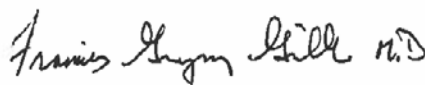


Prior Authorization Review Panel

Prior Authorization Review Panel

CHC-MCO Policy Submission

A separate copy of this form must accompany each policy submitted for review.
Policies submitted without this form will not be considered for review.

Plan: PA Health & Wellness	Submission Date: 02/01/2020
Policy Number:	Effective Date: 01/15/2020 Revision Date: 01/15/2020
Policy Name:	
<p>Type of Submission – <u>Check all that apply</u>:</p> <p> <input checked="" type="checkbox"/> New Policy <input type="checkbox"/> Revised Policy* <input type="checkbox"/> Annual Review - No Revisions <input type="checkbox"/> Statewide PDL - <i>Select this box when submitting policies for Statewide PDL implementation and when submitting policies for drug classes included on the Statewide PDL.</i> </p>	
<p>*All revisions to the policy <u>must</u> be highlighted using track changes throughout the document.</p> <p>Please provide any changes or clarifying information for the policy below:</p> <p style="text-align: center;">New Policy Created</p>	
Name of Authorized Individual (Please type or print): Francis G. Grillo, MD	Signature of Authorized Individual: 

Clinical Policy: Dexrazoxane (Zinecard, Totect)

Reference Number: PA.CP.PHAR.418

Effective Date: 01/2020

Last Review Date: 01/2020

[Coding Implications](#)
[Revision Log](#)

Description

Dexrazoxane (Zinecard[®], Totect[®]) is a cytoprotective agent.

FDA Approved Indications

Zinecard is indicated for reducing the incidence and severity of cardiomyopathy associated with doxorubicin in women with metastatic breast cancer who have received a cumulative doxorubicin dose of 300 mg/m² and will continue receiving doxorubicin to maintain tumor control.

Totect is indicated for the 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 PA Health & Wellness[®] that Zinecard and Totect are **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. Age \geq 18 years;
4. Will be used concurrently with doxorubicin;
5. Member has received a cumulative doxorubicin dose of \geq 300 mg/m²;
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/m² for member receiving doxorubicin 50 mg/m²) 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 (must meet all):

1. Diagnosis of anthracycline-induced extravasation;
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age \geq 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.LTSS.PHAR.01) applies;
2. Member continues to receive doxorubicin;
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/m² for member receiving doxorubicin 50 mg/m²) 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.LTSS.PHAR.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

FDA: Food and Drug Administration

Appendix B: Therapeutic Alternatives

Not applicable

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s):
 - Zinecard: should not be used with non-anthracycline chemotherapy regimens
 - Totect: none reported
- Boxed warning(s): none reported

Appendix D: General Information

- The 2008 American Society of Clinical Oncology (ASCO) clinical practice guidelines for the use of chemotherapy and radiotherapy protectants do not make a recommendation regarding pediatric use of dexrazoxane due to insufficient evidence.
 - Due to variances in the type of pediatric malignancy studied, trial design used, and outcomes assessed, there is not a consistent approach in the clinical literature in terms of what the appropriate cumulative doxorubicin dose threshold at which to initiate dexrazoxane therapy should be, as well what the appropriate dosing of dexrazoxane is in pediatrics.
 - In an open-label, prospective, randomized, placebo-controlled trial (N = 38) by Wexler LH, et al., patients (age ≤ 25 years) with sarcoma who received dexrazoxane had a significantly smaller decline in left ventricular ejection fraction (LVEF) per 100 mg/m² of doxorubicin dose from baseline compared to placebo (1% v. 2.7%, $p < 0.01$). Patients received a dexrazoxane dose of 20 times the dose of doxorubicin. The median doxorubicin dose received by dexrazoxane patients was 410 mg/m² compared to 310 mg/m² in the placebo group.
 - In Choi HS, et al. (N = 89), patients with various solid tumors (predominantly neuroblastomas, peripheral primitive neuroectodermal tumors) were randomized to receive dexrazoxane administered in a 10:1 ratio to doxorubicin or placebo. Dexrazoxane-treated patients were statistically less likely to experience a cardiac event (defined as either increase left ventricular (LV) diastolic diameter for age, increased LV systolic diameter, or fractional shortening less than 28% at any time point of doxorubicin treatment) compared to placebo-treated patients (27.7% v. 52.4%, $p = 0.017$). The incidence of congestive heart failure (CHF) was also lower for those who received dexrazoxane (6.4% v. 14.3%, $p = 0.049$). The 5-year cardiac event free survival rates were significantly improved in the dexrazoxane group (69.2% v. 45.8%, $p = 0.04$). The median cumulative doses of doxorubicin was 290 mg/m² in the dexrazoxane group compared to 294 mg/m² which were not significantly different ($p = 0.387$).
 - Per Asselin BL, et al. dexrazoxane does not appear to compromise antitumor efficacy and did not increase frequency of toxicity or secondary malignancies.

V. Dosage and Administration

Drug Name	Indication	Dosing Regimen	Maximum Dose
dexrazoxane (Zinecard)	Doxorubicin-induced cardiomyopathy	Give Zinecard at a ratio of 10:1 with the doxorubicin dose as an IV infusion over 15 minutes and	Not applicable

Drug Name	Indication	Dosing Regimen	Maximum Dose
		within 30 minutes before doxorubicin is given.	
dexrazoxane (Totect)	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

Drug Name	Availability
dexrazoxane (Zinecard)	Single-dose vial, IV powder for solution: 250 mg, 500 mg
dexrazoxane (Totect)	Single-dose vial, IV powder for solution: 500 mg

VII. References

1. Zinecard Prescribing Information. New York, NY: Pharmacia & Upjohn Co; October 2016. Available at: www.pfizer.com. Accessed March 4, 2019
2. Totect Prescribing Information. Nashville, TN: Cumberland Pharmaceuticals Inc; February 2018. Available at: www.totect.com. Accessed March 4, 2019.
3. American Society of Clinical Oncology Clinical Practice Guidelines for the Use of Chemotherapy and Radiotherapy Protectants. Available at: <http://ascopubs.org/doi/full/10.1200/JCO.1999.17.10.3333>. J Clin Oncol; 10:3333-3355 Accessed March 13, 2019.
4. American Society of Clinical Oncology 2002 Clinical Practice Guideline Update: Use of Chemotherapy and Radiation Therapy Protectants. Available at: <http://ascopubs.org/doi/pdf/10.1200/JCO.2002.04.178>. J Clin Oncol; 20:2895-2903. Accessed March 6, 2019.
5. 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. Accessed March 6, 2019.
6. Micromedex® Healthcare Series [Internet database]. Greenwood Village, Colo: Thomson Healthcare. Updated periodically. Accessed March 6, 2019.
7. Marty M, Espie M, Llombart A, Monnier A, Rapoport BL, and Stahalova V. Multicenter randomized phase III study of the cardioprotective effect of dexrazoxane (Cardioxane®) in advanced/metastatic breast cancer patients treated with anthracycline-based chemotherapy. Ann Oncol 2006; 17:614-622.
8. Wexler LH, Andrich MP, Venzon D, et al. Randomized trial of the cardioprotective agent ICRF-187 in pediatric sarcoma patients treated with doxorubicin. J Clin Oncol. 1996;14(2):362-72.

9. 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.
10. 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.

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
Policy created	01/15/20	