CENTENE® Corporation

Clinical Policy: Hematopoietic Stem and Progenitor Cells, High-Purity Regulatory T-Cells, and Conventional T-Cells (Orca-T)

Reference Number: CP.PHAR.770
Effective Date: FDA Approval Date
Last Review Date: 02.26
Line of Business: Commercial, HIM, Medicaid

Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Hematopoietic stem and progenitor cells, high-purity regulatory T-cells, and conventional T-cells (Orca-T®) is an allogeneic T-cell immunotherapy derived from peripheral blood from either related or unrelated matched donors.

FDA Approved Indication(s) [Pending]

Orca-T is indicated for the treatment of acute myeloid leukemia (AML), acute lymphoblastic leukemia (ALL), and myelodysplastic syndromes (MDS).

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results, or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Orca-T is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria*

**Criteria will mirror the clinical information from the prescribing information once FDA-approved*

A. Acute Myeloid Leukemia, Acute Lymphoblastic Leukemia, and Myelodysplastic Syndromes (must meet all)**:**

1. Diagnosis of one of the following (a or b):*
   a. AML or ALL, and one of the following (i or ii):
      i. Disease is in complete remission (CR) (*see Appendix D*);
      ii. Disease is in complete remission with incomplete hematologic recovery (CRi) (*see Appendix D*);
   b. MDS, and both of the following (i and ii):
      i. Member has ≤ 10% blast burden in the bone marrow;
      ii. One of the following (1 or 2):
         1) Member is indicated for allogeneic hematopoietic stem cell transplantation (HSCT) per 2017 International Expert Panel recommendations (de Witte et al, 2017; *see Appendix E*);
         2) Member has therapy-related/secondary MDS per the World Health Organization classification of myeloid malignancies (*see Appendix E*);

2. Prescribed by or in consultation with a hematologist, oncologist, or transplant specialist;
3. Age ≥ 18 years;*
4. Member has a matched donor (related or unrelated) who is an 8/8 match for human leukocyte antigen (HLA)-A, -B, -C, and -DRB1;*
5. Transplant specialist attestation that member is clinically stable and eligible to undergo myeloablative conditioning and allogeneic HSCT;*
6. Member has not received prior allogeneic HSCT or Orca-T transplant;*
7. Member will receive standard of care therapy for prophylaxis of graft-versus-host disease (e.g., tacrolimus, methotrexate, post-transplant cyclophosphamide, anti-thymocyte globulin, sirolimus, alemtuzumab, mycophenolate mofetil, ursodiol) following Orca-T transplant;*
8. Dose does not exceed the FDA-approved maximum.*

Approval duration: 3 months (one-time transplant per lifetime)

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy*

**Criteria will mirror the clinical information from the prescribing information once FDA-approved*

A. Acute Myeloid Leukemia, Acute Lymphoblastic Leukemia, and Myelodysplastic Syndromes

1. Continued therapy will not be authorized as there is no evidence to support repeat Orca-T transplants.*

Approval duration: Not applicable

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):

a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or

2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

AML: acute myeloid leukemia
ALL: acute lymphoblastic leukemia
CR: complete remission
CRi: complete remission with incomplete hematologic recovery
FDA: Food and Drug Administration
HLA: human leukocyte antigen
HSCT: hematopoietic stem cell transplantation
IPSS-R: Revised International Prognostic Scoring System
MDS: myelodysplastic syndromes

Appendix B: Therapeutic Alternatives

Not applicable

Appendix C: Contraindications/Boxed Warnings [Pending]

- Contraindication(s): pending
- Boxed warning(s): pending

Appendix D: Definition of CR and CRi for AML and ALL

- AML:
  - CR: all of the following:
    - Bone marrow blasts < 5% by morphologic examination
    - Absence of circulating blasts in the peripheral blood by morphologic examination
    - No extramedullary disease (e.g., central nervous system, soft tissue disease)
    - Absolute neutrophil count > 1.0 x 10^9 /L (1,000/µL)
    - Platelet count > 100 x 10^9 /L (100,000/µL)

- CRi: all CR criteria except for residual neutropenia (≤ 1.0 x 10^9/L) and/or thrombocytopenia (≤ 100 x 10^9/L)

- ALL:
  - CR: all of the following:
    - Bone marrow blasts < 5% by morphologic examination
    - Normal maturation of all cellular components in the bone marrow
    - No extramedullary disease (e.g., central nervous system, soft tissue disease)
    - Absolute neutrophil count > 1.0 x 10^9 /L (1,000/µL)
    - Platelet count > 100 x 10^9 /L (100,000/µL)
    - Transfusion independence
  - CRi: all CR criteria except for residual neutropenia (≤ 1.0 x 10^9/L) and/or thrombocytopenia (≤ 100 x 10^9/L).

Appendix E: MDS Allogeneic HSCT Eligibility and Definition of Therapy-Related/Secondary Disease

- MDS allogeneic HSCT eligibility per 2017 International Expert Panel recommendations (de Witte et al, 2017): any one of the following:
  - Revised International Prognostic Scoring System (IPSS-R) ≥ 5 (high or very high)
  - At least one poor risk feature:
    - > 50% increase in blasts from initial diagnosis,
    - High RBC transfusion intensity (≥ 2 units per month for 6 months)
    - Poor prognosis molecular features (SRSF2, RUNX1, U2AF1, ASXL1, TP53)
    - Poor risk cytogenetic features (-7, inv(3)/t(3q)/del(3q), double including -7/del(7q), complex: 3 abnormalities)
    - Very poor risk cytogenetic features (> 3 abnormalities)
  - Failed therapies (erythropoiesis-stimulating agents, lenalidomide, hypomethylating agents, intensive chemotherapy)
- Definition of therapy-related/secondary MDS per the World Health Organization: all of the following (independent of IPSS-R scoring):
  - History of prior treatment with cytotoxic chemotherapy or radiation therapy
  - Morphologic evidence of significant dysplasia (i.e., ≥ 10 % of erythroid precursors, granulocytes, or megakaryocytes) on the peripheral blood smear or bone marrow examination, in the absence of other causes of dysplasia. In the absence of morphologic evidence of dysplasia, a presumptive diagnosis of MDS can be made in patients with otherwise unexplained refractory cytopenias together with certain genetic abnormalities characteristic of therapy-related MDS
  - Blast count in bone marrow ≤ 20%

V. Dosage and Administration [Pending]

Indication	Dosing Regimen	Maximum Dose
AML, ALL, MDS*	Pending	Pending

VI. Product Availability [Pending]

Pending

VII. References

1. Meyer E, Salhotra A, Gandhi A, et al. Orca-T versus allogeneic hematopoietic stem cell transplantation (PRECISION-T): A multicenter, randomized phase 3 trial. Blood. 2025; blood.2025031313. doi: https://doi.org/10.1182/blood.2025031313
2. ClinicalTrials.gov. Precision-T: A randomized study of Orca-T in recipients undergoing allogeneic transplantation for hematologic malignancies (Orca-T). Available at: https://clinicaltrials.gov/study/NCT05316701. Accessed January 14, 2026.
3. National Comprehensive Cancer Network. Hematopoietic Cell Transplantation (HCT) Version 3.2025. Available at: https://www.nccn.org/professionals/physician_gls/pdf/hct.pdf. Accessed January 14, 2026.
4. National Comprehensive Cancer Network. Acute Myeloid Leukemia Version 3.2026. Available at: https://www.nccn.org/professionals/physician_gls/pdf/aml.pdf. Accessed January 14, 2026.
5. National Comprehensive Cancer Network. Hematopoietic Cell Transplantation (HCT) Version 3.2025. Available at: https://www.nccn.org/professionals/physician_gls/pdf/hct.pdf. Accessed January 14, 2026.
6. National Comprehensive Cancer Network. Myelodysplastic Syndromes Version 3.2026. Available at: https://www.nccn.org/professionals/physician_gls/pdf/mds.pdf. Accessed January 14, 2026.
7. de Witte T, Bowen D, Robin M, et al. Allogeneic hematopoietic stem cell transplantation for MDS and CMML: Recommendations from an international expert panel. Blood. 2017 Mar 30;129(13):1753-1762. doi: 10.1182/blood-2016-06-724500. Epub 2017 Jan 17. PMID: 28096091; PMCID: PMC5524528.

Coding Implications [Pending]

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
Pending	Pending

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created pre-emptively	01.14.26	02.26

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and

accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions, and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members, and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.