09-J5000-17

Original Effective Date: 06/15/25

Reviewed: 05/14/25

Revised: 03/15/26

Subject: Revakinagene taroretcel-lwey (Encelto) Intravitreal Implant

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

DESCRIPTION:

Macular telangiectasia is a progressive ocular disease with two forms, type 1 (MacTel1) and type 2 (MacTel2). MacTel1 is a rare congenital disorder, accounting for 20% to 25% of all MacTel cases, that presents with unilateral symptoms and mostly affects the male population. MacTel2 is a more common form with an estimated prevalence of 0.1% in patients over 40 years in the United States. MacTel2 differs from MacTel1 in that it mostly affects females and symptoms present bilaterally with central vision loss; however, patients usually do not experience complete blindness. MacTel2 is a neurodegenerative condition that causes the loss of Müller cells, which are responsible for growth factor secretion, angiogenesis/antiangiogenesis, neurotransmitter metabolism, synaptogenesis, neuroprotection, and photoreceptor survival. Over time, MacTel2 progresses to a proliferative phase, affecting the macular vasculature and causing blood vessels surrounding the fovea to proliferate, dilate, and leak, ultimately leading to macular degeneration. In the proliferative phase intravitreal anti-vascular endothelial growth factor (VEGF) inhibitors have shown to retard the progression of the disease.

On March 5, 2025, the FDA approved revakinagene taroretcel-lwey (Encelto) for the treatment of adults with idiopathic macular telangiectasia type 2 (MacTel2). Revakinagene taroretcel-lwey (Encelto) is an allogeneic encapsulated cell-based gene therapy that is surgically inserted intravitreally as an implant, and it secretes recombinant human ciliary neurotrophic factor (rhCNTF), which is one of several neurotrophic factors endogenously produced by neurons and supporting glial cells. Additionally, it is thought to cause Müller cells to trigger a cascade of signaling events that may promote photoreceptor survival.

According to the manufacturer prescribing information, the efficacy of revakinagene taroretcel-lwey (Encelto) was evaluated in two randomized, multi-center, sham-controlled studies in patients with

MacTel2. Inclusion criteria required at least one study eye with MacTel2, fluorescein leakage, and at least one other characteristic such as hyperpigmentation outside a 500-micron radius from the fovea center, retinal opacification, crystalline deposits, right-angle vessels, or inner/outer lamellar cavities. 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) score of 54 letters or better (20/80 Snellen equivalent) on the Early Treatment Diabetic Retinopathy Study (ETDRS) chart. Patients with neovascular MacTel2 were excluded. Patients were randomized to receive either the revakinagene taroretcel-lwey (Encelto) intravitreal implant or sham procedure under standard operative procedures. Patients in the revakinagene taroretcel-lwey (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. 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. EZ loss is an indicator of PR disruption and macular health. The secondary outcome measure was the mean change in aggregate sensitivity loss of microperimetry within the EZ break area from baseline to Month 24.

For Study 1, a total of 120 patients were randomized and of these, 115 patients underwent the assigned procedure and were included in the analysis of efficacy (revakinagene taroretcel-lwey group = 58 patients and sham group = 57 patients). 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 Caucasian, 5 patients (4%) were Asian, 3 patients (3%) were 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 revakinagene taroretcel-lwey (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 revakinagene taroretcel-lwey (Encelto) group and 35.5 (2, 281.3) dB for the Sham group. The primary and secondary efficacy outcomes for Study 1 are summarized in Table 1.

Table 1: The Primary and Secondary Efficacy Outcomes for Study 1 (N=115)

Efficacy endpoints	**Revakinagene taroretcel-lwey (Encelto) (n= 58)**	**Sham (n=57)**	**Difference between groups**	**P-value[c]**
Rate of change in EZ area loss from baseline over 24 months[a]				
mm^2	0.075	0.166	-0.091	<0.0001
(95% CI)	(0.05, 0.10)	(0.14, 0.19)	(-0.13, -0.06)	
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 revakinagene taroretcel-lwey (Encelto) and four sham patients were excluded due to missing data.

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

For Study 2, a total of 119 patients were randomized and of these, 113 patients underwent the assigned procedure and were included in efficacy evaluation (revakinagene taroretcel-lwey group = 59 patients and sham group = 54 patients). 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 Caucasian, 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 revakinagene taroretcel-lwey (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 revakinagene taroretcel-lwey (Encelto) group and 28.86 (0.33, 221.17) dB for the sham group. The primary and secondary efficacy outcomes for Study 2 are summarized in Table 2.

Table 2: The Primary and Secondary Efficacy Outcomes for Study 2 (N=113)

Efficacy endpoints	**Revakinagene taroretcel-lwey (Encelto)** **(n= 59)**	**Sham** **(n=54)**	**Difference between groups**	**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-months[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 revakinagene taroretcel-lwey (Encelto) and six sham patients were excluded due to missing data.

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

As outline in the revakinagene taroretcel-lwey (Encelto) prescribing information, 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, and iridocyclitis.

POSITION STATEMENT:

The administration of revakinagene taroretcel-lwey (Encelto) intravitreal implant **meets the definition of medical necessity** when **ALL** of the following are met:

1. Member is at least 18 years of age at the time of treatment
2. Diagnosis of macular telangiectasia, type 2, in at least one eye, as evidenced by typical fluorescein leakage and at least **ONE** of the following: - Documentation within the last 6 months must be provided
    a. hyperpigmentation outside a 500-micron radius from the center of the fovea
    b. retinal opacification
    c. crystalline deposits
    d. right angle vessels
    e. inner/outer lamellar cavities
3. Member does **NOT** have neovascular macular telangiectasia
4. 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) - Documentation within the last 6 months must be provided
5. Best corrected visual acuity (BCVA) score of 54 letters or better (20/80 Snellen equivalent) on the Early Treatment Diabetic Retinopathy Study (ETDRS) chart - Documentation within the last 6 months must be provided
6. **NONE** of the following:
    a. Ocular or periocular infection
    b. Known hypersensitivity to Endothelial Serum Free Media (Endo34 SFM)

7. Use of antithrombotic medications (e.g., oral anticoagulants, aspirin, nonsteroidal anti-inflammatory drugs) will be temporarily discontinued prior to the insertion surgery
8. Member has **NOT** previously received intravitreal gene therapy (including revakinagene taroretcel-lwey)
9. Revakinagene taroretcel-lwey will be administered at a Encelto Qualified Treatment Center (QTC) by a certified ophthalmologist
10. The administration of revakinagene taroretcel-lwey (Encelto) will not exceed one implant per affected eye for surgical intravitreal insertion

Approval duration: 9 months to allow for a one-time treatment of both eyes

Revakinagene taroretcel-lwey (Encelto) is considered **experimental or investigational** for any other indications due to insufficient evidence in the peer-reviewed medical literature to support safety, efficacy, and net health outcome.

DOSAGE/ADMINISTRATION:

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

FDA-approved

- Revakinagene taroretcel-lwey (Encelto) is an allogeneic encapsulated cell-based gene therapy indicated for the treatment of adults with idiopathic macular telangiectasia type 2 (MacTel2).
- Revakinagene taroretcel-lwey (Encelto) is an intravitreal implant intended for surgical insertion under aseptic conditions by a qualified ophthalmologist.
- The recommended dose is one revakinagene taroretcel-lwey (Encelto) implant per affected eye containing 200,000 to 440,000 allogeneic retinal pigment epithelial cells expressing recombinant human ciliary neurotrophic factor (rhCNTF).
- Carefully inspect revakinagene taroretcel-lwey (Encelto) prior to use and refer to the instructions for use when preparing for and performing surgical placement or removal of the implant.

Dose Adjustments

- None

Drug Availability

- One single-dose revakinagene taroretcel-lwey (Encelto) implant containing 200,000 to 440,000 allogeneic retinal pigment epithelial cells expressing rhCNTF (NDC: 82958-501-01)

PRECAUTIONS:

Boxed Warning

- None

Contraindications

- Ocular or periocular infections
- Known hypersensitivity to Endothelial Serum Free Media (Endo34 SFM)

Precautions/Warnings

- Revakinagene taroretcel-lwey (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.
- Vitreous Hemorrhage: Temporarily discontinue antithrombotic medication prior to revakinagene taroretcel-lwey (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 revakinagene taroretcel-lwey (Encelto) extrusion. The surgical site should be examined closely and the revakinagene taroretcel-lwey (Encelto) should be surgically repositioned if indicated.

BILLING/CODING INFORMATION:

The following codes may be used to describe:

HCPCS Coding

J3403	Revakinagene taroretcel-lwey, per implant

ICD-10 Diagnosis Codes That Support Medical Necessity

H35.071	Retinal telangiectasis, right eye
H35.072	Retinal telangiectasis, left eye
H35.073	Retinal telangiectasis, bilateral
H35.079	Retinal telangiectasis, unspecified eye

REIMBURSEMENT INFORMATION:

Refer to section entitled **POSITION STATEMENT**.

PROGRAM EXCEPTIONS:

Federal Employee Program (FEP): Follow FEP guidelines.

State Account Organization (SAO): Follow SAO guidelines.

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

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

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

DEFINITIONS:

Gene therapy - Gene therapies treat diseases by modifying or manipulating the expression of a gene or altering the properties of living cells for therapeutic use including: (1) replacing a disease-causing gene with a healthy copy of the gene, (2) inactivating a disease-causing gene that is not functioning properly, or (3) introducing a new or modified gene into the body to help treat a disease.

RELATED GUIDELINES:

None

OTHER:

None

REFERENCES:

1. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2025. URL www.clinicalpharmacilogy-ip.com Accessed 4/30/25.
2. Encelto (revakinagene taroretcel-lwey) [package insert]. Neurotech Pharmaceuticals, Inc. Cumberland (RI): March 2025.
3. DRUGDEX System [Internet]. Greenwood Village (CO): Thomson Micromedex; Updated periodically [cited 2025 April 30].
4. DynaMed [database online]. Ipswich, MA: EBSCO Information Services.; 2025. URL http://www.dynamed.com. Accessed 4/30/25.
5. Orphan Drug Designations and Approval [Internet]. Silver Spring (MD): US Food and Drug Administration; 2025 [cited 2025 April 30]. Available from: http://www.accessdata.fda.gov/scripts/opdlisting/oopd/index.cfm/.

COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 05/14/25.

GUIDELINE UPDATE INFORMATION:

06/15/25	New Medical Coverage Guideline – Revakinagene taroretcel-lwey (Encelto), an allogeneic encapsulated cell-based gene therapy that is intravitreally inserted, for the treatment of adults with idiopathic macular telangiectasia type 2 (MacTel2).
10/01/25	Revision: Added HCPCS code J3403 and removed code J3590.
03/15/26	Revision: Updating ICD-10 billing codes.