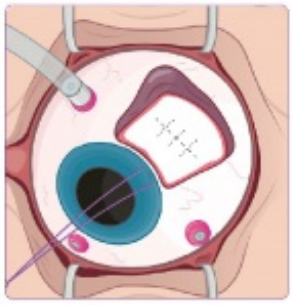

Figure 53 Close sclerotomy

iii. Close the conjunctiva with 6-0 plain gut sutures (or equivalent). See Figure 54.

iv. Administer subconjunctival antibiotic injection per routine.

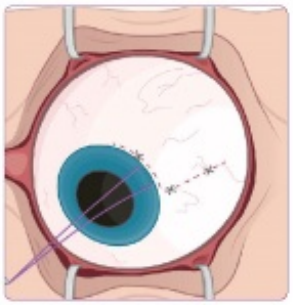

Figure 54 Close incision

3 Postoperative Wound Care

3.1 Antibiotic and steroid application

Warning

- Failure to follow postoperative antibiotic and steroid application can lead to increased risk of injury, inflammation, or infection.

The patient is to use:

- A topical antibiotic solution at a frequency of 1 drop four times a day for 7 days.
- A steroid drop taper of prednisolone acetate 1% (or equivalent) starting the day after surgery with the following taper:
  - 1 drop four times a day for the first 7 days
  - 1 drop three times a day for the next 7 days
  - 1 drop two times a day for the next 7 days
  - 1 drop once a day for the last 7 days.

Explanation of Symbols

Table 6 Symbol description

Symbol	Description
	Prescription only
	Sterile device
	Manufacturer
	Date of Manufacture
	Keep protected from light
	Use By Date
	Do not use if package is damaged
	LOT number
	Global Trade Item Number
	Serial number
	MR Conditional

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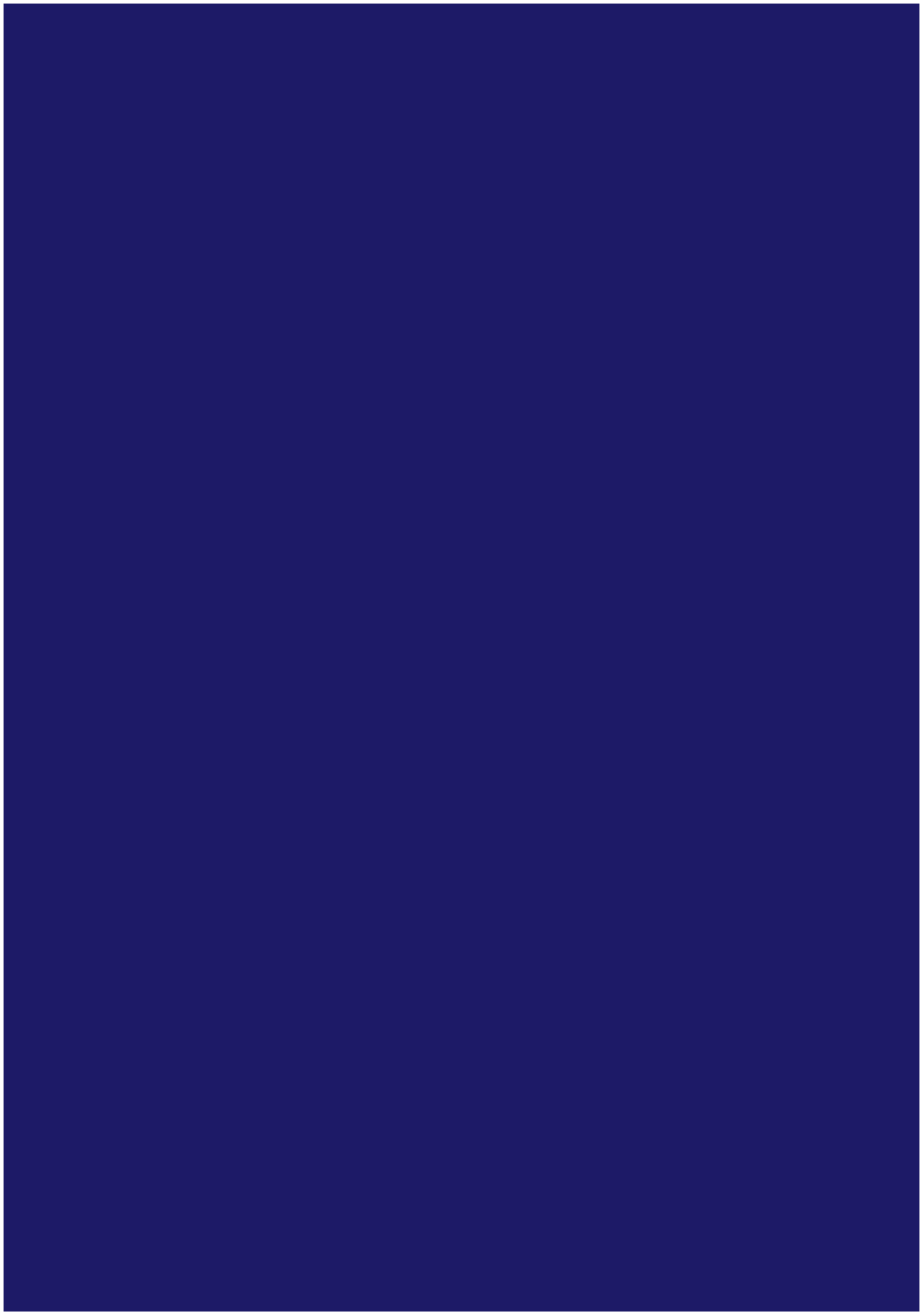
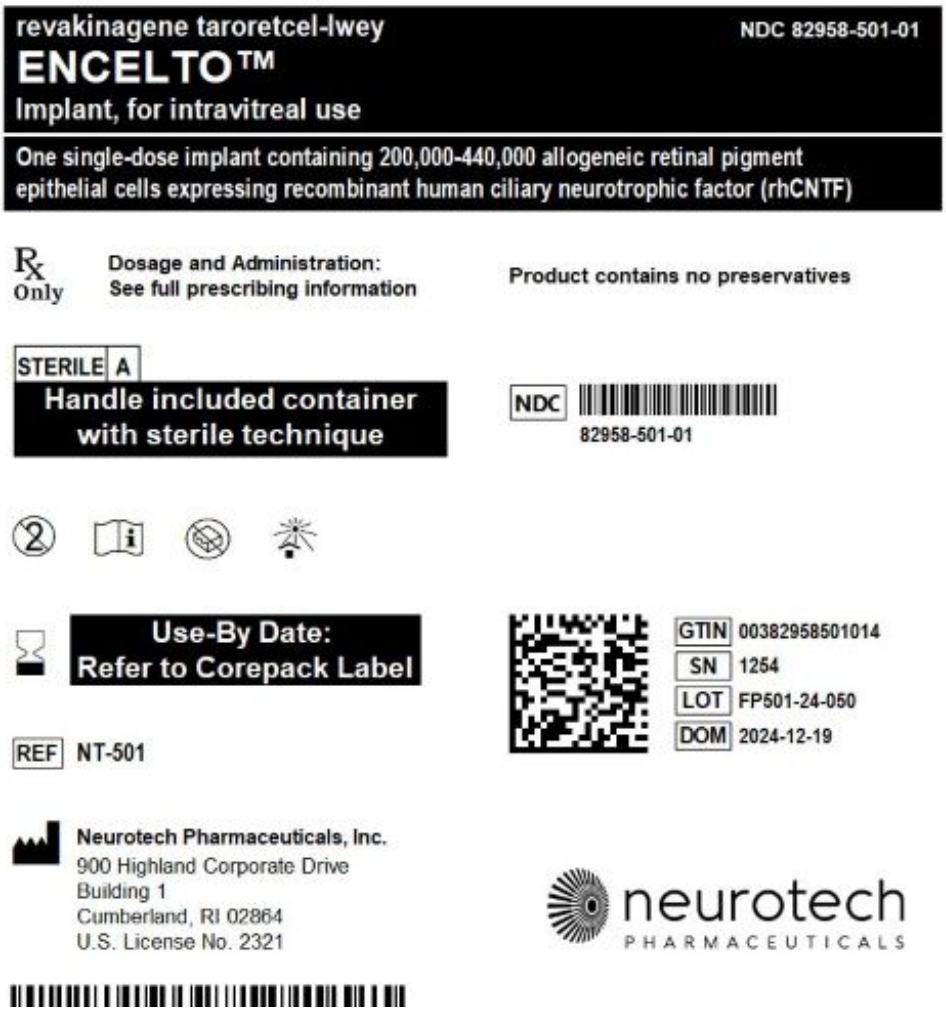
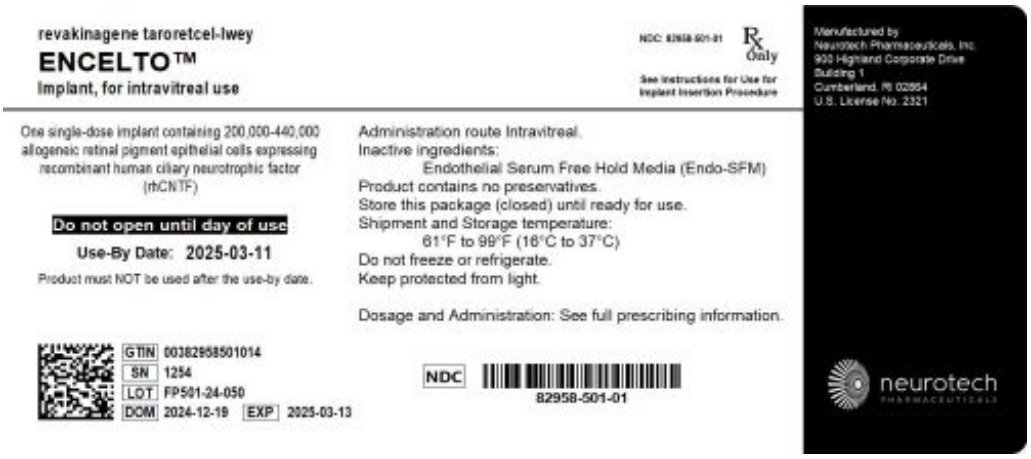


ENCELTO PRODUCT LABEL



ENCELTO COREPACK LABEL



ENCELTO

revakinagene taroretcel-lwey implant

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:82958-501
Route of Administration	INTRAVITREAL		

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
REVAKINAGENE TARORETCEL (UNII: Q7V7NYG6GM) (REVAKINAGENE TARORETCEL - UNII:Q7V7NYG6GM)	REVAKINAGENE TARORETCEL	440000 [arb'U]

Product Characteristics			
Color	white (white to off-white)	**Score**	
Shape	capsule	**Size**	7mm
Flavor		**Imprint Code**	
Contains			

Packaging				
#	**Item Code**	**Package Description**	**Marketing Start Date**	**Marketing End Date**
1	NDC:82958-501-01	1 in 1 CONTAINER	03/12/2025	
1		1 in 1 CAPSULE; Type 5: Device Coated or Otherwise Combined with Biologic		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
BLA	BLA125798	03/12/2025	

Labeler - Neurotech Pharmaceuticals, Inc. (117685116)

Revised: 3/2025 Neurotech Pharmaceuticals, Inc.