Pharmacy Drug Policy

SUBJECT: Tregzi (allogeneic regulatory T cell immunotherapy with HSPC and T cells-vldq)
POLICY NUMBER: PHARMACY-134
EFFECTIVE DATE: 08/2026
LAST REVIEW DATE: 09/25/2026

If the member's subscriber contract excludes coverage for a specific service or prescription drug, it is not covered under that contract. In such cases, medical or drug policy criteria are not applied. This drug policy applies to the following line/s of business:

Policy Application

Category:	☒ Commercial Group (e.g., EPO, HMO, POS, PPO)	☒ Medicare Advantage
	☒ On Exchange Qualified Health Plans (QHP)	☐ Medicare Part D
	☒ Off Exchange Direct Pay	☒ Essential Plan (EP)
	☒ Medicaid & Health and Recovery Plans (MMC/HARP)	☒ Child Health Plus (CHP)
	☐ Federal Employee Program (FEP)	☐ Ancillary Services
	☒ Dual Eligible Special Needs Plan (D-SNP)	

DESCRIPTION:

Tregzi (allogeneic regulatory T cell immunotherapy with HSPC and T cells-vldq) is an allogeneic regulatory T-cell based immunotherapy containing hematopoietic stem and progenitor cells (HSPCs) and T cells indicated for the treatment of hematological malignancies while improving chronic graft-versus-host disease (cGVHD)-free survival in matched donor hematopoietic stem cell transplantation with myeloablative preparative regimen.[1] Administration of Tregzi involves four separate infusion bags for intravenous infusion: HSPCs, regulatory T cells (Tregs), conventional T cells (Tcons), and Tcon diluent. Its recommended dose is a single intravenous infusion of ≥1.0 × 10^6 HSPCs per kg, 1.3 × 10^6 to 3.5 × 10^6 Tregs per kg, and 1.3 × 10^6 to 3.5 × 10^6 Tcons per kg.

Chronic graft-versus-host disease is a major complication of allogeneic hematopoietic stem cell transplant (HSCT) that affects approximately 30% to 70% of HSCT recipients.[2] The condition is characterized by an immune-mediated response that leads to chronic inflammation and fibrosis of multiple organs.[2,3] Management of cGVHD involves treatment with immunosuppressants such as steroids and calcineurin inhibitors.

Approval of Tregzi was supported by the PRECISION-T Phase III Trial where 187 subjects between the ages of 18 and 65 years were enrolled and randomized to receive either Tregzi with single agent tacrolimus or a control arm comprised of a peripheral blood stem cell allograft with tacrolimus and methotrexate (Tac/MTX).[4,5] Subjects were diagnosed with either acute leukemia or myelodysplastic syndrome and received myeloablative conditioning. The primary endpoint evaluated survival free from moderate-to-severe cGVHD (cGFS). Patients treated with Tregzi at the one-year follow-up demonstrated 78% cGFS compared to 38.4% in the convention stem cell transplant plus Tac/MTX arm. Additional efficacy endpoints highlighted a 63.1% cGVHD and relapse-free survival at one year compared to 30.9%, respectively.

Warnings and precautions include a risk of graft failure, GVHD, infusion reactions, secondary malignancies and malignancies of donor origins, and transmission of infectious agents.[1] For further reduction in risk of developing GVHD, it is recommended that patients are treated with a single agent calcineurin inhibitor as prophylaxis. Adverse reactions were generally consistent with conventional hematopoietic stem cell transplants – some of the most common adverse reactions with incidence ≥20% were infections, gastrointestinal disorders (diarrhea, abdominal pain, vomiting, nausea), mucositis, and rash.[1,4]

POLICY:

Tregzi (allogeneic regulatory T cell immunotherapy with HSPC and T cells-vldq) – Medical Benefit
1. Must be prescribed by a hematologist, oncologist, or physician experienced in the treatment of hematologic malignancies **AND** 2. The patient must be eligible for an allogeneic hematopoietic (stem) cell transplant (HSCT) **AND** 3. The patient must receive therapy at an authorized treatment center **AND** 4. Must be at least 18 years of age **AND** 5. Must be diagnosed with one of the following: a. Acute myeloid, lymphoid, or mixed phenotype/undifferentiated leukemia in complete remission (CR) or in complete remission with incomplete hematologic recovery (CRi); See appendix for definitions of CR and CRi b. Myelodysplastic syndromes (MDS) with ≤ 10% blast burden in the bone marrow; **AND** 6. Consideration may be given to other hematological malignancies for which myeloablative allogeneic HSCT is an established treatment per NCCN guidelines 7. Provider must attest the patient will be treated with at least a single agent calcineurin inhibitor (such as tacrolimus) as prophylaxis to decrease the risk of graft versus host disease (GHVD) **AND** 8. Must have been screened and found seronegative for HIV-1 or -2 antibody, HTLV-1 or -2 antibody, Hepatitis B sAg, and Hepatitis C antibody **AND** 9. Must have a matched related or unrelated donor who is an 8/8 match for HLA-A, -B, -C, and DRB1 **AND** 10. Tregzi will not be authorized if the patient meets any of the following: a. Patient had a prior allogeneic hematopoietic stem cell transplant b. Hematopoietic cell transplantation-specific Comorbidity Index (HCT-CI) >4 c. Any uncontrolled autoimmune disease requiring active immunosuppressive treatment d. Current uncontrolled bacterial, viral, or fungal infection 11. Tregzi is indicated for one-time intravenous administration only and therefore will not be authorized for retreatment. Retreatment will be considered experimental/investigational when any FDA approved gene or cellular therapy, or any other gene or cellular therapy under investigation, has been previously administered 12. Tregzi is considered investigational for all other non-FDA approved indications 13. Approval will be for 6 months to allow one-time administration

POLICY GUIDELINES:

1. Utilization Management is contract dependent. Refer to specific contract/benefit language for exclusions.
   a. Coverage criteria may be dependent on the contract renewal date.
   b. Coverage of drugs listed in this policy are contract dependent.
   c. Not all contracts/benefits allow coverage of healthcare professional administered drugs as part of their pharmacy benefit
   d. Not all contracts/benefits cover all medical infusible drugs.
2. Clinical documentation must be submitted for each request (initial and recertification [if applicable]) unless otherwise specified (e.g., provider attestation required). Supporting documentation includes, but is not limited to, progress notes documenting previous treatments and treatment history, diagnostic testing, laboratory test results, genetic testing or biomarker results, imaging and other objective or subjective measures of benefit. Requested dosing must remain consistent with FDA-approved dosing recommendations.

3. This policy does not apply to Medicare Part D and D-SNP pharmacy benefits. The drugs in this policy may apply to all other lines of business including Medicare Advantage.
4. Unless otherwise indicated within drug specific criteria, the drugs listed in this policy are administered by a healthcare professional and therefore are covered under the medical benefit.
5. All utilization management requirements outlined in this policy are compliant with applicable New York State insurance laws and regulations. Policies will be reviewed and updated as necessary to ensure ongoing compliance with all state and federally mandated coverage requirements.
6. For commercial contracts, medical necessity determinations align with the Certificate of Coverage issued by the Health Plan, which states that covered services must be clinically appropriate and not primarily for the convenience of the member, the member's family, or the provider.
7. This policy is based on available evidence as of the last review date. Coverage determinations are subject to applicable plan documents, state and federal regulations, and individual patient circumstances. This policy does not constitute medical advice.
8. This policy is subject to ongoing revision. Newly marketed drugs and existing drugs with new indications may be subject to prior authorization until formal coverage criteria are established. Inclusion of a drug in this policy does not guarantee its current availability on the market, as some agents may be discontinued, withdrawn, or otherwise unavailable. As product status changes, drugs may be removed from the policy.
9. For members with Medicare Advantage, medications with a National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) will be covered pursuant to the criteria outlined by the NCD and/or LCD. NCDs/LCDs for applicable medications can be found on the CMS website at https://www.cms.gov/medicare-coverage-database/search.aspx. In the absence of a Medicare National Coverage Determination (NCD), Local Coverage Determination (LCD), or other Medicare coverage guidance, CMS permits a Medicare Advantage Organization (MAO) to establish its own coverage determinations in accordance with 42 CFR § 422.101(b)(6). Indications that have not been addressed by the applicable medication's LCD/NCD will be covered in accordance with criteria determined by the Health Plan. Step therapy requirements may be imposed in addition to LCD/NCD requirements.
10. Manufacturers may either discontinue participation in, or may not participate in, the Medicaid Drug Rebate Program (MDRP). Under New York State Medicaid requirements, physician-administered drugs must be produced by manufacturers that participate in the MDRP. Products made by manufacturers that do not participate in the MDRP will not be covered under Medicaid Managed Care/HARP lines of business. Drug coverage will not be available for any product from a non-participating manufacturer. For a complete list of New/Reinstated & Terminated Labelers please visit: https://www.medicaid.gov/medicaid/prescriptiondrugs/medicaid-drug-rebate-program/newreinstated-terminated-labeler-information/index.html
11. The requested site of care may impact approval timeframe and is subject to review.
12. The following applies to all gene and cellular therapies unless otherwise specified within the drug-specific coverage criteria:
    a. Administration, Retreatment, and Treatment with Additional or Other Gene/Cellular Therapies
        i. One-Time Administration
            1. Most gene and cellular therapies, whether autologous, allogeneic ("off-the-shelf"), or in vivo gene-transfer therapies, are designed and studied as one-time treatments.
            2. Repeat dosing, reinfusion, or sequential therapy with other gene or cellular products has not been established as safe, effective, or clinically appropriate.
        ii. Retreatment/Repeat Administration
            1. Retreatment with the same gene or cellular therapy product is considered experimental and investigational because:
                a. Clinical trials evaluated these therapies as single-administration interventions
                b. Safety, efficacy, and durability of a second administration have not been established

c. Risks of immune activation, insertional mutagenesis, or vector immunity may be increased with repeat dosing

iii. Treatment with an Additional or Other Gene/Cellular Therapy

1. Treatment with an additional or different gene or cellular therapy after prior exposure to any gene or cellular therapy is also considered experimental and investigational, unless supported by evidence demonstrating (a-c):
   a. Anticipated clinical benefit beyond available standard therapies
   b. Safety of sequential administration
   c. Justification for selecting a second gene/cellular intervention after a prior one
2. This includes, but is not limited to:
   a. Switching between CAR-T products (e.g., CD19 → CD19 or CD19 → BCMA)
   b. Switching between autologous and allogeneic cellular therapies
   c. Sequential use of CAR-T, TCR-T, NK-cell therapies, or other genetically engineered cell therapies
   d. Receiving a gene therapy after previous gene or cellular therapy exposure
   e. Receiving an in vivo gene therapy following any prior vector-based therapy

iv. Prior Gene/Cell Therapy Exposure

1. An individual is generally not eligible for additional gene or cellular therapy if they have previously received:
   a. Any autologous cellular therapy (e.g., CAR-T, TCR-T, TIL),
   b. Any allogeneic genetically modified cellular therapy,
   c. Any in vivo gene therapy (e.g., AAV, lentiviral vector)
   d. Any ex vivo gene-modified cell product
   e. Are being considered for any other gene or cellular therapy without documented evidence supporting safety and anticipated benefit.

13. Approval timeframes may be extended to align authorization periods for drugs administered as part of a multidrug regimen, including when regimen components are administered across different benefits. This provision does not apply when the approval timeframe reflects a drug-specific limitation on duration of therapy.

CODES:

Eligibility for reimbursement is based upon the benefits set forth in the member's subscriber contract. CODES MAY NOT BE COVERED UNDER ALL CIRCUMSTANCES. PLEASE READ THE POLICY AND GUIDELINES STATEMENTS CAREFULLY.
Codes may not be all inclusive as the AMA and CMS code updates may occur more frequently than policy updates.

Code Key:
Experimental/Investigational = (E/I),
Not medically necessary/ appropriate = (NMN).

HCPCS: J3590 (NOC)

UPDATES:

Date	Revision
09/25/2026	Revised / Implemented
08/25/2026	Created
08/13/2026	Reviewed / P&T Committee Approval

APPENDIX:

Definitions of Complete Remission (CR) and Complete Remission with Incomplete Hematologic Recovery (CRi)[6]

Definition of CR for AML and MPAL (meets all criteria, 1-5)

1. Bone marrow blasts <5% by morphologic examination
2. ANC >1.0 × 10^9/L (1,000/μL)
3. Absence of circulating blasts in the peripheral blood by morphologic examination
4. No evidence extramedullary disease
5. Platelet count >100 × 10^9/L (100,000/μL)

CRi is defined as meeting all CR criteria except for residual neutropenia (<1.0 × 10^9/L) and/or thrombocytopenia (<100 × 10^9/L).

Definition of CR for ALL (meets all criteria, 1-6)

1. <5% blasts in the bone marrow
2. Normal maturation of all cellular components in the bone marrow
3. No extramedullary disease (e.g., central nervous system, soft tissue disease)
4. ANC > 1,000/μL
5. Platelet count >100,000/μL
6. Transfusion independence

CRi is defined as meeting all CR criteria except for residual neutropenia (≤1.0 × 10^9/L) and/or thrombocytopenia (≤100 × 10^9/L).

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4. Meyer EH, Salhotra A, Gandhi AP, et al. Orca-T vs allogeneic hematopoietic stem cell transplantation (Precision-T): a multicenter, randomized phase 3 trial. Blood. 2026;147(11):1168-1177. doi:10.1182/blood.2025031313
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6. U.S. Food and Drug Administration. Acute myeloid leukemia: developing drugs and biological products for treatment. Guidance for industry. FDA; October 2022. Accessed August 25, 2026. https://www.fda.gov/regulatory-information/search-fda-guidance-documents/acute-myeloid-leukemia-developing-drugs-and-biological-products-treatment-0