Clinical Policy Title:	dexrazoxane
Policy Number:	RxA.329
Drug(s) Applied:	Totect®
Original Policy Date:	02/07/2020
Last Review Date:	09/14/2021
Line of Business Policy Applies to:	All lines of business

Background

Dexrazoxane (Totect®) is a cytoprotective agent. It 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/m^2 and will continue receiving doxorubicin to maintain tumor control. Do not use Totect® with doxorubicin initiation.

Totect® is also indicated for the treatment of extravasation resulting from intravenous anthracycline chemotherapy.

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
dexrazoxane (Totect®)	Doxorubicin induced cardiomyopathy	Give dexrazoxane at a ratio of 10:1 with the doxorubicin dose as an intravenous infusion over 15 minutes. Give doxorubicin within 30 minutes after completion of dexrazoxane dose.	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 intravenous 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

Dosage Forms

- dexrazoxane: Single-dose vial, IV powder for solution: 250 mg, 500 mg.
- dexrazoxane (Totect®): Single-dose vial, IV powder for solution: 500 mg.

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria. The provision of provider samples does not guarantee coverage under the terms of the pharmacy benefit administered by RxAdvance. All criteria for initial approval must be met in order to obtain coverage.

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 ≥ 18 years;
4. Will be used concurrently with doxorubicin;
5. Member has received a cumulative doxorubicin dose of ≥ 300 mg/m^2;
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).

Approval Duration:
Commercial: 12 months
Medicaid: 12 months

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:
Commercial: 3 days
Medicaid: 3 days

II. Continued Therapy Approval

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

1. Member is currently receiving medication that has been authorized by RxAdvance or member has previously met initial approval criteria listed in this policy;
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/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:
Commercial: 12 months
Medicaid: 12 months

B. Anthracycline-Induced Extravasation

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

Approval Duration

Not applicable

III. Appendices

APPENDIX A: Abbreviation/Acronym Key

FDA: Food and Drug Administration

APPENDIX B: Therapeutic Alternatives

- Not applicable

APPENDIX C: Contraindications/Boxed Warnings

- Contraindication(s):
  - 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/m^2 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/m^2 compared to 310 mg/m^2 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/m^2 in the dexrazoxane group compared to 294 mg/m^2 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.

References

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Review/Revision History	Review/Revised Date	P&T Approval Date
Policy established.	01/2020	02/07/2020
Policy was revised: Currently receiving medication via RxAdvance benefit or member has previously met initial approval criteria	03/2020	
Policy was reviewed: 1. Clinical Policy Title was updated. 2. Line of Business Policy Applies to was updated to all lines of business. 3. Initial and Continued approval duration was updated to include Medicaid, Commercial & HIM approval duration. 4. Continued therapy criteria II.A.1 was rephrased to "Currently receiving medication that has been authorized by RxAdvance…". 5. References were reviewed and updated.	07/19/2020	09/14/2020

Policy was reviewed: 1. Clinical Policy Drugs Applied was updated to remove inactive/unavailable drug Zinecard. 2. Background was updated to include “Do not use Totect® with doxorubicin initiation”. 3. Dosing Information was updated to remove inactive/unavailable drug Zinecard. 4. Dosing Information dosing regimen for indication Doxorubicin induced cardiomyopathy was updated from “Give Zinecard 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” to “Give dexrazoxane at a ratio of 10:1 with the doxorubicin dose as an intravenous infusion over 15 minutes. Give doxorubicin within 30 minutes after completion of dexrazoxane dose”. 5. Dosage Forms was updated to remove inactive/unavailable drug name Zinecard. 6. Statement about provider sample ‘‘The provision of provider samples does not guarantee coverage…” was added to Clinical Policy. 7. Initial Approval Criteria and Continued Therapy Approval Criteria were updated to remove HIM approval duration. 8. Continued Therapy Approval Criteria II.A.1 was rephrased to "Member is currently receiving medication that has been authorized by RxAdvance...". 9. References were reviewed and updated.	05/28/2021	09/14/2021