Medical Policy Bulletin

Title:
Revakinagene taroretcel-lwey (Encelto)
Policy #:
MA08.013

The Company makes decisions on coverage based on the Centers for Medicare and Medicaid Services (CMS) regulations and guidance, benefit plan documents and contracts, and the member's medical history and condition. If CMS does not have a position addressing a service, the Company makes decisions based on Company Policy Bulletins. Benefits may vary based on contract, and individual member benefits must be verified. The Company determines medical necessity only if the benefit exists and no contract exclusions are applicable. Although the Medicare Advantage Policy Bulletin is consistent with Medicare's regulations and guidance, the Company's payment methodology may differ from Medicare.

When services can be administered in various settings, the Company reserves the right to reimburse only those services that are furnished in the most appropriate and cost-effective setting that is appropriate to the member's medical needs and condition. This decision is based on the member's current medical condition and any required monitoring or additional services that may coincide with the delivery of this service.

This Policy Bulletin document describes the status of CMS coverage, medical terminology, and/or benefit plan documents and contracts at the time the document was developed. This Policy Bulletin will be reviewed regularly and be updated as Medicare changes their regulations and guidance, scientific and medical literature becomes available, and/or the benefit plan documents and/or contracts are changed.

Policy

Coverage is subject to the terms, conditions, and limitations of the member's Evidence of Coverage.

In the absence of coverage criteria from applicable Medicare statutes, regulations, NCDs, LCDs, CMS manuals, or other Medicare coverage documents, this policy uses internal coverage criteria developed by the Company in consideration of peer-reviewed medical literature, clinical practice guidelines, and/or regulatory status.

The Company reserves the right to reimburse only those services that are furnished in the most appropriate and cost-effective setting that is appropriate to the member's medical needs and condition.

MEDICALLY NECESSARY

Revakinagene taroretcel-lwey (Encelto®), implanted intravitreally by a qualified ophthalmologist, is considered medically necessary and, therefore, covered for the treatment of adults with idiopathic macular telangiectasia type 2 (MacTel) when ALL of the following are met:

- Individual has a documented diagnosis (via fluorescein angiography, optical coherence tomography [OCT], OCT angiography) of type 2 idiopathic nonproliferative macular telangiectasia in the affected eye(s) with evidence of fluorescein leakage and at least ONE of the other features:
    - Hyperpigmentation that is outside of a 500-micron radius from the center of the fovea
    - Retinal opacification
    - Crystalline deposits
    - Right-angle vessels
    - Inner/outer lamellar cavities
- Individual's best corrected visual acuity (BCVA) is ONE of the following:
    - 54-letter score or better as measured by the Early Treatment Diabetic Retinopathy Study (ETDRS) chart
    - 20/80 or better using the Snellen chart
- Individual does not have evidence of ANY of the following in the affected eye(s):
    - Ocular or periocular infections
    - Known hypersensitivity to Endothelial Serum Free Media (Endo-SFM)
    - Glaucoma

    - Severe nonproliferative or proliferative diabetic retinopathy
    - Uveitis
    - Intraretinal hyperreflectivity by OCT
    - Other ocular disease(s) that may confound the diagnosis, procedures, or outcome of treatment
    - Intraretinal neovascularization or subretinal neovascularization (SRNV), as evidenced by the presence of ANY of the following in either eye:
        - Hemorrhage
        - Hard exudate
        - Subretinal fluid or intraretinal fluid
- Individual has not had ANY of the following in the affected eye(s):
    - Inability to temporarily discontinue antithrombotic medication prior to insertion surgery
    - Vitrectomy
    - Penetrating keratoplasty
    - Trabeculectomy
    - Trabeculoplasty
    - Lens removal in the previous 3 months
    - Yttrium aluminum garnet (YAG) laser within 4 weeks
- Individual has not received a previous implantation of revakinagene taroretcel-lwey (Encelto) in the affected eye(s)

EXPERIMENTAL/INVESTIGATIONAL

All other uses for revakinagene taroretcel-lwey (Encelto) are considered experimental/investigational and, therefore, not covered unless the indication is supported as an accepted off-label use, as defined in the Company medical policy on Off-Label Coverage for Prescription Drugs and Biologics.

REQUIRED DOCUMENTATION

The individual's medical record must reflect the medical necessity for the care provided. These medical records may include, but are not limited to: records from the professional provider's office, hospital, nursing home, home health agencies, therapies, and test reports.

The Company may conduct reviews and audits of services to our members, regardless of the participation status of the provider. All documentation is to be available to the Company upon request. Failure to produce the requested information may result in a denial for the drug.

Guidelines

There is no Medicare coverage determination addressing revakinagene taroretcel-lwey (Encelto); therefore, the Company policy is applicable.

BENEFIT APPLICATION

Subject to the terms and conditions of the applicable Evidence of Coverage, revakinagene taroretcel-lwey (Encelto) is covered under the medical benefits of the Company's Medicare Advantage products when the medical necessity criteria listed in this medical policy are met.

US FOOD AND DRUG ADMINISTRATION STATUS

The US Food and Drug Administration (FDA) approved revakinagene taroretcel-lwey (Encelto) on March 5, 2025, as an allogeneic encapsulated cell-based gene therapy for the treatment of adults with idiopathic macular telangiectasia type 2 (MacTel).

PEDIATRIC USE
The safety and effectiveness of revakinagene taroretcel-lwey (Encelto) in pediatric individuals have not been established.

Description

MACULAR TELANGIECTASIA

Macular telangiectasia (MacTel), or juxtafoveal telangiectasia, is a rare, progressive condition of the macula that usually affects individuals older than 40 years of age. It results in gradual central vision loss with patchy visual field deficits, usually bilaterally, perifoveal telangiectatic retinal vessels, and reduction in visual acuity (VA), often in near vision. Occasionally, the individual will experience subretinal neovascularization. MacTel does not affect peripheral vision. Although MacTel rarely results in total loss of vision, it does impair the quality of life of affected individuals resulting in decreased ability to read, drive, or perform activities of daily living. MacTel is a neurodegenerative disease that results in dysfunction of macular Müller cells and loss of photoreceptors.

The cause of MacTel is not known. There is likely a genetic component. The presence of a systemic disorder (e.g., diabetes, hypertension, obesity) may put an individual at an increased risk of developing the condition. The presence of another ocular condition may also play a role in the development of MacTel.

Because MacTel had features that overlap with other conditions, narrowing down a diagnosis can be challenging. The best way to diagnose MacTel is using a multimodal approach. Optical coherence tomography (OCT), OCT angiography (OCTA), and fluorescein angiography (FA) used together would be the preferred method to use.

MacTel has a relatively good long-term prognosis, so most individuals will not need treatment. For some individuals, laser treatments for leaking blood vessels may be used. This treatment can cause other deleterious side effects, so is not a preferred approach. Steroids, or other medications, can be injected into the eyes as therapy. Because MacTel can lead to the growth of abnormal retinal blood vessels, vascular endothelial growth factor blockers can be used to treat nonproliferative MacTel.

REVAKINAGENE TARORETCEL-LWEY (ENCELTO)

The US Food and Drug Administration (FDA) approved revakinagene taroretcel-lwey (Encelto) on March 5, 2025, as an allogeneic encapsulated cell therapy for the treatment of adults with idiopathic macular telangiectasia type 2 (MacTel). Revakinagene taroretcel-lwey (Encelto) capsules contain 200,000 to 440,000 allogeneic retinal pigment epithelial cells expressing ciliary neurotrophic factor (CNTF) for surgical intravitreal placement. CNTF 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 revakinagene taroretcel-lwey (Encelto) is not completely understood.

CONSIDERATIONS

Revakinagene taroretcel-lwey (Encelto) has yet to be clinically investigated in individuals with:

- Specific lens opacities (i.e., cortical opacity >standard 3; posterior subcapsular opacity >standard 2; nuclear opacity >standard 3) as measured on the age-related eye disease study (AREDS) clinical lens grading system
- Central serous chorioretinopathy
- Pathologic myopia
- Significant corneal or media opacities
- History of ocular herpes

CLINICAL TRIAL INFORMATION

The efficacy and safety of revakinagene taroretcel-lwey (Encelto) was evaluated in two identical phase III, multicenter, randomized, sham-controlled clinical trials (NCT03316300 [NTMT-03-A], NCT03319849 [NTMT-03-B]). Of the 115 individuals enrolled in NTMT-03-A, 58 received the study treatment and 57 received a sham treatment. Of the 113 individuals enrolled in NTMT-03-B, 59 received the study treatment and 54 received a sham treatment. The primary endpoint of both clinical trials was the rate of change in the area of ellipsoid zone (EZ) loss (inner segment/outer segment [IS/OS]; macular photoreceptor loss) from baseline through 24 months. The EZ comprises the outer portion of photoreceptor inner segments that appear on OCT scans due to the dense collection of mitochondria localized to that region, meaning EZ imaging can capture and quantify photoreceptor degradation, the biological basis for vision loss. Longitudinal natural-history studies show EZ loss (area size at baseline, location) correlates with later declines in retinal sensitivity, best corrected visual acuity (BCVA), and the development/enlargement of scotomas in individuals with MacTel type 2. Therefore, the phase

III's secondary trial endpoints included were change in retinal sensitivity and monocular reading speed from baseline through 24 months.

In NTMT-03-A, the active treatment cohort experienced a change of 0.075 mm^2/24 months in EZ area loss and the sham treatment cohort experienced a change of 0.166 mm^2/24 months (difference −0.091 mm^2/24 months [95 percent confidence interval [CI], −0.125 to −0.056; P<0.001]) which was a relative difference of 54.8 percent. In NTMT-03-B, the active treatment cohort experienced a change of 0.111 mm^2/24 months in EZ area loss and the sham treatment cohort experienced a change of 0.160 mm^2/24 months (difference −0.049 mm^2/24 months [95 percent CI, −0.089 to −0.008; P=0.02) which was a relative difference of 30.6 percent. In NTMT-03-A, the mean difference in aggregate sensitivity loss over 24 months in the active treatment cohort was 25.27 db (95 percent CI, 15.64–34.90) versus 43.02 db (95 percent CI, 31.51–54.53) in the sham treatment cohort (difference -17.75 [95 percent CI, −32.58 to −2.91]; P=0.02). In NTMT-03-B, the mean difference in aggregate sensitivity loss over 24 months in the active treatment cohort was 40.02 db (95 percent CI, 25.74–54.30) versus 41.97 db (95 percent CI, 30.03–53.91) in the sham treatment cohort (difference −1.95 [95 percent CI, −20.33 to 16.43]; P=0.84). It has been previously reported that the functional consequence of an EZ defect depends on where the defect is (central versus noncentral) and its baseline size (i.e., small peripheral EZ changes may not translate to noticeable visual loss especially since the foveal center part of the retina is responsible for sharp vision). Therefore, the variability in retinal sensitivity reported across the NTMT-03-A and NTMT-03-B phase III trials may be due to differences in the type of EZ break as researchers fail to report the number of enrolled individuals that had noncentral versus central EZ loss (i.e., central EZ loss has a higher rate of clinically relevant visual loss). In NTMT-03-A, the mean change in reading speed over 24 months in the active treatment cohort was −6.18 words/min (95 percent CI, −14.00 to 1.64) versus −12.20 words/min (95 percent CI−23.71 to −0.68) in the sham treatment cohort (estimated difference 6.02 words/minute [95 percent CI, -7.76 to 19.80]; P=0.39). In NTMT-03-B, the mean change in reading speed over 24 months in the active treatment cohort was −5.46 words/min (95 percent CI, −13.55 to 2.63) versus −18.88 words/min (95 percent CI, −28.46 to −9.30) in the sham cohort (estimated difference 13.04 [95 percent CI, 0.72–25.36]). Although there was less decline in reading speed in the active treatment cohorts versus the sham treatment cohorts, the differences did not reach significance.

Multiple safety measures were assessed. The percentage of individuals who lost 15 or more letters in best corrected visual acuity (BCVA) in 24 months was 13.8 percent in individuals in the active treatment cohort in NTMT-03-A versus 8.8 percent in individuals in the sham treatment cohort (P=0.56). The percentage of individuals who lost 15 or more letters in BCVA in 24 months was 3.4 percent in individuals in the active treatment cohort in NTMT-03-B versus 5.6 percent in individuals in the sham treatment cohort (P=0.67). There were more ocular treatment-emergent adverse events in the two active treatment cohorts versus the two sham treatment cohorts; most were mild. There were more serious ocular treatment-emergent adverse events in the two active treatment cohorts versus none in the sham treatment cohorts, but they were few and most were related to surgical complications, including suture-related complications, vitreous hemorrhage, and one individual whose device extruded and required surgical repositioning. Delayed dark adaptation, a known side effect from the treatment from previous clinical trials, was experienced by 17 percent and 24 percent of individuals in the active treatment cohorts from NTMT-03-A and NTMT-03-B, respectively, versus none and 2 percent of individuals in the sham treatment cohorts from NTMT-03-A and NTMT-03-B, respectively. Miosis, another known side effect from the treatment, was experienced by 17 percent and 14 percent of individuals in the treatment cohorts from NTMT-03-A and NTMT-03-B, respectively, and none in the sham treatment cohorts from either clinical trial.

SUMMARY

MacTel type 2 currently has no other approved disease-modifying therapies. It is a rare, progressive disease that can lead to significant reading/vision impairment despite preserved central acuity early on, meaning there is a clinical need for an intervention that preserves photoreceptors. It is established that the EZ band on OCT maps to the inner-segment ellipsoid packed with photoreceptor mitochondria. EZ is a direct pathophysiologic link to photoreceptor health and has high correlations with retinal sensitivity, BCVA, and the development/enlargement of scotomas at later time points. Although at a varied level and without knowledge of a clinically significant preservation percentage, revakinagene taroretcel-lwey (Encelto) induced a reduction in EZ loss in a statistically significant manner in all the available data. Previous literature has shown that EZ loss predicts future functional decline, meaning both phase III trials meeting their primary endpoint (reduction in EZ loss), demonstrates sufficient efficacy in a condition for which waiting for downstream functional outcomes (e.g., BCVA or retinal sensitivity) to manifest would mean treatment may come too late (i.e., photoreceptor cells do not regenerate). Across phase III trials, the implant and surgical procedure were generally well tolerated; most adverse events were procedure-related and mild. Longitudinal follow-up indicates the device remains functional (implants provide bioactive CNTF to the vitreous for durations exceeding a decade).

OFF-LABEL INDICATIONS

There may be additional indications contained in the Policy section of this document due to evaluation of criteria highlighted in the Company's off-label policy, and/or review of clinical guidelines issued by leading professional organizations and government entities.

References

American Hospital Formulary Service (AHFS). Revakinagene taroretcel-lwey (Encelto®). AHFS Drug Information. [UpToDate Lexidrug Web site]. 08/21/2025. Available at: https://online.lexi.com/lco/action/home [via subscription only]. Accessed August 26, 2025.

Chew EY, Clemons TE, Jaffe GJ, et al. Effect of ciliary neurotrophic factor on retinal neurodegeneration in patients with macular telangiectasia type 2: a randomized clinical trial. *Ophthalmology*. 2019 Apr;126(4):540-549.

Chew EY, Clemons TE, Peto T, et al. Ciliary neurotrophic factor (CNTF) for macular telangiectasia type 2 (MacTel): results from a phase I safety trial. *Am J Ophthalmol*. 2015 Apr;159(4):659-666.

Chew EY, Gillies M, Jaffe GJ, et al. Cell-based ciliary neurotrophic factor therapy for macular telangiectasia type 2. *NEJM Evid*. 2025 Aug;4(8):EVIDoa2400481.

Chew EY, Kim J, Sperduto RD, et al. Evaluation of the Age-Related Eye Disease Study clinical lens grading system AREDS report no. 31. *Ophthalmology*. 2010;117(11):2112-2119.

ClinicalTrials.gov. A study to determine the safety and efficacy of NT-501 in macular telangiectasia type 2 - protocol A. ClinicalTrials.gov Identifier: NCT03316300. First Posted: October 20, 2017. Last Update Posted: September 24, 2024. Available at: https://clinicaltrials.gov/. Accessed August 26, 2025.

ClinicalTrials.gov. A study to determine the safety and efficacy of NT-501 in macular telangiectasia type 2 - protocol B. ClinicalTrials.gov Identifier: NCT03319849. First Posted: October 20, 2017. Last Update Posted: September 24, 2024. Available at: https://clinicaltrials.gov/. Accessed August 26, 2025.

Elsevier's Clinical Pharmacology Compendium. Revakinagene taroretcel-lwey (Encelto®). [Clinical Key Web site]. 07/18/2025. Available at: https://www.clinicalkey.com/#!/ [via subscription only]. Accessed August 26, 2025.

Goerdt L, Berger M, Jungblut J, et al. Skeleton density and ellipsoid zone loss are prognostic for progression in Macular Telangiectasia Type 2. *Sci Rep*. 2024;14(1):17328.

Heeren TFC, Kitka D, Florea D, et al. Longitudinal correlation of ellipsoid zone loss and functional loss in macular telangiectasia type 2. *Retina*. 2018;38(Suppl 1):S20-S26.

Kauper K, Nystuen A, Orecchio L, et al. Long-term durability of ciliary neurotrophic factor-releasing revakinagene taroretcel-lwey in individuals with retinal degenerative disorders. *Invest Ophthalmol Vis Sci*. 2025 Aug 1;66(11):3.

Merative Micromedex® DRUGDEX® (electronic version). Revakinagene taroretcel-lwey (Encelto®). [Micromedex Web site]. 08/20/2025. Available at: https://www.micromedexsolutions.com/micromedex2/librarian [via subscription only]. Accessed August 26, 2025.

Pauleikhoff D, Bonelli R, Dubis AM, et al. Progression characteristics of ellipsoid zone loss in macular telangiectasia type 2. *Acta Ophthalmol*. 2019;97(7):e998-e1005.

Peto T, Heeren TFC, Clemons TE, et al. Correlation of clinical and structural progression with visual acuity loss in macular telangiectasia type 2: MacTel project report no. 6-the MacTel Research Group. *Retina*. 2018;38 Suppl 1(Suppl 1):S8-S13.

Posvar W, Pucker AD. Snellen vs. ETDRS in VA testing: best-corrected visual acuity testing in clinical practice and clinical trials. [the ophthalmologist Web site]. 02/19/2024. Available at: https://theophthalmologist.com/issues/2024/articles/feb/snellen-vs-etdrs-in-va-testing. Accessed August 26, 2025.

Revakinagene taroretcel-lwey (Encelto®) [prescribing information]. Cumberland, RI: Neurotech Pharmaceuticals, Inc.

03/2025. Available at: https://www.encelto.com/. Accessed August 26, 2025.

Sallo FB, Peto T, Egan C, et al. “En face” OCT imaging of the IS/OS junction line in type 2 idiopathic macular telangiectasia. *Invest Ophthalmol Vis Sci*. 2012;53(10):6145-6152.

Singh RP. Waiting on a treatment: how the history of MacTel is leading us into the future. [Modern Retina from Ophthalmology Web site]. 02/17/2025. Available at: https://www.modernretina.com/view/waiting-on-a-treatment-how-the-history-of-mactel-is-leading-us-into-the-future. Accessed August 26, 2025.

Turbert D. What is macular telangiectasia? [American Academy of Ophthalmology Web site]. 09/23/2024. Available at: https://www.aao.org/eye-health/diseases/macular-telangiectasia. Accessed August 26, 2025.

UpToDate® Lexidrug™. Revakinagene taroretcel-lwey (Encelto®). [UpToDate Lexidrug Web site]. 08/01/2025. Available at: https://online.lexi.com/lco/action/home [via subscription only]. Accessed August 26, 2025.

US Food and Drug Administration (FDA). Center for Drug Evaluation and Research. Revakinagene taroretcel-lwey (Encelto®). Prescribing information. [FDA Web site]. 03/05/2025. Available at: https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm. Accessed August 26, 2025.

Coding

Inclusion of a code in this table does not imply reimbursement. Eligibility, benefits, limitations, exclusions, precertification/referral requirements, provider contracts, and Company policies apply.

The codes listed below are updated on a regular basis, in accordance with nationally accepted coding guidelines. Therefore, this policy applies to any and all future applicable coding changes, revisions, or updates.

In order to ensure optimal reimbursement, all health care services, devices, and pharmaceuticals should be reported using the billing codes and modifiers that most accurately represent the services rendered, unless otherwise directed by the Company.

The Coding Table lists any CPT, ICD-10, and HCPCS billing codes related only to the specific policy in which they appear.

CPT Procedure Code Number(s)
N/A

ICD - 10 Procedure Code Number(s)
N/A

ICD - 10 Diagnosis Code Number(s)
H35.071 Retinal telangiectasis, right eye

H35.072 Retinal telangiectasis, left eye

H35.073 Retinal telangiectasis, bilateral

HCPCS Level II Code Number(s)
J3403 Revakinagene tarorectcel-lwey, per implant

Revenue Code Number(s)
N/A

Policy History

Revisions From MA08.013:

06/18/2026	This policy will become effective 06/18/2026. The following new policy has been developed to communicate the Company's coverage criteria for revakinagene taroretcel-lwey (Encelto®).

Version Effective Date:
06/18/2026
Version Issued Date:
06/18/2026
Version Reissued Date:
N/A