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of the Blue Cross and Blue Shield Association

Medical benefit drug policies are a source for BCBSM and BCN medical policy information only. These documents are not to be used to determine benefits or reimbursement. Please reference the appropriate certificate or contract for benefit information. This policy may be updated and therefore subject to change.

P&T Date: 08/13/2026

Tregzi™ (allogeneic regulatory T cell immunotherapy with HSPC and T cells-vldq)

HPCPS: J3590

Policy:

Requests must be supported by submission of chart notes and patient specific documentation.

- A. Coverage of the requested drug is provided when all the following are met:
 - a. FDA approved indication
 - b. FDA approved age
 - c. Prescribed by or in consultation with an oncologist/hematologist
 - d. Matched to a related or unrelated donor who is an 8/8 match for HLA-A, -B, -C, and DRB1
 - e. Plan to undergo myeloablative conditioning
 - f. Must not have any of the following:
 - i. Prior allogeneic hematopoietic stem cell transplant (HSCT)
 - ii. Active infection (e.g. viral, bacterial, fungal) such as CMV, HIV, active hepatitis B or active hepatitis C
 - iii. Any uncontrolled autoimmune disease requiring active immunosuppressive treatment
 - g. Must not have received prior treatment with Tregzi or any other purified regulatory T-cell therapy for the treatment of hematologic malignancies
 - h. Trial and failure, contraindication, OR intolerance to the preferred drugs as listed in BCBSM/BCN's utilization management medical drug list
 - i. Only to be administered at certified bone marrow/stem cell transplant centers
 - j. The requesting physician attests to providing clinical outcome information within the appropriate provider portal as requested by BCBSM
 - k. If new diagnoses are FDA-approved, coverage will be determined based on the FDA approved indication on a case-by-case basis until fully evaluated by the BCBSM Pharmacy and Therapeutics Committee
- B. Quantity Limitations, Authorization Period and Renewal Criteria
 - a. Quantity Limits: Align with FDA recommended dosing
 - b. Authorization Period: Aligns with FDA recommended or guideline supported treatment duration and provided for at least 60 days and up to 6 months at a time with the allowance of only one dose per lifetime
 - c. Renewal Criteria: Not applicable as no further authorization will be provided.

This policy and any information contained herein is the property of Blue Cross Blue Shield of Michigan and its subsidiaries, is strictly confidential, and its use is intended for the P&T committee, its members and BCBSM employees for the purpose of coverage determinations.

***Note: Coverage and approval duration may differ for Medicare Part B members based on any applicable criteria outlined in Local Coverage Determinations (LCD) or National Coverage Determinations (NCD) as determined by Center for Medicare and Medicaid Services (CMS). See the CMS website at <http://www.cms.hhs.gov/>. Determination of coverage of Part B drugs is based on medically accepted indications which have supported citations included or approved for inclusion determined by CMS approved compendia.

Background Information:

- Tregzi is an allogeneic regulatory T cell-based immunotherapy with hematopoietic stem and progenitor cells and T cells indicated for use in matched donor HSCT with myeloablative preparative regimen, for hematopoietic and immunologic reconstitution and to improve chronic graft-versus-host disease (cGVHD)-free survival, in the treatment of adults with hematological malignancies.
- Hematological malignancies cause uncontrolled growth of unhealthy cells in the bone marrow where blood cells are made. They can broadly be categorized as different types of leukemias, lymphomas and myelomas. The Center for International Blood and Marrow Transplant Research (CIBMTR) reported over 23,000 HSCT in 2023, with a significant portion for blood cancers like leukemia. cGVHD occurs in approximately 40% - 50% of patients with hematologic malignancies who undergo allo-HSCT. It is the leading cause of late non-relapse mortality and long-term morbidity in these survivors. Acute myeloid leukemia (AML) is rapidly progressing cancer that starts in the bone marrow and results in an overproduction of abnormal white blood cells. AML is the most common acute leukemia in adults, with about 22,000 new cases diagnosed each year. The percentage of AML patients receiving HSCT more than doubled in the U.S. from 2010 (11.9%) to 2023 (24.5%). Acute lymphoblastic leukemia (ALL) is a fast-growing cancer that affects immature white blood cells (lymphoblasts) in the bone marrow. ALL is the most common leukemia in children under 15, but is rare in adults, with about 3,000-6,000 new cases annually in the U.S. Myelodysplastic syndrome (MDS) is a group of diseases that prevent the bone marrow from producing enough healthy blood cells and can develop into leukemia. Around 12,000 to 15,000 new cases are diagnosed each year in the U.S. and an estimated 10% of these patients receiving HSCT.
- The FDA approval for Tregzi is based on results from the pivotal Phase III study, Precision-T, a randomized, open-label, multi-center study that evaluated the safety, efficacy and tolerability of Tregzi compared to conventional allogeneic hematopoietic stem cell transplant (alloHSCT) in 187 adult (age 18-65) patients with AML, ALL mixed-phenotype acute leukemia (MPAL), and MDS. Patients must have been matched to the related or unrelated donor at an 8/8 HLA-A, -B, -C, and DRB1 match and have had planned to undergo myeloablative conditioning with total body irradiation (TBI)/cyclophosphamide (Cy), TBI/etoposide, or busulfan/fludarabine/thiotepa (BFT). For patients in the Tregzi arm, Tregzi was administered after myeloablative conditioning regimen; single-agent GVHD prophylaxis with tacrolimus was administered following Tregzi infusion (generally Day +3). A standard care arm of unmanipulated donor allograft with dual-agent tacrolimus and methotrexate GVHD prophylaxis was used for comparison. In the Precision-T trial key exclusion criteria included prior alloHSCT, being seropositive for HIV-1 or -2, HTLV-1 or -2, hepatitis B sAg, or hepatitis C antibody, and any uncontrolled autoimmune disease requiring active immunosuppressive treatment.
 - The primary endpoint, survival free of moderate-to-severe cGVHD, was met with a 1-year rate of outcome at 78% (95% CI: 65%, 87%) in the Tregzi plus single-agent tacrolimus group vs 38.4% (95% CI: 26%, 51%) in the standard care arm plus tacrolimus/methotrexate group ($p < 0.00001$).
 - A secondary endpoint of cumulative incidence of moderate-to-severe cGVHD was 12.6% (95% CI: 5%, 23%) and 44.0% (95% CI: 31%, 56%) in the Tregzi and alloHSCT arms, respectively ($p < 0.00002$).
 - The overall survival (OS), another secondary endpoint, was 93.7% (95% CI: 86%, 97%) in the Tregzi arm and 83.2% (95% CI: 73%, 90%) in the alloHSCT arm though results only trended towards significance ($p = 0.11823$).

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- A secondary endpoint of GVHD and relapse-free survival (GRFS) was 63.1% and 30.9% with Tregzi and alloHSCT (p<0.001 in a post hoc analysis), respectively.
- The cumulative incidence of non-relapse mortality (NRM) was 3.4% (95% CI: 0.9%, 8.8%) for Tregzi versus 13.2% (95% CI: 6.8%, 21.6%) for alloHSCT ([95% CI: 0.08, 0.93]; p=0.03 in a post hoc analysis).
- The National Comprehensive Cancer Network (NCCN) guidelines for hematopoietic cell transplantation (Version 2.2026 – April 3, 2026) recommend HSCT for a variety of blood cancers and mention the most common malignancies treated with alloHSCT include AML, MDS, myeloproliferative neoplasms (MPN), and ALL. The appropriateness of HSCT varies with the type of malignancy and remission status, so disease- specific NCCN guidelines should be consulted to determine the appropriate timing of this treatment. Hematopoietic stem cells for allogeneic transplant can be obtained from peripheral blood, bone marrow, or umbilical cord blood (UCB). Several clinical factors should be considered when choosing an optimal graft source including disease state, disease stage, patient comorbidities, and the urgency for transplantation. The use of peripheral blood progenitor cells (PBPC) has largely replaced the use of bone marrow grafts (in particular for autologous HSCT) due to the ease of collection, avoidance of general anesthesia, more rapid engraftment rates, and reduced risk of graft failure. However, allogeneic PBPC transplants are associated with an increased risk of cGVHD compared to bone marrow transplants. There are three potential donor sources for hematopoietic cells: related donor (family members), unrelated volunteers (from donor registries), and UCB units. HLA matching is the most important factor when choosing a donor and HLA-matched siblings remains the preferred donor source, although post-transplant survival is comparable among patients receiving hematopoietic cells from HLA-matched unrelated donors. cGVHD is the leading cause of NRM after alloHSCT. Optimal GVHD care is best delivered by a multidisciplinary team, preferably in medical centers with access to specialized transplant services. Systemic corticosteroids are a mainstay of treatment for GVHD. Steroid-refractory GVHD, even after significant progress with recent FDA approval of several agents, remains associated with significant morbidity, poor quality of life, increased health care costs, and significant mortality. The guidelines suggest that continued research to improve risk stratification, develop new therapies, and enhance supportive care is needed. The guidelines have not been updated to include Tregzi.
- Tregzi is for intravenous use only. A single dose of Tregzi consists of hematopoietic stem and progenitor cells (HSPCs), regulatory T cells (Tregs), conventional T cells (Tcons), and Tcon diluent provided in 4 separate infusion bags labeled for the specific patient. Each patient-specific infusion bag of Tregzi contains a batch dependent concentration of allogeneic cells. Patient-specific dose information can be found within the Certificate of Analysis (COA).
 - HSPCs – intravenous, once, on day 0
 - Tregs – intravenous , once, on day 0 immediately after administration of HSPCs
 - Tcons – intravenous, once, on day +2 to +3 (after the start of HSPC infusion on day 0)
 - Tcon diluent – intravenous, once, administered with Tcons drug product on day +2 to +3 (after HSPC infusion on day 0)
- An appropriate myeloablative preparative regimen should be administered before infusion of Tregzi. The use of corticosteroids as premedication is strongly discouraged per the prescribing information.

References:

1. Tregzi [prescribing information]. Sacramento, CA. Orca Biosystems Inc. June 2026
2. National Comprehensive Cancer Network. Hematopoietic Cell Transplantation (HCT) (Version 2.2026). April 3, 2026. Available at: <https://www.nccn.org> Accessed on July 7, 2026.
3. Ortner N, Holzer H. 2025 U.S. organ and tissue transplants: estimated costs and utilization, emerging issues, and solutions. Milliman; February 2025. Accessed July 2, 2026. Available at: <https://www.milliman.com/en/insight/2025-us-organ-and-tissue-transplants-costs-utilization>
4. Baumrin E, Loren AW, Falk SJ, Mays JW, Cowen EW. Chronic graft-versus-host disease. Part I: Epidemiology, pathogenesis, and clinical manifestations. J Am Acad Dermatol. 2024 Jan;90(1):1-16. doi: 10.1016/j.jaad.2022.12.024. Epub 2022 Dec 23. Retraction in: J Am Acad Dermatol. 2026 Jan 30:S0190-9622(26)00117-9. doi: 10.1016/j.jaad.2026.01.065. PMID: 36572065; PMCID: PMC10287844.
5. Elsevier. Chronic graft versus host disease. ScienceDirect Topics. Accessed July 8, 2026. <https://www.sciencedirect.com/topics/pharmacology-toxicology-and-pharmaceutical-science/chronic-graft-versus-host-disease>
6. Idoroenyi Amanam, Salman Otoukesh, Monzr M. Al Malki, Amandeep Salhotra; Chronic GVHD: review advances in prevention, novel endpoints, and targeted strategies. Hematology Am Soc Hematol Educ Program 2023; 2023 (1): 164–170. doi: <https://doi.org/10.1182/hematology.2023000427>

Policy History												
#	Date	Change Description										
1.2	Effective Date: 08/13/2026	New policy. This criteria replaces previously approved preliminary criteria.										
1.1	Effective Date: 08/03/2026	UM medical management system update for MAPPO and BCNA <table><tr><th>Line of Business</th><th>PA Required in Medical Management System (Yes/No)</th></tr><tr><td>BCBS</td><td>Yes</td></tr><tr><td>BCN</td><td>Yes</td></tr><tr><td>MAPPO</td><td>Yes</td></tr><tr><td>BCNA</td><td>Yes</td></tr></table>	Line of Business	PA Required in Medical Management System (Yes/No)	BCBS	Yes	BCN	Yes	MAPPO	Yes	BCNA	Yes
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BCBS	Yes											
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1.0	Effective Date: 07/13/2026	UM medical management system update for BCBS and BCN <table><tr><th>Line of Business</th><th>PA Required in Medical Management System (Yes/No)</th></tr><tr><td>BCBS</td><td>Yes</td></tr><tr><td>BCN</td><td>Yes</td></tr><tr><td>MAPPO</td><td>No</td></tr><tr><td>BCNA</td><td>No</td></tr></table>	Line of Business	PA Required in Medical Management System (Yes/No)	BCBS	Yes	BCN	Yes	MAPPO	No	BCNA	No
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MAPPO	No											
BCNA	No											

* The prescribing information for a drug is subject to change. To ensure you are reading the most current information it is advised that you reference the most updated prescribing information by visiting the drug or manufacturer website or <http://dailymed.nlm.nih.gov/dailymed/index.cfm>.

Blue Cross Blue Shield/Blue Care Network of Michigan
Medication Authorization Request Form



This form is to be used by participating physicians to obtain coverage for **drugs covered under the medical benefit**. For commercial members only, please complete this form and submit via fax to 1-877-325-5979. If you have any questions regarding this process, please contact BCBSM Provider Relations and Servicing or the Medical Drug Helpdesk at 1-800-437-3803 for assistance.

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PATIENT INFORMATION	PHYSICIAN INFORMATION
Name	Name
ID Number	Specialty
D.O.B. ☐ Male ☐ Female	Address
Diagnosis	City /State/Zip
Drug Name	Phone/Fax: P: () - F: () -
Dose and Quantity	NPI
Directions	Contact Person
Date of Service(s)	Contact Person Phone / Ext.

STEP 1: DISEASE STATE INFORMATION

- Is this request for: ☐ Initiation ☐ Continuation *Date patient started therapy:* _____
- Administered by patient or a medical professional? ☐ patient (self) ☐ health care professional (physician, nurse, etc.)
- Site of administration? ☐ Provider office/Home infusion ☐ Other: _____
☐ Hospital outpatient facility (go to #4) *Reason for Hospital Outpatient administration:* _____
☐ Hospital inpatient facility for Car-T therapy only (for example: Kymriah, Yescarta, or Tecartus) (go to #5)
- Please specify location of administration if hospital outpatient infusion: _____
- Please specify location of administration if hospital inpatient infusion: _____
- Please provide the NPI number for the place of administration: _____
- Initiation AND Continuation of therapy:**
 - What is the patient's diagnosis? _____
 - What other medication has the patient received for their condition? Please list _____
 - Please describe the response to previous therapies: _____
 - Will the patient be receiving any other treatment for the listed condition while on this medication? Please list: _____
 - Please list any labs values important for diagnosing or monitoring this patient's condition: _____
- Continuation of therapy:**
 - Has the patient progressed while on this medication? ☐ yes ☐ no
 - How has the patient's condition changed while on this medication?
☐ Improved: Please describe: _____
☐ Stable: please describe: _____
☐ Worsened; Please describe: _____
☐ Other; Please describe: _____

Chart notes are required for the processing of all requests. Please add any other supporting medical information necessary for our review (required)

Coverage will not be provided if the prescribing physician's signature and date are not reflected on this document.

☐ Request for expedited review: I certify that applying the standard review time frame may seriously jeopardize the life or health of the member or the member's ability to regain maximum function

Physician's Name	Physician Signature	Date
Step 2: Checklist	☐ Form Completely Filled Out ☐ Provide chart notes	☐ Attach test results
Step 3: Submit	By Fax: BCBSM Specialty Pharmacy Mailbox 1-877-325-5979	By Mail: BCBSM Specialty Pharmacy Program P.O. Box 312320, Detroit, MI 48231-2320

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7/26/2018, 9/18/2018; 1/31/2020; 3/17/2020; 8/9/2021