Clinical Policy: Dexrazoxane (Totect)

Reference Number: PA.CP.PHAR.418
Effective Date: 01/2020
Last Review Date: 04/2025

Description
Dexrazoxane is a cytoprotective agent.

FDA Approved Indications
Dexrazoxane 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 PA Health & Wellness® that dexrazoxane 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 2B or higher supported indications (i-vi):
      i. Pediatric ALL and one of the following (1 or 2):
         1) BCR::ABL1-negative B-ALL (one of the following A, B or C):
            A. As part of the DFCI ALL Protocol 16-001 regimen, based on DFCI ALL Protocol 11-001 regimen (HR/VHR arms);
            B. Relapsed or refractory BCR::ABL1 -negative B-ALL;
            C. Any other NCCN category 1, 2A or 2B recommendations not listed;
         2) Relapsed or refractory BCR::ABL1-positive B-ALL in combination with dasatinib (Sprycel®) or imatinib (Gleevec®) as part of COG AALL1331 regimen;
      ii. Pediatric aggressive mature B-cell lymphomas;
      iii. Pediatric Hodgkin lymphoma
      iv. Wilms Tumor (nephroblastoma) and member has a planned cumulative dose of doxorubicin ≥ 150 mg/m^2;
      v. Neuroblastoma;
      vi. Soft tissue sarcoma, and member has a planned cumulative dose of doxorubicin ≥ 250 mg/m^2 (off-label);

4. Will be used concurrently with doxorubicin or other high-dose anthracycline;
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*).

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

B. Anthracycline-Induced Extravasation (off-label) (must meet all)**:**
1. Diagnosis of anthracycline-induced extravasation;
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age ≥ 18 years;
4. Request meets one of the following (a or b):
   a. Dose does not exceed 2,000 mg per day on days 1 and 2, and 1,000 mg on day 3.
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration: 3 days

C. Other diagnoses/indications
1. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

II. Continued Therapy

A. Doxorubicin-Induced Cardiomyopathy (must meet all)**:**
1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.PHARM.01) applies;
2. Member continues to receive doxorubicin or other high-dose anthracycline;
3. Member is responding positively to therapy;
4. 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*).

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. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.PHARM.01) applies.

   Approval duration: Duration of request or 6 months (whichever is less); or

2. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

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 – PA.CP.PMN.53.

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

VI. Product Availability

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

VII. References

1. Dexrazoxane Prescribing Information. Berkeley Heights, NJ: Hikma Pharmaceuticals USA, Inc; January 2025. Available at: https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=68089182-d4a2-4053-8d0d-fc97a901515d. Accessed January 30, 2025.
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 January 30, 2025.

6. National Comprehensive Cancer Network. Pediatric Aggressive Mature B-Cell Lymphomas Version 2.2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/ped_b-cell.pdf. Accessed January 30, 2025.
7. National Comprehensive Cancer Network. Pediatric Acute Lymphoblastic Leukemia Version 2.2025. Available at: https://www.nccn.org/professionals/physician_gls/pdf/ped_all.pdf. Accessed January 30, 2025.
8. National Comprehensive Cancer Network. Pediatric Hodgkin Lymphoma Version 1.2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/ped_hodgkin.pdf. Accessed January 30, 2025.
9. National Comprehensive Cancer Network. Wilms Tumor (Nephroblastoma) Version 2.2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/wilms_tumor.pdf. Accessed January 30, 2025.
10. National Comprehensive Cancer Network. Soft Tissue Sarcoma Version 4.2024. Available at https://www.nccn.org/professionals/physician_gls/pdf/sarcoma.pdf. Accessed January 30, 2025.
11. National Comprehensive Cancer Network. Neuroblastoma Version 2.2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/neuroblastoma.pdf. Accessed January 30, 2025.

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 hydrochloride, per 250 mg

Reviews, Revisions, and Approvals	Date
Policy created	01/2020
1Q 2021 annual review: updated policy in response to expansion of Totect FDA indication for doxorubicin toxicity, which overlaps with Zinecard; references reviewed and updated	01/2021
2Q 2021 annual review: updated section V dosing to include Totect for the indication of doxorubicin-induced cardiomyopathy; references reviewed and updated.	04/2021
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; references reviewed and updated.	04/2022
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	04/2023

Reviews, Revisions, and Approvals	Date
recommendation; removed Zinecard from policy as product has been discontinued; reference reviewed and updated.	
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	04/2024
2Q 2025 annual review: removed brand Totect from criteria as product has been discontinued and obsolete; for doxorubicin-induced cardiomyopathy, clarified anthracycline-induced extravasation is an off-label use now that Totect has been discontinued; removed Hodgkin lymphoma in adults age > 60 years per NCCN; removed redirections to generic dexrazoxane now that product is only available as generic; references reviewed and updated.	04/2025