Clinical Policy Title:	pegaspargase, calaspargase pegol-mknl
Policy Number:	RxA.347
Drug(s) Applied:	Oncaspar®, Asparlas™
Original Policy Date:	03/06/2020
Last Review Date:	09/14/2021
Line of Business Policy Applies to:	All lines of business

Background

Pegaspargase (Oncaspar®) and calaspargase pegol-mknl (Asparlas™) are an asparagine specific enzyme.

Oncaspar® is indicated as a component of a multi-agent chemotherapeutic regimen for the treatment of pediatric and adult patients with:

- First-line treatment of acute lymphoblastic leukemia (ALL)
- ALL and hypersensitivity to native forms of L-asparaginase

Asparlas™ is indicated as a component of a multi-agent chemotherapeutic regimen for the treatment of ALL in pediatric and young adult patients age 1 month to 21 years.

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
pegaspargase (Oncaspar®)	ALL	Age ≤ 21 years: 2,500 IU/m^2 intramuscularly or intravenously no more frequently than every 14 days. Age > 21 years: 2,000 IU/m^2 intramuscularly or intravenously no more frequently than every 14 days.	Age ≤ 21 years: 2,500 IU/m^2 every 14 days Age >21 years: 2,000 IU/m^2 every 14 days
calaspargase pegol-mknl (Asparlas™)	ALL	Age 1 month to 21 years: 2,500 IU/m^2 intravenously no more frequently than every 21 days.	2,500 IU/m^2 every 21 days

Dosage Forms

- pegaspargase (Oncaspar®): Single-dose vial: 3,750 IU/5 mL solution.
- calaspargase pegol-mknl (Asparlas™): Single-dose vial: 3,750 units/5 mL solution.

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. Prescribed by or in consultation with an oncologist or hematologist;
3. Request meets one of the following (a, b, or c):*
   a. Request is for Oncaspar®: dose does not exceed 2,500 IU/m^2 every 14 days (age ≤ 21 years) or 2,000 IU/m^2 every 14 days (age > 21 years);
   b. Request is for Asparlas™: dose does not exceed 2,500 IU/m2 every 21 days (age 1 month to 21 years);
   c. 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: 6 months
Medicaid: 6 months

B. Extranodal NK/T-Cell Lymphoma (off-label) (must meet all)**:**

1. Diagnosis of one of the following NK/T-cell lymphoma subtypes (a, b, or c):
   a. Nasal type;
   b. Extranasal type;
   c. Aggressive NK-cell leukemia;
2. Request is for Oncaspar®;
3. Prescribed by or in consultation with an oncologist or hematologist;
4. Age 18 years of age or older;
5. Prescribed as a component of any of the following regimens (a, b, c or d):*
   a. Modified-SMILE (steroid [dexamethasone], methotrexate, ifosfamide, pegaspargase, etoposide);
   b. P-GEMOX (gemcitabine, pegaspargase, oxaliplatin);
   c. DDGP (dexamethasone, cisplatin, gemcitabine, pegaspargase);
   d. AspaMetDex (pegaspargase, methotrexate, dexamethasone);
6. *Prior authorization may be requiredDose is within FDA maximum limit for any FDA-approved indication or 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: 6 months
Medicaid: 6 months

C. Hepatosplenic T-Cell Lymphoma (off-label) (must meet all):

1. Request is for Oncaspar®;
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age 18 years of age or older;

4. Prescribed as a component of any of the following regimens (a, b, c or d):*
   a. Modified-SMILE (steroid [dexamethasone], methotrexate, ifosfamide, pegaspargase, etoposide);
   b. P-GEMOX (gemcitabine, pegaspargase, oxaliplatin);
   c. DDGP (dexamethasone, cisplatin, gemcitabine, pegaspargase);
   d. AspaMetDex (pegaspargase, methotrexate, dexamethasone);
   *Prior authorization may be required
5. Dose is within FDA maximum limit for any FDA-approved indication or 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: 6 months
Medicaid: 6 months

II. Continued Therapy Approval

A. All Indications in Section I (must meet all)**:**

1. Member is currently receiving medication that has been authorized by RxAdvance, or documentation supports that member is currently receiving Oncaspar® or Asparlas™ 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. Request is for Oncaspar®: new dose does not exceed 2,500 IU/m^2 every 14 days (age ≤ 21 years) or 2,000 IU/m^2 every 14 days (age > 21 years);
   b. Request is for Asparlas™: new dose does not exceed 2,500 IU/m2 every 21 days (age 1 month to 21 years);
   c. New 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 NCCNApproval duration:
Commercial: 12 months
Medicaid: 12 months

III. Appendices

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

APPENDIX B: Therapeutic Alternatives

- Not applicable

APPENDIX C: Contraindications/Boxed Warnings

- Contraindication(s):
  - History of serious allergic reactions to Oncaspar® or to pegylated L-asparaginase therapy;
  - History of serious thrombosis with prior L-asparaginase therapy;
  - History of serious pancreatitis with prior L-asparaginase therapy;
  - History of serious hemorrhagic events with prior L-asparaginase therapy;
  - Severe hepatic impairment.

- Boxed warning(s):
  - None reported.

APPENDIX D: General Information

- Hypersensitivity: Observe patients for one hour after administration. Discontinue Asparlas™ in patients with serious hypersensitivity reactions.
- Pancreatitis: Discontinue Asparlas™ in patients with pancreatitis. Monitor blood glucose.
- Thrombosis: Discontinue Asparlas™ for severe or life-threatening thrombosis.
- Hemorrhage: Discontinue Asparlas™ for severe or life-threatening hemorrhage. Evaluate for etiology and treat.
- Hepatotoxicity: Monitor for toxicity through recovery from cycle. Discontinue Asparlas™ for severe liver toxicity.

IV. References

1. Oncaspar Prescribing Information. Boston, MA: Servier Pharmaceuticals LLC; June 2020. Available at: https://www.oncaspar.com/prescribing_information.pdf. Accessed May 31, 2021.
2. Asparlas Prescribing Information. Boston, MA: Servier Pharmaceuticals LLC; June 2020. Available at: https://asparlas.com/resource/1616938898000/asparlas/files/Asparlas_PI.pdf . Accessed May 31, 2021.
3. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed May 31, 2021.
4. National Comprehensive Cancer Network. Acute Lymphoblastic Leukemia Version 1.2021. Available at https://www.nccn.org/professionals/physician_gls/pdf/all.pdf. Accessed May 31, 2021.
5. National Comprehensive Cancer Network. Pediatric Acute Lymphoblastic Leukemia Version 2.2021. Available at: https://www.nccn.org/professionals/physician_gls/pdf/ped_all.pdf. Accessed May 31, 2021.
6. National Comprehensive Cancer Network. T-Cell Lymphomas Version 1.2021. Available at https://www.nccn.org/professionals/physician_gls/pdf/t-cell.pdf. Accessed May 31, 2021.

Review/Revision History	Review/Revised Date	P&T Approval Date
Policy established.	01/2020	03/06/2020
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 "Member is currently receiving medication that has been authorized by RxAdvance…". 5. References were reviewed and updated.	07/19/2020	09/14/2020

Review/Revision History	Review/Revised Date	P&T Approval Date
Policy was reviewed 1. Statement about provider sample ‘‘The provision of provider samples does not guarantee coverage…” was added to Clinical Policy. 2. Initial Approval Criteria I.B.1 was updated from “Diagnosis of NK/T-cell lymphoma, nasal type” to “Diagnosis of one of the following NK/T-cell lymphoma subtypes (a, b, or c)…”. 3. Initial Approval Criteria I.B.1.a was updated to include “Nasal type;”. 4. Initial Approval Criteria I.B.1.b was updated to include “Extranasal type;”. 5. Initial Approval Criteria I.B.1.c was updated to include “Aggressive NK-cell leukemia;”. 6. Initial Approval Criteria I.B.2 was updated to include “Request is for Oncaspar®;”. 7. Initial Approval Criteria I.B.5.c was updated to include “DDGP (dexamethasone, cisplatin, gemcitabine, pegaspargase);”. 8. Initial Approval Criteria I.C was updated to include off-label indication, “Hepatosplenic T-Cell Lymphoma (off-label) (must meet all):”. 9. Initial Approval Criteria and Continued Therapy Approval Criteria were updated to remove HIM approval duration.	05/31/2021	09/14/2021

Review/Revision History	Review/Revised Date	P&T Approval Date
10. Continued Therapy Approval Criteria II.A.1 was rephrased to "Member is currently receiving medication that has been authorized by RxAdvance...". 11. Appendix D was updated to include warnings and precautions, "Hypersensitivity: Observe patients for one hour after administration…", "Pancreatitis: Discontinue Asparlas™ in patients with pancreatitis…", "Thrombosis: Discontinue Asparlas™ for severe or life-threatening thrombosis…", "Hemorrhage: Discontinue Asparlas™ for severe or life-threatening hemorrhage…", and "Hepatotoxicity: Monitor for toxicity through recovery from cycle…". 12. References were reviewed and updated.		