Blincyto® (blinatumomab)
(Intravenous)

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Document Number: SHP-0382

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I. Length of Authorization [1,9,10]

Acute Lymphoblastic Leukemia (ALL)

- Relapsed or refractory disease:
  - Initial coverage will be provided for 30 weeks for a total of five cycles (2 cycles of induction followed by 3 cycles of consolidation)
  - Continued coverage will be provided every 24 weeks for a maximum of two additional authorizations (4 cycles of continued therapy)
- Consolidation therapy (Adult) and MRD+ (Pediatric):
  - Coverage will be provided for 24 weeks for a total of four cycles (1 cycle of induction followed by 3 cycles of consolidation)
- Infant ALL in combination with an Interfant regimen:
  - Coverage will be provided for 28 days

II. Dosing Limits

A. Quantity Limit (max daily dose) [NDC Unit]:

- Blincyto 35 mcg powder for injection: 28 vials per 42 day supply

B. Max Units (per dose and over time) [HCPCS Unit]:

- Acute Lymphoblastic Leukemia (ALL) (Adult/Pediatric)

  Cycle 1 – 5 (Induction/Consolidation)
  - 980 billable units per 42 days

  Cycle 6 – 9 (Continued Therapy)
  - 980 billable units per 84 days

III. Initial Approval Criteria [1]

Submission of medical records (chart notes) related to the medical necessity criteria is REQUIRED on all requests for authorizations. Records will be reviewed at the time of submission. Please provide documentation related to diagnosis, step therapy, and clinical markers (i.e. genetic and mutational testing) supporting initiation when applicable. Medical records may be submitted via direct upload through the PA web portal or by fax.

Coverage is provided in the following conditions:

Universal Criteria [1]

- Patient has not received a live vaccine within 2 weeks prior to initiating therapy and will not receive concurrent treatment with lives vaccine while on therapy; **AND**

Acute Lymphoblastic Leukemia (ALL) – Adult* † ‡ Φ [1-8,6e,7e]

- Patient is at least 15 years of age; **AND**
- Patient has B-cell precursor ALL; **AND**
  - Used as consolidation therapy following a complete response to induction therapy; **AND**
    - Patient has positive minimal residual disease (MRD+); **AND**
      - Used as a single agent; **OR**
      - Patient has MRD (presence of leukemic cells) greater than or equal to 0.1% as measured by flow cytometry or polymerase chain reaction (PCR); **AND**
    - Patient has negative minimal residual disease (MRD-); **AND**
      - Used as a single agent for Ph- disease; **AND**
      - Patient received induction therapy with inotuzumab ozogamicin + mini-hyperCVD; **OR**
  - Patient has relapsed or refractory disease; **AND**
    - Used as a single agent for Ph+ disease; **AND**
      - Patient was relapsed or refractory to at least one second-generation or later TKI (e.g., dasatinib, nilotinib, bosutinib, ponatinib); **OR**
      - Patient was intolerant to a second-generation or later TKI AND intolerant or refractory to imatinib; **OR**
    - Used as a single agent for Ph- disease; **OR**
    - Used in combination with inotuzumab ozogamicin + mini-hyperCVD for Ph+ or Ph- disease

***NCCN recommendations for ALL may be applicable to adolescent and young adult (AYA) patients within the age range of 15-39 years.*

Pediatric Acute Lymphoblastic Leukemia (ALL) † ‡ Φ [1-9]

- Patient is at least 1 month of age; **AND**
  - Used as a single agent; **AND**
    - Patient has B-cell precursor ALL; **AND**
      - Patient has minimal residual disease positive (MRD+) ALL; **AND**
        - Patient has MRD (presence of leukemic cells) greater than or equal to 0.1% as measured by flow cytometry or polymerase chain reaction (PCR); **AND**
          - Patient is in first or second complete remission; **OR**
          - Used after or at the end of consolidation therapy; **OR**
      - Patient has relapsed or refractory disease; **OR**
  - Used in combination with an Interfant regimen (e.g., Interfant-06, Interfant-99, etc.) for infant ALL

**NCCN recommendations for Pediatric ALL may be applicable to certain adolescent and young adult (AYA) patients up to 30 years of age.*

Preferred therapies and recommendations are determined by review of clinical evidence. NCCN category of recommendation is taken into account as a component of this review. Regimens deemed equally efficacious (i.e., those having the same NCCN categorization) are considered to be therapeutically equivalent.

† FDA Approved Indication(s); ‡ Compendium Recommended Indication(s); Φ Orphan Drug

IV. Renewal Criteria [1,2,9,10]

Coverage may be renewed based upon the following criteria:

- Patient continues to meet the universal and other indication-specific relevant criteria such as concomitant therapy requirements (not including prerequisite therapy), performance status, etc. identified in section III; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: Cytokine Release Syndrome (CRS), neurological toxicities, serious infections, pancreatitis, tumor lysis syndrome (TLS), neutropenia/febrile neutropenia, elevated liver enzyme, leukoencephalopathy, etc.; **AND**
- Treatment response or stabilization of disease as indicated by CBC, bone marrow cytogenic analysis, QPCR, or FISH; **AND**

Acute Lymphoblastic Leukemia (Adult/Pediatric) – Relapsed or refractory disease

- Patient has not exceeded 4 cycles of continued therapy or 9 total cycles of therapy for the treatment of relapsed or refractory disease

Adult Acute Lymphoblastic Leukemia – Consolidation therapy

- Coverage may not be renewed

Pediatric Acute Lymphoblastic Leukemia – MRD+

- Coverage may not be renewed

Pediatric Acute Lymphoblastic Leukemia – With an Interfant regimen

- Coverage may not be renewed

V. Dosage/Administration [1,9,10]

Indication	Dose
Adult ALL	**Relapsed/Refractory Disease*** ➢ Weight greater than or equal to 45 kg – Cycle 1 (induction): • 9 mcg daily x 7 days, then 28 mcg daily x 21 days in a 42 day cycle – Cycles 2-5 (induction/consolidation): • 28 mcg daily x 28 days in a 42 day cycle. – Cycles 6-9 (continued therapy): • 28 mcg daily x 28 days in an 84 day cycle. ➢ Weight less than 45 kg – Cycle 1(induction) : • 5 mcg/m2/day (not to exceed 9 mcg/day) x 7 days, then 15 mcg/m2/day (not to exceed 28 mcg/day) x 21 days in a 42 day cycle – Cycles 2-5 (induction/consolidation): • 15 mcg/m2/day (not to exceed 28 mcg/day) x 28 days in a 42 day cycle. – Cycles 6-9 (continued therapy): • 15 mcg/m2/day (not to exceed 28 mcg/day) x 28 days in an 84 day cycle. **Up to 9 total cycles of therapy.*
	Consolidation Therapy* ➢ Weight greater than or equal to 45 kg – Cycle 1(induction): • 28 mcg daily x 28 days in a 42-day cycle – Cycles 2-4 (consolidation): • 28 mcg daily x 28 days in a 42 day cycle. ➢ Weight less than 45 kg – Cycle 1(induction) : • 15 mcg/m2/day (not to exceed 28 mcg/day) x 28 days in a 42 day cycle. – Cycles 2-4 (consolidation): • 15 mcg/m2/day (not to exceed 28 mcg/day) x 28 days in a 42 day cycle. **Up to 4 total cycles of therapy.*
Pediatric ALL	**Relapsed/Refractory Disease (single agent)*** ➢ Weight greater than or equal to 45 kg – Cycle 1 (induction): • 9 mcg daily x 7 days, then 28 mcg daily x 21 days in a 42 day cycle

	– Cycles 2-5 (induction/consolidation): • 28 mcg daily x 28 days in a 42 day cycle – Cycles 6-9 (continued therapy): • 28 mcg daily x 28 days in an 84 day cycle ➢ Weight less than 45 kg – Cycle 1 (induction) : • 5 mcg/m²/day (not to exceed 9 mcg/day) x 7 days, then 15 mcg/m²/day (not to exceed 28 mcg/day) x 21 days in a 42 day cycle – Cycles 2-5 (induction/consolidation): • 15 mcg/m²/day (not to exceed 28 mcg/day) x 28 days in a 42 day cycle – Cycles 6-9 (continued therapy): • 15 mcg/m²/day (not to exceed 28 mcg/day) x 28 days in an 84 day cycle **Up to 9 total cycles of therapy.*
	MRD+ (single agent)* ➢ Weight greater than or equal to 45 kg – Cycle 1 (induction): • 28 mcg daily x 28 days in a 42-day cycle – Cycles 2-4 (consolidation): • 28 mcg daily x 28 days in a 42 day cycle ➢ Weight less than 45 kg – Cycle 1 (induction): • 15 mcg/m²/day (not to exceed 28 mcg/day) x 28 days in a 42 day cycle – Cycles 2-4 (consolidation): • 15 mcg/m²/day (not to exceed 28 mcg/day) x 28 days in a 42 day cycle **Up to 4 total cycles of therapy.*
	In Combination with an Interfant Regimen (Infant ALL): 15 mcg/m²/day (not to exceed 28 mcg/day) x 28 days

VI. Billing Code/Availability Information

HCPCS Code:

- J9039 – Injection, blinatumomab, 1 microgram; 1 billable unit = 1 microgram

NDC:

- Blincyto 35 mcg single-dose powder for injection: 55513-0160-xx

VII. References (STANDARD)

1. Blincyto [package insert]. Thousand Oaks, CA; Amgen, February 2022. Accessed March 2023.
2. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) blinatumomab. National Comprehensive Cancer Network, 2023. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most

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6. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) for Pediatric Acute Lymphoblastic Leukemia 2.2023. National Comprehensive Cancer Network, 2023. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed March 2023.
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8. von Stackelberg A, Locatelli F, Zugmaier G, et al. Phase I/Phase II Study of Blinatumomab in Pediatric Patients With Relapsed/Refractory Acute Lymphoblastic Leukemia. J Clin Oncol. 2016;34(36):4381-4389. doi:10.1200/JCO.2016.67.3301.
9. Van Der Sluis IM, De Lorenzo P, Kotecha RS, et al. A phase 2 study to test the feasibility, safety and efficacy of the of the addition of blinatumomab to the Interfant06 backbone in infants with newly diagnosed KMT2A-rearranged acute lymphoblastic leukemia. a collaborative study of the Interfant Network. Blood 2021;138:361.
10. Advani AS, Moseley A, O'Dwyer KM, et al. SWOG 1318: A Phase II Trial of Blinatumomab Followed by POMP Maintenance in Older Patients With Newly Diagnosed Philadelphia Chromosome-Negative B-Cell Acute Lymphoblastic Leukemia. J Clin Oncol. 2022 May 10;40(14):1574-1582.

VIII. References (ENHANCED)

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2e. Kantarjian H, DeAngelo D, Stelljes M, et al. Inotuzumab Ozogamicin versus Standard Therapy for Acute Lymphoblastic Leukemia. N Engl J Med 2016; 375:740-753. DOI: 10.1056/NEJMoa1509277.

3e. Maude S, Laetsch T, Buechner J, et al. Tisagenlecleucel in Children and Young Adults with B-Cell Lymphoblastic Leukemia. N Engl J Med 2018; 378:439-448. DOI: 10.1056/NEJMoa1709866.

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6e. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Acute Lymphoblastic Leukemia Version 1.2022. National Comprehensive Cancer Network, 2023. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed March 2023.

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13e. Magellan Health, Magellan Rx Management. Blincyto Clinical Literature Review Analysis. Last updated March 2023. Accessed March 2023.

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
C83.50	Lymphoblastic (diffuse) lymphoma unspecified site
C83.51	Lymphoblastic (diffuse) lymphoma lymph nodes of head, face, and neck
C83.52	Lymphoblastic (diffuse) lymphoma intrathoracic lymph nodes
C83.53	Lymphoblastic (diffuse) lymphoma intra-abdominal lymph nodes
C83.54	Lymphoblastic (diffuse) lymphoma lymph nodes of axilla and upper limb
C83.55	Lymphoblastic (diffuse) lymphoma lymph nodes of inguinal region and lower limb
C83.56	Lymphoblastic (diffuse) lymphoma intrapelvic lymph nodes
C83.57	Lymphoblastic (diffuse) lymphoma spleen
C83.58	Lymphoblastic (diffuse) lymphoma lymph nodes of multiple sites
C83.59	Lymphoblastic (diffuse) lymphoma extranodal and solid organ sites
C91.00	Acute lymphoblastic leukemia not having achieved remission
C91.01	Acute lymphoblastic leukemia, in remission
C91.02	Acute lymphoblastic leukemia, in relapse

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determination (NCD), Local Coverage Determinations (LCDs), and Local Coverage Articles (LCAs) may exist and compliance with these policies is required where applicable. They can be found at: https://www.cms.gov/medicare-coverage-database/search.aspx. Additional indications may be covered at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD/LCA): N/A

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdictio	**Applicable State/US Territory**	**Contractor**
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT,	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdictio	**Applicable State/US Territory**	**Contractor**
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA, LLC
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA, LLC
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC