Clinical Policy: Dexrazoxane (Totect)

Reference Number: CP.PHAR.418
Effective Date: 03.19.19
Last Review Date: 05.24
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

Dexrazoxane (Totect®) is a cytoprotective agent.

FDA Approved Indications

Totect is indicated for:

- Reducing the incidence and severity of cardiomyopathy associated with doxorubicin administration in women with metastatic breast cancer who have received a cumulative doxorubicin dose of 300 mg/m^2 and who will continue to receive doxorubicin therapy to maintain tumor control. Do not use Totect with doxorubicin initiation.
- Treatment of extravasation resulting from intravenous anthracycline chemotherapy.

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 dexrazoxane and Totect is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Doxorubicin-Induced Cardiomyopathy (must meet all)**:**

1. Prescribed to reduce the incidence or severity of cardiomyopathy associated with doxorubicin;
2. Prescribed by or in consultation with an oncologist or hematologist;
3. One of the following (a or b):
   a. Age ≥ 18 years, and member has received a cumulative doxorubicin dose of ≥ 300 mg/m^2;
   b. Prescribed for one of the following NCCN 2A or higher supported indications (i-vii):
      i. Pediatric acute lymphoblastic leukemia (ALL) and one of the following (1 or 2):
         1) Ph-negative ALL: as part of the DFCI ALL Protocol 11-001 or 16-001 in members with an anticipated cumulative anthracycline dose ≥ 250 mg/m^2 of doxorubicin equivalent or radiation with potential impact to the heart (e.g., radiation to chest, abdomen, spine, or total body irradiation);
         2) Relapsed or refractory Ph-positive ALL: in combination with Sprycel® (dasatinib) or imatinib (Gleevec®) as part of COG AALL1331 regimen with an anticipated cumulative anthracycline dose ≥ 250 mg/m^2 of

doxorubicin equivalent or radiation with potential impact to the heart (e.g., radiation to chest, abdomen, spine, or total body irradiation);
   ii. Pediatric aggressive mature B-cell lymphomas;
   iii. Pediatric Hodgkin lymphoma;
   iv. Hodgkin lymphoma in adults age > 60 years, in combination with ABVD regimen (doxorubicin, bleomycin, vinblastine, dacarbazine) or CHOP regimen (cyclophosphamide, doxorubicin, vincristine, prednisone);
   v. Wilms Tumor (nephroblastoma), and member has a planned cumulative dose of doxorubicin ≥ 150 mg/m^2;
   vi. Neuroblastoma;
   vii. Soft tissue sarcoma, and member has a planned cumulative dose of doxorubicin ≥ 250 mg/m^2;
4. Will be used concurrently with doxorubicin;
5. For Totect requests, member must use dexrazoxane, if available, unless contraindicated or clinically significant adverse effects are experienced;
6. Request meets one of the following (a or b):*
   a. Dose does not exceed 10 times the dose of doxorubicin (e.g., dexrazoxane 500 mg/m^2 for member receiving doxorubicin 50 mg/m^2) given with each doxorubicin dose;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration: 12 months or duration of doxorubicin therapy, whichever is less

B. Anthracycline-Induced Extravasation (must meet all)**:**
1. Diagnosis of anthracycline-induced extravasation;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Dose does not exceed 2,000 mg per day on days 1 and 2, and 1,000 mg on day 3.

Approval duration: 3 days

C. 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

A. Doxorubicin-Induced Cardiomyopathy (must meet all)**:**

1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B);*
2. Member continues to receive doxorubicin;
3. Member is responding positively to therapy;
4. For Totect requests, member must use dexrazoxane, if available, unless contraindicated or clinically significant adverse effects are experienced;
5. Request meets one of the following (a or b):*
   a. Dose does not exceed 10 times the dose of doxorubicin (e.g., dexrazoxane 500 mg/m^2 for member receiving doxorubicin 50 mg/m^2) given with each doxorubicin dose;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration: 12 months or duration of doxorubicin therapy, whichever is less

B. Anthracycline-Induced Extravasation

1. Re-authorization is not permitted. Member must meet the initial approval criteria.

Approval duration: Not applicable

C. 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 – 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
ALL: acute lymphoblastic leukemia
FDA: Food and Drug Administration

Appendix B: Therapeutic Alternatives
Not applicable

Appendix C: Contraindications/Boxed Warnings
None reported

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Doxorubicin-induced cardiomyopathy	Give dexrazoxane at a ratio of 10:1 with the doxorubicin dose as an IV infusion over 15 minutes and within 30 minutes before doxorubicin is given.	Not applicable
Anthracycline-induced extravasation	Day 1: 1,000 mg/m^2 Day 2: 1,000 mg/m^2 Day 3: 500 mg/m^2 Give Totect as an IV infusion over 1-2 hours and within 6 hours of extravasation. Treatment on days 2 and 3 should start at the same hour (+/-3 hours) as day 1.	Day 1: 2,000 mg Day 2: 2,000 mg Day 3: 1,000 mg

VI. Product Availability

Single-dose vial, IV powder for solution: 500 mg

VII. References

1. Totect Prescribing Information. Yardville, PA: Clinigen, Inc; November 2020. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/022025s019lbl.pdf. Accessed February 12, 2024.
2. American Society of Clinical Oncology 2008 Clinical Practice Guideline Update: Use of Chemotherapy and Radiation Therapy Protectants. Available at: http://ascopubs.org/doi/pdf/10.1200/JCO.2008.17.2627. J Clin Oncol; 27:127-145.
3. Choi HS, Park ES, Kang HJ, et al. Dexrazoxane for preventing anthracycline cardiotoxicity in children with solid tumors. J Korean Med Sci. 2010;25(9):1336-42.

4. Asselin BL, Devidas M, Chen L, et al. Cardioprotection and Safety of Dexrazoxane in Patients Treated for Newly Diagnosed T-Cell Acute Lymphoblastic Leukemia or Advanced-Stage Lymphoblastic Non-Hodgkin Lymphoma: A Report of the Children's Oncology Group Randomized Trial Pediatric Oncology Group 9404. J Clin Oncol. 2016;34(8):854-62.
5. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: https://nccn.org/. Accessed February 12, 2024.
6. National Comprehensive Cancer Network. Pediatric Aggressive Mature B-Cell Lymphomas Version 1.2023. Available at: https://www.nccn.org/professionals/physician_gls/pdf/ped_b-cell.pdf. Accessed February 12, 2024.
7. National Comprehensive Cancer Network. Pediatric Acute Lymphoblastic Leukemia Version 4.2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/ped_all.pdf. Accessed February 12, 2024.
8. National Comprehensive Cancer Network. Pediatric Hodgkin Lymphoma Version 2.2023. Available at: https://www.nccn.org/professionals/physician_gls/pdf/ped_hodgkin.pdf. Accessed February 12, 2024.
9. National Comprehensive Cancer Network. Wilms Tumor (Nephroblastoma) Version 1.2023. Available at: https://www.nccn.org/professionals/physician_gls/pdf/wilms_tumor.pdf. Accessed February 12, 2024.
10. National Comprehensive Cancer Network. Soft Tissue Sarcoma Version 2.2022. Available at https://www.nccn.org/professionals/physician_gls/pdf/sarcoma.pdf. Accessed February 12, 2024.
11. National Comprehensive Cancer Network. Neuroblastoma Version 1.2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/neuroblastoma.pdf. Accessed February 12, 2024.

Coding Implications

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
J1190	Injection, dexrazoxane, 250 mg

Reviews, Revisions, and Approvals	Date	P&T Approval Date
2Q 2020 annual review: no significant changes; HIM-Medical Benefit revised to HIM line of business; references reviewed and updated.	02.15.20	05.20
RT4: updated policy in response to expansion of Totect FDA indication for doxorubicin toxicity, which overlaps with Zinecard.	11.16.20	
2Q 2021 annual review: references for HIM line of business off-label use revised from HIM.PHAR.21 to HIM.PA.154; updated section V dosing to include Totect for the indication of	01.31.21	05.21

Reviews, Revisions, and Approvals	Date	P&T Approval Date
doxorubicin-induced cardiomyopathy; references reviewed and updated.		
2Q 2022 annual review: per NCCN added off-label supported uses in patients under 18 years of age in Ph-negative ALL, aggressive mature B-cell lymphomas, Hodgkin lymphoma, or Wilms Tumor (nephroblastoma); removed appendix D that provided references to studies with inconclusive doxorubicin thresholds for use in pediatric patients as such use is supported by NCCN; removed Zinecard from policy as product has been discontinued; references reviewed and updated.	02.14.22	05.22
Template changes applied to other diagnoses/indications and continued therapy section.	09.23.22	
2Q 2023 annual review: updated FDA approved indication to mirror PI; clarified that use is limited to the pediatric population for Ph-negative ALL and Hodgkin lymphoma; added off-label use for soft tissue sarcoma to criteria under doxorubicin-induced cardiomyopathy per NCCN 2A recommendation; reference reviewed and updated.	01.25.23	05.23
2Q 2024 annual review: for doxorubicin-induced cardiomyopathy, added redirection to generic dexrazoxane, added the following NCCN 2A indications: relapsed/refractory Ph-positive ALL, Hodgkin lymphoma in adults age > 60 years, and neuroblastoma; references reviewed and updated	02.12.24	05.24

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.