

Medical Drug Clinical Criteria

Subject:	Asparagine Specific Enzymes		
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Overview

This document addresses the use of asparagine specific enzymes, Oncaspar (pegaspargase), Rylaze (asparaginase [*erwinia chrysanthemi*]), and Asparlas (calaspargase pegol-mknl). These products are enzymes that work by depleting blood plasma levels of asparagine. Normal cells create more asparagine; however, some leukemic cells are not able to synthesize this amino acid and subsequently die. Asparagine specific enzymes are primarily used to treat acute lymphoblastic leukemia (ALL).

The native form of asparaginase, marketed as Elspar, is no longer commercially available in the US. Oncaspar is an E.coli-derived pegylated form of asparaginase approved in 1994 to treat individuals with ALL and hypersensitivity to native asparaginase. It now carries an indication to be used as a component of multi-agent chemotherapeutic regimen for first-line treatment of ALL. Erwinaze is an E.chrysanthemi-derived form of asparaginase approved in 2011 to treat individuals with ALL and hypersensitivity to E.coli-derived asparaginase. It is administered more frequently than pegylated forms of the enzyme. Rylaze, another E.chrysanthemi-derived asparaginase product, was approved in 2021 for individuals with hypersensitivity to E.coli-derived asparaginase. It is administered via IM injection every 48 hours. Asparlas (calaspargase pegol) was recently FDA approved as another first line option in ALL for patients aged 1 month to 21 years. Similar to Oncaspar, Asparlas is an E.coli-derived pegylated form of asparaginase with a slightly different mPEG moiety which allows it to be dosed no more frequently than every 3 weeks compared with the biweekly dosing of Oncaspar.

The National Comprehensive Cancer Network® (NCCN) provides additional recommendations with a category 2A level of evidence for the use of asparagine specific enzymes. NCCN notes that asparaginase-based chemotherapy regimens are recommended for extranodal NK/T-cell lymphomas, nasal type (a rare subtype of non-hodgkins lymphoma), with pegaspargase-based regimens preferred. NCCN also notes that Asparlas may be substituted for pegaspargase in patients ≤21 years of age for more sustained asparaginase activity. NCCN removed the 2A recommendation for Asparlas in Extranodal NK/T-cell lymphomas, and nasal type for Asparlas and Oncaspar

Definitions and Measures

Acute leukemia: A type of leukemia where the number of leukemic cells develops rapidly and these abnormal cells do not perform the normal functions of the white blood cells.

Hypersensitivity: An exaggerated response by the immune system to a drug or other substance.

Leukemia: A type of cancer that starts in blood-forming tissue, such as the bone marrow, and causes large numbers of abnormal blood cells to be produced and enter the bloodstream.

Lymphoid leukemia: Leukemia that starts in lymphoid cells is called lymphoid, lymphoblastic, or lymphocytic leukemia.

Clinical Criteria

When a drug is being reviewed for coverage under a member's medical benefit plan or is otherwise subject to clinical review (including prior authorization), the following criteria will be used to determine whether the drug meets any applicable medical necessity requirements for the intended/prescribed purpose.

Erwinaze (asparaginase [*erwinia chrysanthemi*]); Rylaze (asparaginase *erwinia chrysanthemi* (recombinant)-rywn)

Requests for **Erwinaze (asparaginase [*erwinia chrysanthemi*])** or **Rylaze (asparaginase *erwinia chrysanthemi* (recombinant)-rywn)** may be approved if the following criteria are met:

- I. ____ Individual has a diagnosis of one of the following:
A. aAcute lymphoblastic lymphoma or acute lymphocytic (lymphoblastic) leukemia (ALL) (Label); **OR**

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~~+B. Extranodal Natural Killer T-cell lymphoma (ENKL) (NCCN 2A);~~

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AND

- II. Individual has developed a documented systemic allergic reaction or anaphylaxis to prior treatment with *E. Coli* – derived asparaginase;

AND

- III. Individual does not have any of the following contraindications:
- A. History of serious thrombosis with prior L-asparaginase therapy; **OR**
 - B. History of serious pancreatitis with prior L-asparaginase therapy; **OR**
 - C. History of serious hemorrhagic events with prior L-asparaginase therapy.

Requests for ~~Erwinaze (asparaginase [erwinia chrysanthemi])~~ or Rylaze (asparaginase erwinia chrysanthemi (recombinant)-rywn) may not be approved if above criteria are not met and for all other indications.

Oncaspar (pegaspargase)

Requests for Oncaspar (pegaspargase) may be approved if the following criteria are met:

- I. Individual has a diagnosis of one of the following:
- A. Acute lymphoblastic lymphoma or acute lymphocytic (lymphoblastic) leukemia (ALL); **OR**
 - B. Extranodal natural killer T-cell lymphoma (ENKL) (NCCN 2A); **OR**
 - ~~C. Hepatosplenic T-Cell Lymphoma (NCCN 2A);~~

AND

- II. Individual does not have any of the following contraindications:
- A. History of serious thrombosis with prior L-asparaginase therapy; **OR**
 - B. History of serious pancreatitis with prior L-asparaginase therapy; **OR**
 - C. History of serious hemorrhagic events with prior L-asparaginase therapy; **OR**
 - D. Severe hepatic impairment.

Requests for Oncaspar (pegaspargase) may not be approved if above criteria are not met and for all other indications.

Asparlas (calaspargase pegol-mknl)

Requests for Asparlas (calaspargase pegol-mknl) may be approved if the following criteria are met:

- I. Individual is age 1 month to 21 years (Label, NCCN 2A); **AND**
- II. Individual has a diagnosis of acute lymphoblastic lymphoma or acute lymphocytic (lymphoblastic) leukemia (ALL);

AND

- III. Individual does not have any of the following contraindications:
- A. History of serious hypersensitivity reactions, including anaphylaxis, to pegylated L-asparaginase therapy; **OR**
 - B. History of serious thrombosis with prior L-asparaginase therapy; **OR**
 - C. History of serious pancreatitis with prior L-asparaginase therapy; **OR**
 - D. History of serious hemorrhagic events with prior L-asparaginase therapy; **OR**
 - E. Severe hepatic impairment.

Requests for Asparlas (calaspargase pegol-mknl) may not be approved if above criteria are not met and for all other indications.

Coding

The following codes for treatments and procedures applicable to this document are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

HCPCS

J9019	Injection, asparaginase (Erwinaze), 1,000 iu
J9020	Injection, asparaginase, not otherwise specified, 10,000 units
J9021	Injection, asparaginase, recombinant, (Rylaze), 0.1 mg
J9266	Injection, pegaspargase, per single dose vial (Oncaspar)

J9118 Injection, calaspargase pegol-mknl, 10 units [Asparlas]

ICD-10 Diagnosis

C83.50-C83.59	Lymphoblastic (diffuse) lymphoma
C86.1	Hepatosplenic T-cell lymphoma
C91.00-C91.02	Acute Lymphoblastic Leukemia (ALL)

Document History

Revised: 02/23/2024

Document History:

- 02/23/2024 – Annual Review: Remove Erwinaze, no longer available. Add NCCN 2A use in ENKT cell lymphoma for Rylaze. Update Oncaspar criteria to remove NCCN recommendation for use in Hepatosplenic T-cell lymphoma. Add references. Wording and formatting updates. Coding Reviewed: No changes.
- 02/24/2023 – Annual Review: Update criteria for Erwinaze, Oncaspar and Asparlas. Coding Reviewed: Added ICD-10-CM C86.1. Removed ICD-10-CM C86.0.
- 02/25/2022 – Annual Review: No changes. Coding Reviewed: No changes.
- 08/20/2021 – Select Review: Add new agent Rylaze to clinical criteria; update criteria to align with label. Coding reviewed: Added HCPCS J3590, J9999, C9399 for Rylaze. Coding Reviewed: Added J9021. Removed J3590, J9999, C9399.
- 02/19/2021 – Annual Review: No changes. No changes. Coding Reviewed: No changes.
- 02/21/2020 – Annual Review: Roll in criteria from ING-CC-0138 Asparlas (calaspargase pegol-mknl). No changes to criteria. Coding Reviewed: Added HCPCS code J9118 for Asparlas.
- 05/17/2019 – Annual Review: First review of asparaginase specific enzymes. Add new contraindication to Oncaspar criteria. Add references for off label indications.

References

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2. DailyMed. Package inserts. U.S. National Library of Medicine, National Institutes of Health website. <http://dailymed.nlm.nih.gov/dailymed/about.cfm>. Accessed: December 28, 2023.
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4. Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc.; 2023; Updated periodically.
5. NCCN Clinical Practice Guidelines in Oncology™. © 2023 National Comprehensive Cancer Network, Inc. For additional information visit the NCCN website: <http://www.nccn.org/index.asp>. Accessed on December 28, 2023.
 - a. Acute Lymphoblastic Leukemia. V3.2023. Revised October 09, 2023.
 - b. Pediatric Acute Lymphoblastic leukemia. V3.2024. Revised October 31, 2023.
 - c. T-Cell Lymphomas. V1.2024. Revised December 21, 2023.

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