Molina Clinical Policy
Tregzi (allogeneic regulatory T cell immunotherapy with HSPC and T cells-vldq): MEDICARE
Policy No. 488b

Last Approval: 10/21/2026
Next Review Due By: August 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 the Federal government or CMS for Medicare. 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 covers the use of Tregzi in adults with hematologic malignancies undergoing allogeneic hematopoietic stem cell transplantation (HSCT). Tregzi is a donor-derived, HLA-matched, cell therapy intended to improve chronic graft-versus-host disease (cGVHD)-free survival, while reconstituting both hematopoietic and immunologic systems (Tregzi prescribing information, 2026).

Allogeneic hematopoietic stem cell transplantation is a potentially curative treatment for several high-risk hematologic malignancies, including acute myeloid leukemia (AML), acute lymphoblastic leukemia (ALL), myelodysplastic syndrome (MDS), and other blood cancers. Although transplantation can eradicate malignant hematopoietic cells and restore normal blood formation, it carries the risk of graft-versus-host disease (GVHD), one of the most serious complications of the procedure. GVHD occurs when immunocompetent donor T lymphocytes recognize the recipient's tissues as foreign and mount an immune response against them. Chronic GVHD is a complex immune-mediated disorder characterized by persistent inflammation, immune dysregulation, and fibrosis that can affect multiple organ systems (Yishan et al 2026). Unlike acute GVHD, which generally develops within the first 100 days after transplantation, chronic GVHD typically develops months after transplant and can follow a prolonged, relapsing, or progressive course. Chronic GVHD is associated with substantial morbidity, reduced quality of life, prolonged need for immunosuppressive therapy, recurrent infections, and increased non-relapse mortality.

Historically, chronic GVHD develops in approximately 30% to 70% of transplant recipients and remains a leading cause of long-term morbidity among transplant survivors (Yishan et al. 2026). More than 8,000 allogeneic hematopoietic stem cell transplants are performed annually in the United States for hematologic malignancies (Spellman et al.2025).

Standard prophylaxis against GVHD following allogenic HSCT generally consists of pharmacologic immunosuppressive regimens, commonly involving calcineurin inhibitors such as tacrolimus in combination with agents including methotrexate, mycophenolate mofetil, post-transplant cyclophosphamide, or other immunosuppressive therapies. Although these approaches reduce GVHD risk, they do not eliminate it and may delay immune reconstitution while increasing susceptibility to bacterial, viral, and fungal infections (Meyer et al. 2026). Patients who develop chronic GVHD often require prolonged corticosteroid therapy and additional immunosuppressive treatments, which can further contribute to treatment-related morbidity.

Tregzi represents a novel cellular-engineering approach to GVHD prevention. Rather than primarily relying on broad pharmacologic immune suppression, Tregzi leverages regulatory T-cell biology to promote immune tolerance and reduce chronic GVHD. This approach addresses a major unmet need in the care of patients undergoing curative transplantation for hematologic malignancies. Tregzi also preserves engraftment, immune reconstitution, and graft-versus-leukemia activity. Tregzi manufacturing isolates the different cell components (regulatory T cells (Tregs) and conventional T cells (Tcons)) and gives them to the recipient in a unique order (Tregs first) to promote the Treg effect and enhance immune downregulation prior to giving the conventional T cells. Tacrolimus is still used in Tregzi therapy but after infusing conventional T-cells.

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COVERAGE POLICY

All transplants require prior authorization from the Corporate Transplant Department. Solid organ transplant requests will be reviewed by the Corporate Senior Medical Director or qualified clinical designee. All other transplants will be reviewed by the Corporate Senior Medical Director or covering Medical Director. If the criteria are met using appropriate NCD and/or LCD guidelines, State regulations, and/or MCP policies the Corporate Senior Medical Director's designee can approve the requested transplant.

Office visits with participating Providers do NOT require prior authorization. Providers should see the Member in office visits as soon as possible and without delay. Failure to see the Member in office visits may be considered a serious quality of care concern.

Criteria for Tregzi
Tregzi may be **considered medically necessary** when ALL the following criteria are met:

1. Approved for allogeneic HSCT using a myeloablative conditioning regimen, as defined by NCCN (e.g., TBI ≥5 Gy single dose or ≥8 Gy fractionated; or busulfan >8 mg/kg PO, >6.4 mg/kg IV, or plasma-exposure equivalent). Regimens used in the pivotal trial include, but are not limited to:
   a. TBI/Cy (Total Body Irradiation plus Cyclophosphamide)
   b. TBI/Etoposide (Total Body Irradiation plus Etoposide)
   c. BFT (Busulfan, Fludarabine, and Thiotepa)
   (Note: Other myeloablative regimens selected by the treating transplant program are acceptable. Reduced-intensity and non-myeloablative regimens are not covered.)

2. Member has an 8/8 match for HLA-A, -B, -C, and DRB1 related or unrelated donor

3. Member is diagnosed with ONE of the following:
   a. Acute myeloid, lymphoid, or mixed phenotype leukemia in complete remission (CR) or CR with incomplete hematologic recovery, with or without the presence of known minimal residual disease
   b. Myelodysplastic syndromes (MDS) and/or have therapy-related/secondary MDS, with ≤ 10% blast burden in the bone marrow

4. Member is 18 years of age or older

5. Member has not had a prior allogeneic HSCT

6. Member is not currently receiving corticosteroids or other immunosuppressive therapy. Note: Topical corticosteroids or oral systemic corticosteroid doses ≤ 10 mg/day are allowed.

7. Member does not have a planned donor lymphocyte infusion (DLI)

8. Member does not have a planned pharmaceutical in vivo or ex vivo T cell depletion
9. Member does not have positive anti-donor HLA antibodies against a mismatched allele in the selected donor

10. Member does not have a documented allergy or hypersensitivity to ANY of the following:
    a. Iron dextran or bovine, murine, algal or Streptomyces avidinii proteins
    b. Tacrolimus

QUANTITY LIMITATIONS: Provided as a single dose. Each dose has multiple components with each component administered once and is patient specific. Additional infusions of Tregzi will not be authorized.

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CONTINUATION OF THERAPY: Tregzi is indicated as a one-time infusion only. Repeat administration has not been studied and safety and efficacy of additional doses have not been established; additional infusions are therefore not authorized.

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

In the pivotal Phase 3 PRECISION-T trial, (NCT05316701) Tregzi demonstrated substantial improvements compared with conventional transplantation. All trial participants had either acute leukemias or myelodysplastic syndrome and met criteria for allogeneic hematopoietic stem cell transplant. The comparator in the clinical trial was a conventional, unmanipulated peripheral blood graft using tacrolimus plus methotrexate. The total number of participants were 187. There were 93 participants in the Tregzi cohort and 94 in standard allogenic HSCT with tacrolimus and methotrexate (Meyer et al. (2026)). The primary endpoint was survival free from moderate to severe chronic GVHD. At one year, chronic GVHD-free survival was achieved in 78% of Tregzi-treated patients compared with 38.4% of patients receiving standard transplantation, while moderate-to-severe chronic GVHD occurred in 12.6% versus 44.0%, respectively. Overall survival was 93.9% with Tregzi versus 83.1% with standard graft with tacrolimus and methotrexate. In addition, there were significantly less infectious complications and less nonrelapse mortality in the Tregzi group. These findings suggest that Tregzi may improve long-term transplant outcomes by decreasing the incidence of chronic GVHD, reducing dependence on prolonged immunosuppression, and preserving effective hematopoietic recovery.

The Phase 1b PRECISION-T trial (NCT04013685) was a multicenter study that evaluated the safety, tolerability, and preliminary efficacy of Orca-T, a donor-derived cellular therapy composed of purified hematopoietic stem and progenitor cells, regulatory T cells, and conventional T cells, in 155 patients undergoing myeloablative allogeneic hematopoietic stem cell transplantation for hematologic malignancies, including AML, ALL, MDS, CML, and BPDCN (Blastic Plasmacytoid Dendritic Cell Neoplasm). Results demonstrated successful engraftment, favorable immune reconstitution, low rates of acute and chronic graft-versus-host disease (GVHD), and encouraging relapse-free survival, supporting the hypothesis that regulatory T-cell enrichment can reduce alloreactive immune responses without compromising graft-versus-leukemia activity. The favorable safety and efficacy signals observed in this study provided the foundation for the subsequent randomized Phase 3 PRECISION-T trial (NCT05316701), which ultimately supported FDA approval of Tregzi.

Several ongoing and planned studies continue to evaluate Orca-T/Tregzi across a range of transplant settings and hematologic malignancies, including the Phase 2 SERENE-T trial (NCT07216443), a Phase 1 study in patients with advanced hematologic malignancies undergoing allogeneic hematopoietic cell transplantation (NCT06551584), a Phase 1 study evaluating Orca-T in combination with donor-derived CD19/CD22 CAR-T cells in B-cell acute lymphoblastic leukemia (NCT05507827), a Phase 1 study of Orca-T following chemotherapy and total marrow and lymphoid irradiation (NCT06195891), a Phase 1 study of reduced-intensity allogeneic transplantation using a T-cell-depleted graft with regulatory T-cell augmentation (NCT05088356), and an Expanded Access Program for patients with advanced hematologic malignancies (NCT07346105).

National and Specialty Organizations

Tregzi was only recently approved and guidelines to date do not mention its use in clinical practice.

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CODING & BILLING INFORMATION

CPT (Current Procedural Terminology)

Code	Description
96413	Chemotherapy administration, intravenous infusion technique; up to 1 hour, single or initial substance/drug
96415	Chemotherapy administration, intravenous infusion technique; each additional hour (List separately in addition to code for primary procedure)
81378	HLA Class I and II typing, high resolution (i.e., alleles or allele groups), HLA-A, -B, -C, and -DRB1

HCPCS (Healthcare Common Procedure Coding System)

Code	Description
C9399	Unclassified drugs or biologicals [when specified as Tregzi (allogeneic regulatory T cell immunotherapy with HSPC and T cells-vldq)]
J3590	Unclassified biologics [when specified as Tregzi (allogeneic regulatory T cell immunotherapy with HSPC and T cells-vldq)]

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

10/21/2026 New policy. IRO peer review completed on 8/10/26 by a practicing physician board certified in Hematology and Medical Oncology.

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