Molina Clinical Policy
Encelto (revakinagene taroretcel-lwey)
Policy No. 470

Last Approval: 04/08/2026
Next Review Due By: April 2027

DISCLAIMER

This Molina Clinical Policy (MCP) is intended to facilitate the Utilization Management process. Policies are not a supplementation or recommendation for treatment; Providers are solely responsible for the diagnosis, treatment, and clinical recommendations for the Member. It expresses Molina's determination as to whether certain services or supplies are medically necessary, experimental, investigational, or cosmetic for purposes of determining appropriateness of payment. The conclusion that a particular service or supply is medically necessary does not constitute a representation or warranty that this service or supply is covered (e.g., will be paid for by Molina) for a particular Member. The Member's benefit plan determines coverage – each benefit plan defines which services are covered, which are excluded, and which are subject to dollar caps or other limits. Members and their Providers will need to consult the Member's benefit plan to determine if there are any exclusion(s) or other benefit limitations applicable to this service or supply. If there is a discrepancy between this policy and a Member's plan of benefits, the benefits plan will govern. In addition, coverage may be mandated by applicable legal requirements of a State, the Federal government or CMS for Medicare and Medicaid Members. CMS's Coverage Database can be found on the CMS website. The coverage directive(s) and criteria from an existing National Coverage Determination (NCD) or Local Coverage Determination (LCD) will supersede the contents of this MCP and provide the directive for all Medicare members. References included were accurate at the time of policy approval and publication.

OVERVIEW

This policy reviews the use of Encelto (revakinagene taroretcel-lwey) in non-neovascular macular telangiectasis type 2. Macular telangiectasia (MT) is a rare cause of progressive, central vision loss. Vision loss begins with difficulties in reading after the age of 40 but becomes more extensive over time. The disorder has been attributed to a disturbance of vascular growth and neurodegeneration in the central portion of the retina (macula). The macula (center of the retina) is responsible for central, color vision and high acuity vision. Photoreceptor degeneration, prominent in the macula, results from dysfunction of Muller cells that provide nutrition and tropic factors. It is now thought that MT results from primary neurodegeneration secondary to loss of trophic factor support from Muller cells. This is followed by disorganized retinal vessel formation and vessel dysfunction. The are multiple subtypes of MT and it is important to know the subtype of MT that revakinagene treats. MT is divided broadly into two subtypes, macular telangiectasia type 1 (MT-1) and macular telangiectasia type 2 (MT-2). There is a further subdivision of MT-2 into neovascular and non-neovascular types. Revakinagene treats the MT-2, non-neovascular type by supplying a trophic factor called ciliary neurotrophic factor to the retinal region.

Revakinagene is an encapsulated, cell-based gene therapy surgically implanted in the eye. The manufacturer's proprietary cell line is genetically engineered to produce the CNTF trophic factor within an encapsulation that allows CNTF to diffuse out to retinal cells. CNTF is neuroprotective and helps maintain photoreceptors and retinal ganglion cells. This therapy slows the progression of MT-2 but is not a cure. Each implant houses 200,000 to 440,000 allogeneic retinal pigment epithelial cells with the recombinant human CNTF gene. Implants are removeable should problems arise.

Regulatory Status
Encelto was FDA approved March 5, 2025. Prior to Encelto, there was no known treatment for MT-2 (Chew 2019).

COVERAGE POLICY

Revakinagene taroretcel-lwey may be **considered medically necessary** when ALL the following criteria are met:

1. Member must have a diagnosis of macular telangiectasia type 2 with evidence of fluorescein leakage typical of macular telangiectasia or other features including retinal opacification, crystalline deposits, right angle vessels, inner lamellar cavities or hyperpigmentation not involving the center of the fovea, but no evidence of intraretinal/subretinal neovascularization

2. Member is between 21 years and 80 years of age

3. Member must be medically able to undergo ophthalmic surgery for the ocular implant

4. In the eye (s) to be treated, Member must have an ellipsoid zone break and en face lesion size as measured by

Optical Coherence Tomography (OCT) of at least 0.16 mm^2 – 4.00 mm^2.(See supplemental information below for definitions of terminology)

5. Member has not received steroid intravitreal therapy for non-neovascular macular telangiectasia within the last 3 months or intravitreal anti-VEGF therapy in the eye to be treated or anti-VEGF in the untreated eye within the last 3 months.

6. Member does not have evidence of ocular disease (other than macular telangiectasia) that may be vision threatening

7. Member does not have evidence of intraretinal/subretinal neovascularization in either eye

8. Member does not have evidence of central serous chorio-retinopathy (CSCR) in either eye

9. Member does not have evidence of pathologic myopia in either eye

10. Member does not have significant corneal or media opacities in either eye

11. Member does not have a vitrectomy, penetrating keratoplasty, trabeculectomy or trabeculoplasty

12. Member does not have any of the following lens opacities: cortical opacity > standard 3, posterior subcapsular opacity > standard 2, or a nuclear opacity > standard 3 as measured on the AREDS clinical lens grading system (Age-Related Eye Disease Study); Member has not undergone lens removal in the study eye(s) in the previous 3 months or YAG laser within 4 weeks

13. Member is not on chemotherapy

14. Member is not pregnant or breastfeeding

15. Member is not on immunosuppressive therapy

16. Member is not immunodeficient

17. Member does not have a known history of HIV

18. Member does not have a history of ocular Herpes virus

19. Member does not have Active or suspected ocular or periocular infections

20. Member does not have a known hypersensitivity to Endothelial Serum Free Media (Endo-SFM)

Limitations and Exclusions

QUANTITY LIMITATIONS: The recommended dose is one ENCELTO implant per affected eye. Additional implants of Encelto will not be authorized.

Continuation of Therapy

Encelto is indicated as a one-time implant. Repeat treatment or re-administration of an implant is not supported by labeling or compendia and is not considered medically necessary.

DOCUMENTATION REQUIREMENTS: Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational, or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

SUMMARY OF MEDICAL EVIDENCE

Encelto's FDA approval was based on data from several studies. In 2025, data from two, phase 3 trials with identical protocols, were combined & published. They demonstrated a reduced rate of photoreceptor loss in MT participants as measured by ellipsoid zone size in the Encelto treated group versus control (Chew et al 2025; NCT03316300 & NCT03319849). The ellipsoid zone loss (photoreceptor biomarker) was the primary endpoint measure. The greater the size of EZ loss the greater the photoreceptor loss. Healthy eyes have no EZ loss. Those with MT have a known historical rate of EZ loss over time. Encelto slowed the rate of EZ loss by -0.049 mm^2 /24 months & -0.091 mm^2 24/ months in each of the two treated groups. The control eye rate of EZ loss was .160 mm^2 / 24 months to 0.166 mm^2 / 24 months. This difference was statistically significant P<0.001) between treated and untreated eyes. There were 117 individuals in the treatment group and 116 in the control arms. The mean ages were 58 and 60 years old. Safety endpoints included loss of BCVA (best corrected visual acuity). BCVA loss was not statistically significantly different between treatment and controls groups. Self reported miosis and delayed dark adaptation were experienced in the treated eyes more than the controls. One participant had a suture related complication and vitreous hemorrhage, and another participant had device extrusion that was repositioned. No eye infections occurred. Overall this study showed Encelto efficacy with a 30.6 - 54.8% reduction in EZ area loss and adequate tolerability and safety.

Chew et al (2019). reported data a phase 2 study (NCT01949324) looking at safety & efficacy revakinagene therapy in subjects with bilateral macular telangiectasia type 2 This study was a prospective, multi-center, single-masked sham-controlled study. There were 68 participants, but only sixty-five participants completed the study; two participants died (unrelated to treatment) and three participants eyes were ineligible (either because of neovascularization or lesion size). All remaining study members were 21 to 80 years of age, with at least one study eye having a diagnosis of MT-2 (99 study eyes). Participants also had an IS/OS PR break and en face ellipsoid zone between 0.16 mm^2 and 4.00 mm^2. Participants meeting inclusion criteria were randomized (1:1) to receive NT-501 implant or sham procedure. Study eyes received NT-501 implant or sham procedure on Day 0 and are assessed at Day 1, week 1, month 1, month 3, month 6, month 12, month 18, and 24 months.

The primary endpoint was the difference in the area of neurodegeneration as measured by the change in the ellipsoid zone (area of IS/OS loss) assessed by en face imaging by SDOCT (spectral domain OCT). This measurement was carried out in the study eye(s) at month 24 and compared to baseline.

Secondary outcomes included comparisons of visual function between treated and untreated groups. Comparative changes in the ellipsoid zone from baseline to month 12, retinal sensitivity, and reading speed from baseline to months 12 and 24 were part of secondary outcomes. Other outcomes were proportion of study eyes with a 35% or more increase in the ellipsoid zone, best corrected visual acuity, proportion of study eyes with 15 or more letter loss in BCVA, proportion of study eyes with 10 or more letter loss in BCVA.

Study results: There was a 31 percent greater progression of neurodegeneration in the sham treated eye as compared to Encelto treated eyes. The mean retinal sensitivity loss in the sham group was 45% greater than the treated group. Reading speed in the sham group also deteriorated as compared to the treated group by 13.9 words per minute. Visual field testing and electroretinography suggested no major safety concerns. No implants required removal. Two adverse events likely related to CNTF were self -reported delayed dark adaptation (18.8%) and pupil miosis (18.8%).

The first clinical trial, NCT01327911, was a safety study of less than 10 patients as reported by Chew et al (2015). Key enrollment criteria were the presence of macular telangiectasia type 2 in adults ages 21 or older. The primary endpoint was ocular safety after Encelto implant. No implants required removal. Participants were evaluated by electroretinogram (ERG) and best corrected visual acuity. There were 4 participants with transient decrements in ERG parameters, but all returned to baselines by month 3. The study was not powered to answer questions about efficacy.

Singerman et al (2026) published results from combined, extended studies including participants form both NCT03071965 and NCT01327911 trials. Six participants from these studies were followed over 9 years after encelto was implanted to the worst of two eyes. The second untreated eye served as control. The combined studies were focused on phase 1 safety assessments. All implants were retained. Adverse events were assessed by comparing the disease course post encelto treatment with the natural course of disease looking for additional sequelae attributable to the implant. No study eyes had a BCVA (Best corrected visual acuity) loss of greater than 15 letters compared to

baseline, at any study visit up through month 96. One eye did have BCVA loss greater than 15 letters at month 108. BCVA was better in the treated eyes. No serious treatment emergent adverse events were noted. No new safety signals were seen. Although not powered for efficacy, the EZ loss was consistently lower in the treated eyes.

National and Specialty Organizations

This therapy is so recently approved that it does not appear in any guidelines to date.

SUPPLEMENTAL INFORMATION

The Ellipsoid Zone (EZ):
On a standard retinal imaging scan (OCT - a type of ultrasound for the eye), healthy photoreceptors produce a bright, continuous white line in the outer retina called the ellipsoid zone (EZ). This bright line corresponds to the junction between the inner and outer segments of photoreceptors. When this line is intact, photoreceptors are alive and functioning. When it becomes disrupted, thinned, or absent, photoreceptors are damaged or dead and vision is affected accordingly.

In macular telangiectasia type 2 photoreceptors die which is visible on OCT as a shrinking bright line and the size of that shrinking line is how disease is measured and whether treatments are working. The area of EZ loss on OCT is the single best structural marker of disease severity and progression in MT. It maps directly onto where patients have scotomas on visual field testing.

En Face Imaging:
Standard OCT gives you a cross-sectional side view of the retina. En face OCT instead gives a bird's-eye view from above, looking straight down at the ellipsoid zone. It shows the true geographic extent of photoreceptor loss rather than just one slice through it. In a healthy eye, a uniformly bright, uninterrupted surface is seen. In macular telangiectasia, the EZ lesion appears as a dark patch or void within that bright surface since the bright reflective signal is gone because the photoreceptors have died.

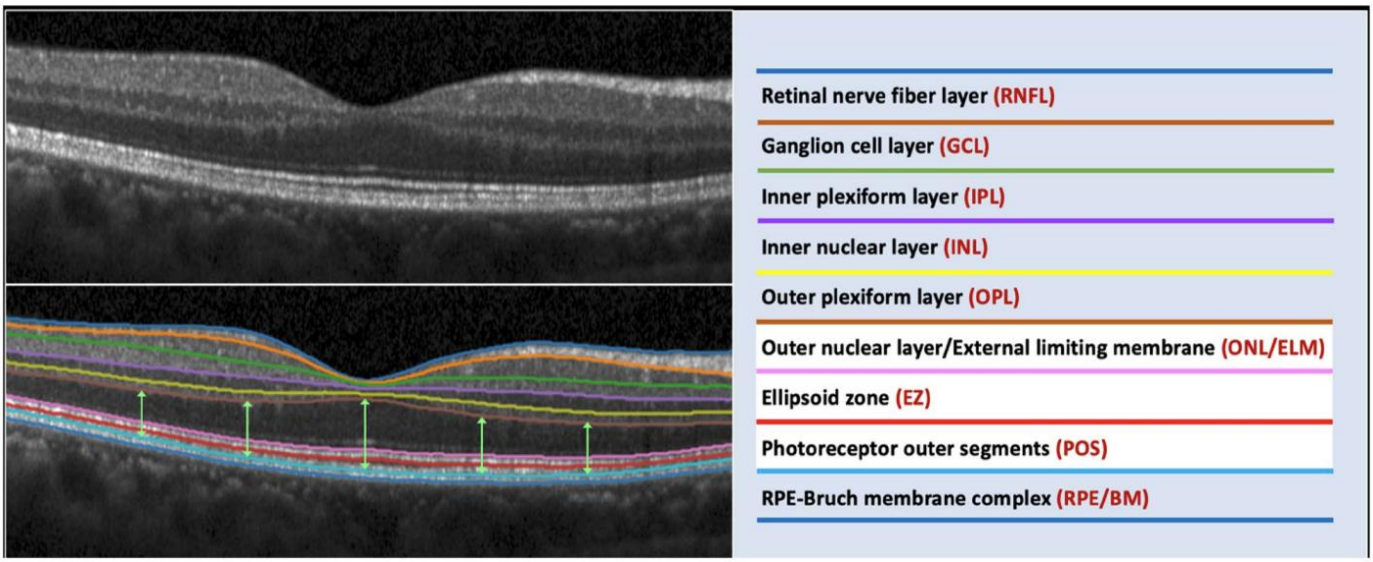

Figure 1. Graph showing the automatic delineation of the nine retinal layers and bands by optical coherence tomography and a deep learning and an interior point method-based algorithm. Nine layers of the retina were segmented, included the retinal nerve fiber layer (RNFL), the ganglion cell layer (GCL), the inner plexiform layer (IPL), the inner nuclear layer (INL), the outer plexiform layer (OPL), the outer nuclear layer/external limiting membrane (ONL/ELM), the ellipsoid zone (EZ), the photoreceptor outer segments band (POS), and the retinal pigment epithelium-Bruch membrane (RPE/BM). The photoreceptor layer is composed of three structures, including ONL, EZ and POS, shown as arrow (left figure), and the zones in white background (right figure). (Adopted from Wang et al, 2023)

AREDS (**Age-Related Eye Disease Study**)
The AREDS Clinical Lens Grading Protocol was developed for grading the presence and severity of nuclear, cortical and PSC lens opacities in a clinical setting. Details available at Chew et al (2010 - PMID: 20561686)

CODING & BILLING INFORMATION

CPT (Current Procedural Terminology)

Code	Description
67027	Implantation of intravitreal drug delivery system (e.g., ganciclovir implant), includes concomitant removal of vitreous

HCPCS (Healthcare Common Procedure Coding System)

Code	Description
J3403	Revakinagene taroretcel-lwey, per implant

CODING DISCLAIMER. Codes listed in this policy are for reference purposes only and may not be all-inclusive. Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement. Listing of a service or device code in this policy does not guarantee coverage. Coverage is determined by the benefit document. Molina adheres to Current Procedural Terminology (CPT®), a registered trademark of the American Medical Association (AMA). All CPT codes and descriptions are copyrighted by the AMA; this information is included for informational purposes only. Providers and facilities are expected to utilize industry standard coding practices for all submissions. When improper billing and coding is not followed, Molina has the right to reject/deny the claim and recover claim payment(s). Due to changing industry practices, Molina reserves the right to revise this policy as needed.

APPROVAL HISTORY

04/08/2026 No changes to criteria except correcting a typographical error and moving terminology definitions of ellipsoid zone to the supplemental section. Edited introduction for clarity and updated medical summary.
04/09/2025 New policy. IRO Peer Review on April 7, 2025 by a practicing physician board-certified in ophthalmology.

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