Clinical Policy Title:	asparaginase erwinia chrysanthemi
Policy Number:	RxA.377
Drug(s) Applied:	Erwinaze®
Original Policy Date:	03/06/2020
Last Review Date:	09/14/2021
Line of Business Policy Applies to:	All lines of business

Background

Asparaginase *Erwinia chrysanthemi* (Erwinaze®) is an asparagine specific enzyme. It is indicated as a component of a multi-agent chemotherapeutic regimen for the treatment of patients with acute lymphoblastic leukemia (ALL) who have developed hypersensitivity to *E. coli*-derived asparaginase.

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
asparaginase *Erwinia chrysanthemi* (Erwinaze®)	Acute lymphoblastic leukemia	To substitute for pegaspargase: The recommended dose for each planned dose of pegaspargase is 25,000 international units/m^2 administered intramuscularly or intravenously three times weekly (Monday/Wednesday/Friday) for six doses. To substitute for native E coli-derived asparaginase, 25,000 international units/m^2 intravenously or intramuscularly for each scheduled dose of native E coli-derived asparaginase	25,000 IU/m^2/dose

Dosage Forms

- 10,000 international units lyophilized powder single-dose vial for reconstitution.

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. Acute lymphoblastic leukemia (must meet all)**:**

1. Diagnosis of ALL;
2. Request meets one of the following (a or b):
   a. Member has developed hypersensitivity to an *E. coli* derived asparaginase product pegaspargase (Oncaspar®);
   b. As a component of multi-agent chemotherapeutic regimen for the induction therapy in adults ≥ 65 years of age or with substantial comorbidities;
3. Prescribed by or in consultation with an oncologist or hematologist;
4. Request meets one of the following (a or b):
   a. Dose should not exceed 25,000 International Units per m^2 administered three times per week;
   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
Commercial: 3 months
Medicaid: 3 months

II. Continued Therapy Approval

A. Acute lymphoblastic leukemia (must meet all)**:**

1. Member is currently receiving medication that has been authorized by RxAdvance, or documentation supports that member is currently receiving Erwinaze® for a covered indication and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. If request is for a dose increase, request meets one of the following (a, b, or c):
   a. New dose should not exceed 25,000 International Units per m^2 administered three times per week;
   b. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

Approval duration
Commercial: 6 months
Medicaid: 6 months

III. Appendices

APPENDIX A: Abbreviation/Acronym Key
ALL: Acute lymphoblastic leukemia
FDA: Food and Drug Administration
NCCN: National Comprehensive Cancer Network

APPENDIX B: Therapeutic Alternatives
Below are suggested therapeutic alternatives based on clinical guidance. Please check drug formulary for preferred agents and utilization management requirements.

Drug Name	Dosing Regimen	Dose Limit/Maximum Dose
Oncaspar® (pegaspargase)	2,500 International Units/m^2 intramuscularly or intravenously, administered no more frequently than every 14 days, as part of a multi-agent chemotherapeutic regimen.	Varies

Therapeutic alternatives are listed as generic (Brand name®) when the drug is available by both generic and brand, Brand name® when the drug is available by brand only and generic name when the drug is available by generic only.

APPENDIX C: Contraindications/Boxed Warnings

- Contraindication(s):
  - Serious hypersensitivity reactions to Erwinaze®, including anaphylaxis;
  - Serious pancreatitis with prior L-asparaginase therapy;
  - Serious thrombosis with prior L-asparaginase therapy;
  - Serious hemorrhagic events with prior L-asparaginase therapy;

- Boxed warning(s):
  - None reported.

APPENDIX D: General Information

- Warnings & Precautions:
  - Hypersensitivity Reactions: Monitor for signs or symptoms. Discontinue Erwinaze® for serious reaction;
  - Pancreatitis: Monitor for symptoms. Discontinue if pancreatitis occurs;
  - Glucose Intolerance: Monitor and manage medically;
  - Thrombosis: Discontinue for severe or life-threatening thrombosis. Provide anticoagulation therapy as indicated;
  - Hemorrhage: Discontinue for severe or life-threatening hemorrhage;

References

1. Erwinaze® Prescribing Information. Palo Alto, CA: Jazz Pharmaceuticals, Inc.; December 2019. Available at http://www.Erwinaze.com . Accessed June 1, 2021.
2. Oncaspar Prescribing Information. Gaithersburg, MD: Sigma-Tau Pharmaceuticals, Inc.; June 2020. Available at https://www.oncaspar.com/prescribing_information.pdf . Accessed June 1, 2021.
3. Asparaginase Erwinia chrysanthemi. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at ww.nccn.org. Accessed June 1, 2021.
4. Acute lymphoblastic leukemia (Version 1.2021). National Comprehensive Cancer Network Guidelines. Available at https://www.nccn.org/professionals/physician_gls/pdf/all.pdf . Accessed June 1, 2021.

Review/Revision History	Review/Revised Date	P&T Approval Date
Policy established.	01/2020	03/06/2020
Policy was reviewed: 1) Policy description table updated 2) Continuation therapy criteria II.A.1. rephrased to “Member is currently receiving medication that has been authorized by RxAdvance”. 3) Initial therapy and continued therapy approval duration added for commercial, medicaid and HIM separately	07/23/2020	09/14/2020

4) References were updated		
Policy was reviewed: 1) Dosing Information dosing regimen was updated to include “To substitute for native E coli-derived asparaginase…” 2) Dosage Forms was updated from “per vial” to “single-dose vial for reconstitution…” 3) Statement about provider sample ‘‘The provision of provider samples does not guarantee coverage…” was added to Clinical Policy. 4) Initial Approval Criteria I.A.2.b was updated to include “for the induction therapy in adults ≥ 65 years of age or with substantial comorbidities” 5) Initial Approval Criteria I.A.3 was consolidated with I.A.2.b to form new criteria I.A.2, “Request meets one of the following (a or b):”. *6)* Initial Approval Criteria I.A was updated to include the disclaimer “*Prescribed regimen must be FDA-approved or recommended by NCCN.” 7) Initial Approval Criteria and Continued Therapy Approval Criteria were updated to remove HIM approval duration. 8) Appendix A was updated to include NCCN. 9) Therapeutic alternative verbiage was updated to "Below are suggested therapeutic alternatives based on clinical guidance..". 10) Appendix B footnote was updated to, ”Therapeutic alternatives are listed as generic (Brand name®) when the drug is available by both generic and brand, Brand name® when the drug is available by brand only and generic name when the drug is available by generic only”.Appendix D was updated to include “Warnings & Precautions”. 11) References were reviewed and updated.	06/01/2021	09/14/2021