revakinagene taroretcel-lwey (Encelto™)

Medicare Advantage Medical Policy #MA-224
Original Effective Date: 09/01/2026
Current Effective Date: 09/01/2026

Applies to all products administered or underwritten by the Health Plan, unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

Blue Advantage does not cover investigational or experimental services, including any drug, device, procedure, or service provided under the investigational arm of a clinical trial or study unless mandated by the Centers for Medicare and Medicaid Services. Coverage is limited to routine services for Category A IDE studies and to devices and related services for Category B IDE studies when not supplied by the trial sponsor. Approved IDE studies are posted on www.cms.gov/medicare/coverage/evidence.

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on review of available data, the Health Plan may consider the use of revakinagene taroretcel-lwey (Encelto™)‡ for the treatment of adults with idiopathic macular telangiectasia (MacTel) type 2 to be **eligible for coverage.****

Patient Selection Criteria

Coverage eligibility for revakinagene taroretcel-lwey (Encelto) will be considered when ALL of the following criteria are met:

- Patient has documentation of a diagnosis of idiopathic Macular Telangiectasia Type 2 as evidenced by fluorescein leakage AND at least ONE of the following:
  - hyperpigmentation outside a 500-micron radius from the center of the fovea; OR
  - retinal opacification; OR
  - crystalline deposits; OR
  - inner/outer lamellar cavities; AND
- Patient is 18 years of age or older; AND
- Patient meets ONE of the following:
  - Patient has a best-corrected visual acuity (BCVA) of 54 letters or better using Early Treatment Diabetic Retinopathy Study (ETDRS) charts; OR
  - Patient has a best-corrected visual acuity (BCVA) of 20/80 or better using the Snellen chart; AND
- Patient has an inner segment/outer segment photoreceptor break (loss) in ellipsoid zone (EZ) between 0.16 and 2.00 mm^2 as measured by spectral domain-optical coherence tomography (SD-OCT); AND
- Patient does NOT have evidence of neovascular (proliferative) MacTel type 2; AND
- Patient has not previously received intravitreal gene therapy; AND
- Dose will not exceed one implant (200,000 to 440,000 allogeneic retinal pigment epithelial cells expressing rhCNTF) per affected eye

When Services Are Considered Not Medically Necessary

Based on review of available data, the Health Plan considers the use of revakinagene taroretcel-lwey (Encelto) when any of the following criteria are NOT met to be **not medically necessary.****

- Patient has documentation of a diagnosis of idiopathic Macular Telangiectasia Type 2 as evidenced by fluorescein leakage AND at least ONE of the following:
  - hyperpigmentation outside a 500-micron radius from the center of the fovea; OR
  - retinal opacification; OR
  - crystalline deposits; OR
  - inner/outer lamellar cavities
- Patient meets ONE of the following:
  - Patient has a best-corrected visual acuity (BCVA) of 54 letters or better using Early Treatment Diabetic Retinopathy Study (ETDRS) charts; OR
  - Patient has a best-corrected visual acuity (BCVA) of 20/80 or better using the Snellen chart
- Patient has an inner segment/outer segment photoreceptor break (loss) in ellipsoid zone (EZ) between 0.16 and 2.00 mm^2 as measured by spectral domain-optical coherence tomography (SD-OCT)
- Patient does NOT have evidence of neovascular MacTel type 2
- Patient has not previously received intravitreal gene therapy

When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Health Plan considers the use of revakinagene taroretcel-lwey (Encelto) when the patient selection criteria are not met (with the exception of those denoted above as **not medically necessary**)** to be **investigational.***

Background/Overview

Encelto is an allogeneic encapsulated cell-based gene therapy indicated for the treatment of adults with idiopathic macular telangiectasia type 2. Encelto is the first approved treatment for MacTel and a first-in-class cell-based therapy for retinal neurodegeneration. 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), 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 and slow disease progression; however, the mechanism of action for Encelto is not completely understood.

There are two primary forms of macular telangiectasia that have been identified. Both are associated with blood vessel abnormalities in the retina. MacTel type 1 is a very rare congenital disorder that occurs unilaterally and almost exclusively in males. Type 1 is associated with the dilation of blood vessels and the formation of aneurysms in various parts of the retina, which may leak fluid, resulting in macular edema. MacTel type 2 is a rare macular degenerative disease associated with the loss of Müller cells, which are responsible for growth factor secretion, angiogenesis/antiangiogenesis, neurotransmitter metabolism, synaptogenesis, neuroprotection, and photoreceptor survival. Over time, MacTel type 2 may progress to a proliferative (neovascular) form, affecting the macular vasculature and causing blood vessels surrounding the fovea (the center of the macula) to proliferate, dilate, and leak, ultimately leading to macular degeneration. The disease does not cause total blindness but significantly impacts quality of life due to progressive central vision loss. Type 2 is typically diagnosed in middle age and is more common in females. MacTel type 2 occurs bilaterally but may not affect each eye in the same way or to the same degree. In the United States, MacTel type 2 has a prevalence of about 0.1% in individuals over 40 years of age.

Rare but serious adverse reactions have occurred with Encelto, including suture-related complications and implant extrusion. Bilateral treatment with Encelto has been evaluated in a Phase 2 clinical trial. A quality control review of the results is continuing. According to Neurotech, preliminary safety results 6 months after insertion of the second implant demonstrate that bilateral treatment was generally safe and well tolerated, with visual acuity remaining relatively constant. All participants in the bilateral clinical trial had received a single Encelto implant during a prior clinical trial. Therefore, the implants were inserted at different points in time. It is unclear whether insertion of bilateral implants at the same time is advisable due to the potential for adverse effects.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)
Encelto was approved in March 2025 for the treatment of adults with idiopathic macular telangiectasia (MacTel) type 2.

Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, technology evaluation centers, reference to regulations, other plan medical policies, and accredited national guidelines.

The efficacy of Encelto was evaluated in two studies, Study 1 and Study 2. Enrollment criteria for both studies were identical. Patients were required to have at least one study eye with MacTel type 2, 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. In addition, 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.

Study 1
Study 1 was a randomized, multi-center, sham-controlled study which enrolled adults with MacTel. Patients were randomized to receive either Encelto intravitreal implant or sham procedure under standard operative procedures. 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. EZ loss is an indicator of PR disruption and macular health. At Month 24, the rate of change in EZ loss rate was 0.075 mm^2/year in the Encelto group and 0.166 mm^2/year in the sham group. This represents a statistical significance between groups with a difference: -0.091 mm^2/year (95% CI: −0.13 to −0.06; $p < 0.0001$), indicating a 54.8% reduction in photoreceptor degeneration

Study 2
Study 2 was a randomized, multi-center, sham-controlled study which enrolled adults with MacTel. Patients were randomized to receive either Encelto intravitreal implant or sham procedure under standard peri-operative procedures. 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

454 PR loss) over 24 months, as measured by SD-OCT. At Month 24, Encelto slowed EZ loss by 30.6% compared to sham. This was statistically significant, though less pronounced than the 54.8% reduction seen in Study 1.

References

1. Encelto [package insert]. Neurotech Pharmaceuticals, Inc. Cumberland, RI. Updated March 2025.
2. Encelto New Drug Review. IPD Analytics. Updated April 2025.

Policy History

Original Effective Date: 09/01/2026
Current Effective Date: 09/01/2026
06/16/2026 UM Committee review and approval. New policy.
Next Scheduled Review Date: 06/2027

Coding

The five character codes included in the Health Plan Medical Policy Coverage Guidelines are obtained from Current Procedural Terminology (CPT®)‡, copyright 2025 by the American Medical Association (AMA). CPT is developed by the AMA as a listing of descriptive terms and five character identifying codes and modifiers for reporting medical services and procedures performed by physician.

The responsibility for the content of the Health Plan Medical Policy Coverage Guidelines is with the Health Plan and no endorsement by the AMA is intended or should be implied. The AMA disclaims responsibility for any consequences or liability attributable or related to any use, nonuse or interpretation of information contained in the Health Plan Medical Policy Coverage Guidelines. Fee schedules, relative value units, conversion factors and/or related components are not assigned by the AMA, are not part of CPT, and the AMA is not recommending their use. The AMA does not directly or indirectly practice medicine or dispense medical services. The AMA assumes no liability for data contained or not contained herein. Any use of CPT outside of the Health Plan Medical Policy Coverage Guidelines should refer to the most current Current Procedural Terminology which contains the complete and most current listing of CPT codes and descriptive terms. Applicable FARS/DFARS apply.

Codes used to identify services associated with this policy may include (but may not be limited to) the following:

Code Type	Code
CPT	No codes
HCPCS	J3403
ICD-10 Diagnosis	All Related Diagnoses

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
    1. Consultation with technology evaluation center(s);
    2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
    3. Reference to federal regulations.

**Medically Necessary (or "Medical Necessity") - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

A. In accordance with nationally accepted standards of medical practice;
B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, "nationally accepted standards of medical practice" means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

NOTICE: If the Patient's health insurance contract contains language that differs from the Health Plan's Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Health Plan recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.

NOTICE: Federal and State law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage.

NOTICE: All codes listed on the Medical Policy require prior authorization. This ensures appropriate utilization and alignment with current clinical guidelines.

NOTICE: If an authorization for an ongoing course of treatment has been provided to a member and the member changes from one health plan to another health plan (e.g., a member moves from carrier A to Blue Advantage), Blue Advantage may honor the previous health plan's authorization for the same service under the same type of in-network benefit for a 90-day transition period. Documentation of the authorization for the ongoing course of treatment from the previous health plan must be provided to us by the member or their provider and the services provided for the course of treatment must otherwise be a covered service under the Blue Advantage health plan.

Medicare Advantage Members
Established coverage criteria for Medicare Advantage members can be found in Medicare coverage guidelines in statutes, regulations, National Coverage Determinations (NCD)s, and Local Coverage Determinations (LCD)s. To determine if a National or Local Coverage Determination addresses coverage for a specific service, refer to the Medicare Coverage Database at the following link: https://www.cms.gov/medicare-coverage-database/search.aspx. You may wish to review the Guide to the MCD Search here: https://www.cms.gov/medicare-coverage-database/help/mcd-bene-help.aspx.

When coverage criteria are not fully established in applicable Medicare statutes, regulations, NCDs or LCDs, internal coverage criteria may be developed. This policy is to serve as the summary of evidence, a list of resources and an explanation of the rationale that supports the adoption of this internal coverage criteria.