**CLINICAL GUIDELINES FOR MEDICAL NECESSITY**

**MEDICAL POLICY**

# Pegaspargase (Oncaspar®)

Version: 1.0

**EFFECTIVE DATE: 3/1/2025**

NantHealth® | Eviti®

## Please note the following:

## Pegaspargase (Oncaspar®)

**Note: For Medicare members/enrollees, to ensure consistency with the Medicare National Coverage Determinations (NCD) and Local Coverage Determinations (LCD), all applicable NCDs, LCDs, and Medicare Coverage Articles should be reviewed prior to applying the criteria set forth in this clinical policy. Please refer to the CMS website at http://www.cms.gov for additional information.**

**Note: For Medicaid members/enrollees, circumstances when state Medicaid coverage provisions conflict with the coverage provisions within this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.**

## Pegaspargase (Oncaspar): Discussion

Pegylated formulations of E. coli L-asparaginase have been developed, including pegaspargase, which extends the circulation time of the enzyme and diminishes immunogenicity. The favorable pharmacokinetic and immunogenicity profile of pegylated formulations over E. coli L-asparaginase helps reduce hypersensitivity reactions, the development of neutralizing antibodies, and the administration frequency, while maintaining its anti-leukemic efficacy.[1]

Adverse reactions include anaphylaxis or serious hypersensitivity reactions, thrombosis, pancreatitis, hemorrhage, and hepatotoxicity, including hepatic veno-occlusive disease. The most common grade >3 adverse reactions are hypoalbuminemia, elevated transaminase, febrile neutropenia, hypertriglyceridemia, hyperglycemia, increased bilirubin increased, pancreatitis, abnormal clotting studies, embolic and thrombotic events, hypersensitivity, sepsis, and infections.

Pegaspargase is approved by the Food and Drug Administration (FDA) for acute lymphoblastic leukemia.[2]

The National Comprehensive Cancer Network (NCCN) endorses pegaspargase for the following cancer types: acute lymphoblastic leukemia (ALL), extranodal natural killer (NK)/T cell lymphoma, and pediatric ALL.[3,4,5]

## Pegaspargase: Definitions

- **AYA (Adolescents and Young Adults)** - Individuals within the range of 15 to 39 years of age.
- **National Comprehensive Cancer Network (NCCN)** - An alliance of more than 30 leading cancer centers devoted to patient care, research, and education. The NCCN guidelines are utilized for Radiation Therapy and Medical Oncology standards. NCCN consensus clinical standards are periodically updated, and NantHealth, Inc. reviews these and updates its policies within a timely manner.
- **Food and Drug Administration (FDA)** - The FDA is responsible for protecting the public health by assuring the safety, efficacy, and security of human and veterinary drugs, biological products, medical devices, our nation's food supply, cosmetics, and products that emit radiation.

## Pegaspargase: Policy

**Note:** Coverage of pegaspargase will be provided for an FDA-approved indication or National Comprehensive Cancer Network (NCCN) guidelines when it is a Category 1, 2A, or 2B recommendation or when all criteria are met.

Pegaspargase will be considered for coverage when the following criteria are met:

### Acute Lymphoblastic Leukemia

1. Prescribed by or in consultation with an oncologist; AND

For **FDA** required criteria coverage:

2. At least 18 years of age; AND
3. First-line therapy; OR
4. Hypersensitivity to asparaginase;[2] OR

For **NCCN** required criteria coverage:

5. Component of European Study for Philadelphia-positive acute lymphoblastic leukemia (EsPhALL) + tyrosine kinase inhibitors (TKI) for one of the following:
   a) Induction (cyclophosphamide, cytarabine, dexamethasone, doxorubicin, mercaptopurine, pegaspargase, thioguanine, vincristine)
   b) Consolidation (cyclophosphamide, cytarabine, daunorubicin, dexamethasone, etoposide, ifosfamide, high-dose methotrexate, pegaspargase, vincristine)

   The above regimen is used for AYA without substantial comorbidities with Philadelphia chromosome-positive B-ALL during frontline therapy or relapsed/refractory (R/R) therapy if not previously given.

   **Note:**

   1. Imatinib use in first-line treatment should be restricted to those who cannot tolerate broader acting TKIs.
   2. There is data to support the benefit of rituximab for CD20-positive disease in addition to chemotherapy (excluding immunotherapy) (especially if age <60 years); OR

6. Component for one of the following:
   a) Cancer and Leukemia Group B (CALGB)10403: induction (daunorubicin, pegaspargase, prednisone, vincristine; with intrathecal (IT) cytarabine, IT methotrexate)
   b) CALGB 10403: extended induction (daunorubicin, pegaspargase, prednisone, vincristine)
   c) CALGB 10403: consolidation (cyclophosphamide, cytarabine, mercaptopurine, pegaspargase, vincristine; with IT methotrexate)
   d) CALGB 10403: interim maintenance (methotrexate, pegaspargase, vincristine; with IT methotrexate)

e) CALGB 10403: delayed intensification (cyclophosphamide, cytarabine, dexamethasone, doxorubicin, pegaspargase, thioguanine, vincristine; with IT methotrexate)
f) Dana Farber Cancer Institute (DFCI) ALL regimen based on DFCI Protocol 00-01 (preferred in frontline for Philadelphia chromosome-negative B-ALL): induction (doxorubicin, pegaspargase, prednisone, vincristine, with IT chemotherapy (cytarabine, methotrexate, hydrocortisone), with or without high-dose methotrexate/leucovorin)
g) DFCI ALL regimen based on DFCI Protocol 00-01 (preferred in frontline for Philadelphia chromosome-negative B-ALL): consolidation (dexamethasone, doxorubicin, mercaptopurine, methotrexate, pegaspargase, vincristine, with IT chemotherapy (cytarabine, methotrexate, hydrocortisone)
h) Programa Espanol de Tratamiento en Hematologia (Spanish Program for Hematology Treatment [PETHEMA]) ALL-96 (if age <30 years): induction (cyclophosphamide, daunorubicin, pegaspargase, prednisone, vincristine)
i) PETHEMA ALL-96 (if age <30 years): consolidation 2 (dexamethasone, vincristine, daunorubicin, cyclophosphamide, pegaspargase)
j) PETHEMA ALL-96 (if age <30 years): maintenance 1 (mercaptopurine, vincristine, methotrexate, prednisone, pegaspargase)
k) University of Southern California/Memorial Sloan-Kettering Cancer Center (USC/MSKCC) ALL regimen based on Children's Cancer Group (CCG)-1882 regimen (if age ≥18 years): induction phase 1 (daunorubicin, augmented pegaspargase, prednisone, vincristine; with IT hydrocortisone, IT methotrexate)
l) USC/MSKCC ALL regimen based on CCG-1882 regimen (if age ≥18 years): induction phase 2 (cyclophosphamide, cytarabine, mercaptopurine, augmented pegaspargase, prednisone, vincristine; with IT hydrocortisone, IT methotrexate)
m) USC/MSKCC ALL regimen based on CCG-1882 regimen (if age ≥18 years): intensification∞ 1 & 2 (leucovorin, high-dose methotrexate, augmented pegaspargase, prednisone)
n) USC/MSKCC ALL regimen based on CCG-1882 regimen (if age ≥18 years): re-induction 1 & 2 (cyclophosphamide, cytarabine, daunorubicin, dexamethasone, augmented pegaspargase, thioguanine, vincristine; with IT hydrocortisone, IT methotrexate)

The above regimens are used for AYA without substantial comorbidities with Philadelphia chromosome-negative B-ALL or T-ALL during frontline therapy or if in late relapse (>3 years from initial diagnosis) if the regimen was used in frontline therapy.

**Note:** Blinatumomab alternating with frontline consolidation therapy should be incorporated as a post-remission approach for Philadelphia chromosome-negative B-ALL based-on data from Eastern Cooperative Oncology Group (ECOG)1910 if minimal/measurable residual disease negative/unavailable for Philadelphia chromosome-negative B-ALL; OR

7. Component of COG AALL0434 for one of the following:
   a) Induction (daunorubicin, pegaspargase, prednisone, vincristine)
   b) Consolidation (cyclophosphamide, cytarabine, mercaptopurine, pegaspargase, vincristine; with or without nelarabine)

   The above regimen is used for AYA without substantial comorbidities with Philadelphia chromosome-negative B-ALL or T-ALL during frontline therapy or if in late relapse (>3 years from initial diagnosis) if the regimen was used in frontline therapy; OR

8. Component for one of the following:
   a) Group for Research on Adult Acute Lymphoblastic Leukemia (GRAALL) 2005): induction and late intensification (cyclophosphamide, daunorubicin, pegaspargase, prednisone, vincristine)
   b) GRAALL-2005: consolidation (cyclophosphamide, cytarabine, dexamethasone, etoposide, mercaptopurine, high-dose methotrexate, leucovorin, pegaspargase, vincristine)
   c) GRAALL-2005: interphase 2 (methotrexate, leucovorin, pegaspargase)
   d) Linker 4-drug regimen (B-ALL): induction (cyclophosphamide, daunorubicin, prednisone, pegaspargase, vincristine)
   e) Linker 4-drug regimen (B-ALL): consolidation (cytarabine, etoposide, mercaptopurine, high-dose methotrexate, pegaspargase)
   f) Linker 4-drug regimen (T-ALL): induction 1A & consolidation 2A (daunorubicin, vincristine, dexamethasone or prednisone, pegaspargase, IT methotrexate)

   The above regimens are used for (AYA and adults age <60 years) without substantial comorbidities with Philadelphia chromosome-negative B-ALL or T-ALL during frontline therapy or if in late relapse (>3 years from initial diagnosis) if the regimen was used in frontline therapy.

   **Note:**
   1. Used with rituximab for CD20-positive B-ALL (excluding interphase 2 of GRAALL-2005)
   2. Blinatumomab alternating with frontline consolidation therapy should be incorporated as a post-remission approach for Philadelphia chromosome-negative B-ALL based on data from ECOG1910 if minimal/measurable residual disease negative/unavailable for Philadelphia chromosome-negative B-ALL; OR

9. Component of dose-adjusted GRAALL-2014 for one of the following:
   a) Induction (cyclophosphamide, daunorubicin, vincristine, prednisone, pegaspargase)
   b) Consolidation (cyclophosphamide, cytarabine, dexamethasone, etoposide, mercaptopurine, high-dose methotrexate, leucovorin, pegaspargase, vincristine, with or without nelarabine); OR

   The above regimen is used for adults age <65 years without substantial comorbidities with T-ALL during frontline therapy or if in late relapse (>3 years from initial diagnosis) if the regimen was used in frontline therapy; OR

10. Component of USC/MSKCC ALL regimen based on CCG-1882 regimen for one of the following:
    a) Induction phase 1 (daunorubicin, augmented pegaspargase, prednisone, vincristine; with IT hydrocortisone, IT methotrexate)
    b) Induction phase 2 (cyclophosphamide, cytarabine, mercaptopurine, augmented pegaspargase, prednisone, vincristine; with IT hydrocortisone, IT methotrexate)
    c) Intensification 1 & 2 (leucovorin, high-dose methotrexate, augmented pegaspargase, prednisone)
    d) Re-induction 1 & 2 (cyclophosphamide, cytarabine, daunorubicin, dexamethasone, augmented pegaspargase, thioguanine, vincristine; with IT hydrocortisone, IT methotrexate)

The above regimen is used for adults age <60 years without substantial comorbidities with Philadelphia chromosome-negative B-ALL during frontline therapy or if in late relapse (>3 years from initial diagnosis) if the regimen was used in frontline therapy.

**Note:**

1. There is data to support the benefit of rituximab for CD20-positive disease in addition to chemotherapy (excluding immunotherapy) (especially if age <60 years)
2. Blinatumomab alternating with frontline consolidation therapy should be incorporated as a post-remission approach for Philadelphia chromosome-negative B-ALL based on data from ECOG1910; OR

11. Component of dose-adjusted CALGB 8811 Larson for one of the following:
    a) Course 1 induction (cyclophosphamide, daunorubicin, pegaspargase, prednisone, vincristine)
    b) Course 2 early intensification (cyclophosphamide, cytarabine, mercaptopurine, pegaspargase, vincristine, IT methotrexate)

    The above regimen is used for adult patients age <65 years without substantial comorbidities with Philadelphia chromosome-negative B-ALL or T-ALL during frontline therapy or if in late relapse (>3 years from initial diagnosis) if the regimen was used in frontline therapy.

    **Note:**

    1. There is data to support the benefit of rituximab for CD20-positive B-ALL in addition to chemotherapy (excluding immunotherapy) (especially if age <60 years)
    2. Blinatumomab alternating with frontline consolidation therapy should be incorporated as a post-remission approach for Philadelphia chromosome-negative B-ALL based on data from ECOG1910; OR

12. Component of MRC UKALLXII/ECOG2993 for one of the following:
    a) Induction phase 1 (daunorubicin, vincristine, prednisone, pegaspargase, IT methotrexate)
    b) Intensification (methotrexate, leucovorin, pegaspargase)

    The above regimen is used for adults age <65 without substantial comorbidities with Philadelphia chromosome-negative B-ALL or T-ALL during frontline therapy or if in late relapse (>3 years from initial diagnosis) if the regimen was used in frontline therapy.

    **Note:** There is data to support the benefit of rituximab for CD20-positive B-ALL in addition to chemotherapy (excluding immunotherapy) (especially if age <60 years); OR

13. Component of ECOG1910 (preferred in frontline for adults aged <65 years without substantial comorbidities) for one of the following:
    a) Induction (cyclophosphamide, cytarabine, daunorubicin, dexamethasone, mercaptopurine, pegaspargase if age <55 years, vincristine, rituximab for CD20-positive disease)

b) Consolidation - if minimal/measurable residual disease negative/unavailable for Philadelphia chromosome-negative B-ALL (cyclophosphamide, cytarabine, daunorubicin, dexamethasone, etoposide, mercaptopurine, high-dose methotrexate, leucovorin, pegaspargase, vincristine, rituximab for CD20-positive disease, alternating with blinatumomab); OR

The above regimen is used for Philadelphia chromosome negative B-ALL for one of the following:

1. Frontline therapy (AYA without substantial comorbidities and adults)
2. Refractory therapy in adults age ≥65 years or adults with substantial comorbidities
3. If in late relapse (>3 years from initial diagnosis) if the regimen was used in frontline therapy (AYA without substantial comorbidities and adults); OR

14. Relapsed/refractory therapy for T-ALL as a component of bortezomib containing regimen for one of the following:
    a) Block 1 Reinduction: vincristine, doxorubicin, prednisone, bortezomib, pegaspargase; with IT hydrocortisone (if CNS positive), IT cytarabine, IT methotrexate
    b) Block 3 Reinduction: cytarabine, pegaspargase; OR

15. Component of ALL-INITIAL-1: consolidation (cyclophosphamide, cytarabine, dexamethasone, idarubicin, high-dose methotrexate, leucovorin, pegaspargase, vincristine, with rituximab for CD20-positive disease); OR

    The above regimen is used for adults age ≥ 65 or adults with substantial comorbidities with Philadelphia chromosome-negative B-ALL during frontline or refractory therapy or if in late relapse (>3 years from initial diagnosis) if the regimen was used in frontline therapy.

    **Note:** Blinatumomab alternating with frontline consolidation therapy should be incorporated as a post-remission approach for Philadelphia chromosome-negative B-ALL based on data from ECOG1910 if minimal/measurable residual disease negative/unavailable; OR

16. Component for one of the following:
    a) Acute lymphoblastic leukemia older patients (ALLOLD07) regimen: consolidation (cytarabine, high-dose methotrexate, leucovorin, pegaspargase)
    b) Modified DFCI 91-01 protocol: induction (dexamethasone, pegaspargase, vincristine, IT cytarabine, intrathecal (IT) methotrexate, IT hydrocortisone; with or without doxorubicin, methotrexate)
    c) Modified DFCI 91-01 protocol: consolidation (dexamethasone, doxorubicin, mercaptopurine, pegaspargase, vincristine, IT cytarabine, IT methotrexate, IT hydrocortisone)
    d) CALGB 9111: induction (cyclophosphamide, daunorubicin, prednisone, pegaspargase, vincristine)
    e) CALGB 9111: consolidation (cyclophosphamide, cytarabine, dexamethasone, doxorubicin, mercaptopurine, pegaspargase, thioguanine, vincristine)

    The above regimens are used for adults age ≥65 or adults with substantial comorbidities with Philadelphia chromosome-negative B-ALL or T-ALL for one of the following:

1. Frontline therapy
2. Refractory therapy or if in late relapse (>3 years from initial diagnosis) if the regimen was used in frontline therapy.

**Note:** Blinatumomab alternating with frontline consolidation therapy should be incorporated as a post-remission approach for Philadelphia chromosome-negative B-ALL based-on data from ECOG1910 if minimal/measurable residual disease negative/unavailable for Philadelphia chromosome-negative B-ALL; OR

17. Component of European Working Group for Adult ALL (EWALL) for consolidation (cytarabine, high-dose methotrexate, pegaspargase)

    The above regimen is used for adults age ≥65 years or adults with substantial comorbidities with B-ALL for one of the following:

    1. Frontline therapy
    2. Relapsed/refractory therapy for Philadelphia chromosome-positive B-ALL, if not previously given
    3. Refractory therapy for Philadelphia chromosome-negative B-ALL if in late relapse (>3 years from initial diagnosis) for Philadelphia chromosome-negative B-ALL if the regimen was used in frontline therapy.

    **Note:**

    1. Used with a TKI for Philadelphia chromosome-positive B-ALL
    2. TKI options include: bosutinib, dasatinib, imatinib, nilotinib, or ponatinib
    3. Imatinib use in first-line should be restricted to those who cannot tolerate broader acting TKIs
    4. Blinatumomab alternating with frontline consolidation therapy should be incorporated as a post-remission approach for Philadelphia chromosome-negative B-ALL based on data from ECOG1910 if minimal/measurable residual disease (MRD) negative/unavailable for Philadelphia chromosome-negative B-ALL; OR

18. Component of dose-adjusted HyperCVAD for maintenance (hyperfractionated cyclophosphamide, dexamethasone, doxorubicin, mercaptopurine, methotrexate, pegaspargase, prednisone, vincristine; with or without nelarabine)

    The above regimen is used for T-ALL for one of the following:

    1. AYA without substantial comorbidities during frontline therapy or as a consideration if in late relapse (>3 years from initial diagnosis) if the regimen was used in frontline therapy.
    2. Adults age <65 years without substantial comorbidities during frontline therapy or as a consideration if in late relapse (>3 years from initial diagnosis) if the regimen was used in frontline therapy.
    3. Adults age ≥65 years or adults with substantial comorbidities during frontline therapy, refractory therapy, or as a consideration if in late relapse (>3 years from initial diagnosis) if regimen used in frontline; OR

19. Component for one of the following:
    a) Augmented HyperCVAD: hyperfractionated cyclophosphamide, mesna, intensified vincristine, doxorubicin, intensified dexamethasone, pegaspargase, IT methotrexate, IT cytarabine alternating with high-dose methotrexate, leucovorin, intensified vincristine, intensified dexamethasone, cytarabine, pegaspargase, IT methotrexate, IT cytarabine
    b) MOpAD: methotrexate, vincristine, pegaspargase, dexamethasone.

    The above regimens may be considered for Philadelphia chromosome-positive B-ALL if refractory to TKIs, are used for Philadelphia chromosome-negative B-ALL, and may be appropriate/considered for T-ALL during relapsed/refractory (R/R) therapy.

**Note:** MOpAD used with rituximab for CD20-positive B-ALL.[3]

**Extranodal NK/T-Cell Lymphomas**

1. At least 18 years of age; AND
2. Prescribed by or in consultation with an oncologist; AND

For **NCCN** required criteria coverage:

3. A component of modified-SMILE (steroid [dexamethasone], methotrexate, ifosfamide, pegaspargase, etoposide) for one of the following:
    a) Induction therapy as a component of combined modality therapy with sequential chemoradiation for stage I-II nasal disease in patients fit for chemotherapy, stage III/IV nasal disease, or stage I-IV extranasal disease
    b) Induction therapy as a component of combination chemotherapy with or without radiation for stage III/IV nasal disease or stage I-IV extranasal disease
    c) Additional therapy (if regimen not previously used) in patients with a positive biopsy following partial response to induction therapy or no response to induction therapy
    d) Aggressive NK-cell leukemia (ANKL); OR
4. A component of GELAD (gemcitabine, etoposide, pegaspargase, dexamethasone) for induction therapy as a component of combined modality therapy with sandwich chemoradiation for one of the following:
    a) Stage I-II nasal disease in patients fit for chemotherapy
    b) Stage III/IV nasal disease
    c) Stage I-IV extranasal disease; OR
5. A component of P-GEMOX (gemcitabine, pegaspargase, oxaliplatin) for one of the following:
    a) Induction therapy as a component of combined modality therapy with sandwich chemoradiation for stage I-II nasal disease in patients fit for chemotherapy, stage III/IV nasal disease, or stage I-IV extra nasal disease
    b) Induction therapy as a component of combination chemotherapy with or without radiation for stage III/IV nasal disease or stage I-IV extra nasal disease
    c) Additional therapy (if regimen not previously used) for patients with a positive biopsy following partial response to induction therapy or no response to induction therapy
    d) Aggressive NK-cell leukemia (ANKL); OR
6. A component of DDGP (dexamethasone, cisplatin, gemcitabine, pegaspargase) for one of the following:

a) Induction therapy as a component of combined modality therapy with sequential chemoradiation followed by RT for stage I-II nasal disease in patients fit for chemotherapy, or for stage III/IV nasal disease, or stage I-IV extranasal disease
b) Induction therapy as a component of combination chemotherapy with or without radiation for stage III/IV nasal disease or stage I-IV extranasal disease
c) Additional therapy (if regimen not previously used) in patients with a positive biopsy following partial response to induction therapy or no response to induction therapy
d) Aggressive NK-cell leukemia (ANKL); OR

7. A component of AspaMetDex (pegaspargase, methotrexate, dexamethasone) (for selected patients who cannot tolerate more intensive chemotherapy) for one of the following:
   a) Induction therapy as a component of combination chemotherapy with or without radiation for stage III/IV nasal disease or stage I-IV extra nasal disease
   b) Additional therapy (if regimen not previously used) in patients with a positive biopsy following partial response to induction therapy or no response to induction therapy
   c) Aggressive NK-cell leukemia (ANKL); OR
8. Relapsed/refractory disease (if not used in first-line therapy) following additional therapy with an alternate combination chemotherapy regimen (asparaginase-based) not previously used, as a component for one of the following:
   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).[4]

**Pediatric Acute Lymphoblastic Leukemia (ALL)**

1. Less than 18 years of age; AND
2. Prescribed by or in consultation with an oncologist; AND

For **NCCN** required criteria coverage:

3. Induction therapy as a component for one of the following:
   a) Standard arm of Children's Oncology Group (COG) AALL1731 regimen, based on COG AALL0932 regimen (SR arm) for B-cell receptor (BCR)::ABL1-negative B-ALL
   b) Standard arm of COG AALL1732 regimen, based on COG AALL1131 regimen (HR arm) for BCR::ABL1-negative B-ALL
   c) Dana Farber Cancer Institute (DFCI) ALL Protocol 16-001 regimen, based on DFCI ALL Protocol 11-001 regimen for BCR::ABL1-negative B-ALL
   d) Total Therapy XVII regimen, based on Total Therapy XVI regimen for BCR::ABL1-negative B-ALL
   e) COG AALL1131 regimen + dasatinib for BCR::ABL1-like B-ALL
   f) DFCI ALL Protocol 16-001 regimen (VHR arm) + dasatinib for BCR::ABL1-like B-ALL with ABL class kinase fusion
   g) Total Therapy XVII regimen + dasatinib for BCR::ABL1-like B-ALL with ABL class kinase fusion
   h) Total Therapy XVII regimen ± ruxolitinib for BCR::ABL1-like B-ALL with mutations associated with Janus kinase (JAK)-STAT pathway activation

i) COG AALL0622 regimen + dasatinib or imatinib for BCR::ABL1-positive B-ALL
j) Total Therapy XVII regimen + dasatinib for BCR::ABL1-positive B-ALL
k) COG AALL1231 regimen for T-ALL
l) COG AALL0434 regimen for T-ALL
m) DFCI ALL Protocol 16-001 regimen, based on DFCI ALL Protocol 11-001 regimen for T-ALL
n) St. Jude Children's Research Hospital (SJCRH) regimen, based on Total Therapy XVII protocol for T-ALL
o) Interfant regimens for infant ALL ± blinatumomab; OR

4. Consolidation therapy as a component for one of the following:
   a) Standard arm of COG AALL1731 regimen, based on COG AALL0932 regimen (SR-Avg/High arm) for BCR::ABL1-negative B-ALL
   b) Standard arm of COG AALL1732 regimen, based on COG AALL1131 regimen (HR arm) for BCR::ABL1-negative B-ALL
   c) DFCI ALL Protocol 16-001 regimen, based on DFCI ALL Protocol 11-001 regimen (SR arm or HR/VHR arms) for BCR::ABL1-negative B-ALL
   d) COG AALL1131 regimen + dasatinib for BCR::ABL1-like B-ALL and cytokine receptor-like factor 2 (CRLF2)- with ABL class kinase fusion
   e) COG AALL1521 regimen ± ruxolitinib for BCR::ABL1-like B-ALL and CRLF2+ or CRLF2- with JAK2 fusions, erythropoietin receptor (EPOR) rearrangements, SH2B3 gene alterations, interleukin-7 receptor (IL7R) insertions/deletions
   f) DFCI ALL Protocol 16-001 regimen + dasatinib for BCR::ABL1-like B-ALL with ABL class kinase fusion
   g) Standard arm of COG AALL1631 (based on COG AALL1122/European Study for Philadelphia-positive acute lymphoblastic leukemia (EsPhALL regimen) with EsPhALL backbone + imatinib or dasatinib for BCR::ABL1-positive B-ALL
   h) COG AALL0622 regimen + dasatinib for BCR::ABL1-positive B-ALL
   i) Total Therapy XVII regimen (SR/HR arm) + dasatinib for BCR::ABL1-positive B-ALL
   j) COG AALL1231 regimen for T-ALL
   k) COG AALL0434 regimen for T-ALL
   l) SJCRH regimen, based on Total Therapy XVII Protocol for T-ALL
   m) Interfant regimens for infant ALL (LR arm, intermediate risk and HR arms, post-consolidation, and HR arm not undergoing hematopoietic stem cell transplantation (HSCT) ± blinatumomab; OR
5. Relapsed/refractory BCR::ABL1-negative B-ALL, or in combination with dasatinib or imatinib for relapsed/refractory BCR::ABL1-positive B-ALL as a component for one of the following regimens:
   a) United Kingdom Acute Lymphoblastic Leukemia R3 (UKALL R3)
   b) Children's Oncology Group (COG) AALL01P2
   c) Acute Lymphoblastic Leukemia Relapse Berlin-Frankfurt-Munster 90 (ALL-REZ BFM 90)
   d) COG AALL07P1
   e) COG AALL1331
   f) High dose cytarabine-based
   g) Venetoclax containing ~~regimen~~ (venetoclax, vincristine, pegaspargase, and prednisone or dexamethasone); OR
6. Relapsed/refractory T-ALL as a component for one of the following:
   a) Bortezomib-containing regimen (e.g., bortezomib, vincristine, doxorubicin, pegaspargase, and prednisone or dexamethasone)

b) UKALL R3 Block 1
c) Berlin-Frankfurt-Munich (BFM) Intensification Block 1
d) Venetoclax containing regimen (venetoclax, vincristine, pegaspargase, and prednisone or dexamethasone)
e) Daratumumab containing regimen (daratumumab, vincristine, pegaspargase, doxorubicin, and prednisone or dexamethasone).[5]

## Authorization Period and Renewal Criteria

1. Initial Authorization Period: 12 months
2. Renewal Criteria: No evidence of disease progression or unacceptable toxicity
3. Renewal Authorization Period: 12 months

## Pegaspargase: References

1. Heo YA et al. A Review in Acute Lymphoblastic Leukemia. https://pmc.ncbi.nlm.nih.gov/articles/PMC6531401/. Accessed February 19, 2025.
2. Pegaspargase Package Insert. https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/103411s5207lbl.pdf. Accessed February 19, 2025.
3. National Comprehensive Cancer Network. Acute Lymphoblastic Leukemia. https://www.nccn.org/professionals/physician_gls/pdf/all.pdf. Accessed February 19, 2025.
4. National Comprehensive Cancer Network. T-Cell Lymphomas. https://www.nccn.org/professionals/physician_gls/pdf/t-cell.pdf. Accessed February 19, 2025.
5. National Comprehensive Cancer Network. Pediatric Acute Lymphoblastic Leukemia. https://www.nccn.org/professionals/physician_gls/pdf/ped_all.pdf. Accessed February 19, 2025.

## Pegaspargase: Coding (CPT®, ICD-10, and HCPCS) *

*Procedure codes appearing in medical policy documents are only included as a general reference. This list may not be all-inclusive and is subject to updates. In addition, the codes listed are not a guarantee of payment. CPT codes are available through the AMA.

| Code | Description |
|---|---|
| C86.0 | Extranodal NK/T-cell lymphomas |
| C91.0 | Acute lymphoblastic leukemia |
| J9266 | Pegaspargase |

## Pegaspargase: Revision and Review History

| No. | Description | Date(s) |
|---|---|---|
| 1 | Original Effective Date: | 3/1/2025 |
| 2 | Policy Review Dates: | |
| 3 | Policy Revision Dates: | |
| 4 | Department Owner: | Medical Affairs |
| 5 | NH Advisory Committee: | 3/20/2025 |
| 6 | Revision Changes: | |