

Blincyto® (blinatumomab) (Intravenous)

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Document Number: IC-0382

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I. Length of Authorization ^{1,9,10}

Acute Lymphoblastic Leukemia (ALL)

- Relapsed or refractory disease (single agent):
 - 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)
- Relapsed or refractory disease (as a component of COG ALL1331 regimen):
 - Coverage will be provided every 56 days for a maximum of 3 cycles
- 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

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 live vaccine while on therapy; **AND**

Acute Lymphoblastic Leukemia (ALL) – Adult † ‡ ◊ ^{1-8,6e,7e}

- Patient is at least 18 years of age*; **AND**
- Patient has B-cell precursor ALL; **AND**
 - Used as consolidation therapy; **AND**
 - Patient has positive minimal residual disease (MRD+); **AND**
 - Used as a single agent; **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); **OR**
 - Patient has negative minimal residual disease (MRD-); **AND**
 - Used as a single agent for Ph- disease; **AND**
 - Used as a component of ECOG1910 regimen; **OR**
 - Used as a component of 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

**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) † ‡ ◊ ¹⁻¹¹

- 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 consolidation therapy; **OR**
- Patient has relapsed or refractory disease; **AND**
 - Patient has Ph⁻ disease; **OR**
 - Patient has Ph⁺ disease intolerant/refractory to TKI; **OR**
- Used as a component of COG AALL1331 regimen; **AND**
 - Patient has B-cell precursor ALL; **AND**
 - Patient has bone marrow relapse with or without extramedullary relapse; **AND**
 - Patient has Ph⁻ disease; **OR**
- Used in combination with an Interfant regimen (e.g., Interfant-06, Interfant-99, etc.) for infant ALL with KMT2A status (11q23) rearranged

**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); Ⓢ 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 [including Immune Effector Cell-Associated Neurotoxicity (ICANS)], 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 (single agent)

- Patient has not exceeded 4 cycles of continued therapy or 9 total cycles of therapy

Pediatric Acute Lymphoblastic Leukemia – Relapsed or refractory disease (as a component of COG ALL1331 regimen)

- Patient has not exceeded 3 cycles of therapy

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 ^{1,9-11}

Indication	Dose
Adult ALL	<p><u>Relapsed/Refractory Disease*</u></p> <ul style="list-style-type: none"> ➤ Weight greater than or equal to 45 kg <ul style="list-style-type: none"> – <u>Cycle 1 (induction):</u> <ul style="list-style-type: none"> • 9 mcg daily x 7 days, then 28 mcg daily x 21 days in a 42 day cycle – <u>Cycles 2-5 (induction/consolidation):</u> <ul style="list-style-type: none"> • 28 mcg daily x 28 days in a 42 day cycle. – <u>Cycles 6-9 (continued therapy):</u> <ul style="list-style-type: none"> • 28 mcg daily x 28 days in an 84 day cycle. ➤ Weight less than 45 kg <ul style="list-style-type: none"> – <u>Cycle 1(induction) :</u> <ul style="list-style-type: none"> • 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 – <u>Cycles 2-5 (induction/consolidation):</u> <ul style="list-style-type: none"> • 15 mcg/m²/day (not to exceed 28 mcg/day) x 28 days in a 42 day cycle. – <u>Cycles 6-9 (continued therapy):</u> <ul style="list-style-type: none"> • 15 mcg/m²/day (not to exceed 28 mcg/day) x 28 days in an 84 day cycle. <p><i>*Up to 9 total cycles of therapy.</i></p>
	<p><u>Consolidation Therapy*</u></p> <ul style="list-style-type: none"> ➤ Weight greater than or equal to 45 kg <ul style="list-style-type: none"> – <u>Cycle 1(induction):</u> <ul style="list-style-type: none"> • 28 mcg daily x 28 days in a 42-day cycle – <u>Cycles 2-4 (consolidation):</u>

	<ul style="list-style-type: none"> • 28 mcg daily x 28 days in a 42 day cycle. <p>➤ Weight less than 45 kg</p> <ul style="list-style-type: none"> - <u>Cycle 1(induction)</u> : <ul style="list-style-type: none"> • 15 mcg/m²/day (not to exceed 28 mcg/day) x 28 days in a 42 day cycle. - <u>Cycles 2-4 (consolidation):</u> <ul style="list-style-type: none"> • 15 mcg/m²/day (not to exceed 28 mcg/day) x 28 days in a 42 day cycle. <p><i>*Up to 4 total cycles of therapy.</i></p>
Pediatric ALL	<p><u>Relapsed/Refractory Disease:</u></p> <p><u>Used as a single agent*:</u></p> <p>➤ Weight greater than or equal to 45 kg</p> <ul style="list-style-type: none"> - <u>Cycle 1 (induction):</u> <ul style="list-style-type: none"> • 9 mcg daily x 7 days, then 28 mcg daily x 21 days in a 42 day cycle - <u>Cycles 2-5 (induction/consolidation):</u> <ul style="list-style-type: none"> • 28 mcg daily x 28 days in a 42 day cycle - <u>Cycles 6-9 (continued therapy):</u> <ul style="list-style-type: none"> • 28 mcg daily x 28 days in an 84 day cycle <p>➤ Weight less than 45 kg</p> <ul style="list-style-type: none"> - <u>Cycle 1 (induction)</u> : <ul style="list-style-type: none"> • 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 - <u>Cycles 2-5 (induction/consolidation):</u> <ul style="list-style-type: none"> • 15 mcg/m²/day (not to exceed 28 mcg/day) x 28 days in a 42 day cycle - <u>Cycles 6-9 (continued therapy):</u> <ul style="list-style-type: none"> • 15 mcg/m²/day (not to exceed 28 mcg/day) x 28 days in an 84 day cycle <p><u>Used as a component of COG AALL1331 regimen:</u></p> <ul style="list-style-type: none"> - <u>Cycles 1-3 (continuation and maintenance therapy):</u> <ul style="list-style-type: none"> • 15 mcg/m²/day x 28 days in a 56 day cycle <p><i>*Up to 9 total cycles of therapy.</i></p> <p><u>MRD+ (single agent)*</u></p> <p>➤ Weight greater than or equal to 45 kg</p> <ul style="list-style-type: none"> - <u>Cycle 1 (induction):</u> <ul style="list-style-type: none"> • 28 mcg daily x 28 days in a 42-day cycle - <u>Cycles 2-4 (consolidation):</u> <ul style="list-style-type: none"> • 28 mcg daily x 28 days in a 42 day cycle <p>➤ Weight less than 45 kg</p> <ul style="list-style-type: none"> - <u>Cycle 1 (induction):</u> <ul style="list-style-type: none"> • 15 mcg/m²/day (not to exceed 28 mcg/day) x 28 days in a 42 day cycle - <u>Cycles 2-4 (consolidation):</u> <ul style="list-style-type: none"> • 15 mcg/m²/day (not to exceed 28 mcg/day) x 28 days in a 42 day cycle <p><i>*Up to 4 total cycles of therapy.</i></p> <p><u>In Combination with an Interfant Regimen (Infant ALL):</u></p> <p>15 mcg/m²/day (not to exceed 28 mcg/day) x 28 days</p>

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, June 2023. Accessed February 2024.
2. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) blinatumomab. National Comprehensive Cancer Network, 2024. 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 February 2024.
3. Jen EY, Xu Q, Schetter A, Przepiora D, et al. FDA Approval: Blinatumomab for Patients with B-cell Precursor Acute Lymphoblastic Leukemia in Morphologic Remission with Minimal Residual Disease. *Clin Cancer Res.* 2019 Jan 15;25(2):473-477. doi: 10.1158/1078-0432.CCR-18-2337. Epub 2018 Sep 25.
4. Kantarjian H, Stein A, Gökbuget N, et al. Blinatumomab versus Chemotherapy for Advanced Acute Lymphoblastic Leukemia. *N Engl J Med* 2017; 376:836-847. doi: 10.1056/NEJMoa1609783.
5. Martinelli G, Boissel N, Chevallier P, et al. Complete Hematologic and Molecular Response in Adult Patients With Relapsed/Refractory Philadelphia Chromosome-Positive B-Precursor Acute Lymphoblastic Leukemia Following Treatment With Blinatumomab: Results From a Phase II, Single-Arm, Multicenter Study. *J Clin Oncol.* 2017 Jun 1;35(16):1795-1802. doi: 10.1200/JCO.2016.69.3531. Epub 2017 Mar 29.
6. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) for Pediatric Acute Lymphoblastic Leukemia 4.2024. National Comprehensive Cancer Network, 2024. 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 February 2024.
7. Topp MS, Gökbuget N, Stein AS, et al. Safety and activity of blinatumomab for adult patients with relapsed or refractory B-precursor acute lymphoblastic leukaemia: a multicentre, single-arm, phase 2 study. *Lancet Oncol.* 2015;16(1):57-66.

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.
11. Hogan LE, Brown PA, Ji L, et al. Children's Oncology Group AALL1331: Phase III trial of blinatumomab in children, adolescents, and young adults with low-risk B-Cell ALL in first relapse. *J Clin Oncol.* 2023;41(25):4118-4129.

VIII. References (ENHANCED)

- 1e. Gökbuget N, Dombret H, Bonifacio M, et al. Blinatumomab for minimal residual disease in adults with B-cell precursor acute lymphoblastic leukemia. *Blood.* 2018 Apr 5;131(14):1522-1531. doi: 10.1182/blood-2017-08-798322. Epub 2018 Jan 22.
- 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.
- 4e. Jeha S, Gaynon P, Razzouk, B, et al. Phase II Study of Clofarabine in Pediatric Patients With Refractory or Relapsed Acute Lymphoblastic Leukemia. *Journal of Clinical Oncology* 2006 24:12, 1917-1923.
- 5e. Benjamini O, Dumlao TL, Kantarjian H, et al. Phase II trial of hyper CVAD and dasatinib in patients with relapsed Philadelphia chromosome positive acute lymphoblastic leukemia or blast phase chronic myeloid leukemia. *Am J Hematol.* 2014 Mar;89(3):282-7.
- 6e. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Acute Lymphoblastic Leukemia Version 4.2023. National Comprehensive Cancer Network, 2024. 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 February 2024.
- 7e. Brown PA, Ji L, Xu X, et al. A Randomized Phase 3 Trial of Blinatumomab Vs. Chemotherapy As Post-Reinduction Therapy in High and Intermediate Risk (HR/IR) First

Relapse of B-Acute Lymphoblastic Leukemia (B-ALL) in Children and Adolescents/Young Adults (AYAs) Demonstrates Superior Efficacy and Tolerability of Blinatumomab: A Report from Children's Oncology Group Study AALL1331. *Blood* 2019; 134 (Supplement_2): LBA-1. doi: <https://doi.org/10.1182/blood-2019-132435>.

- 8e. Topp MS, Kufer P, Gökbuget N, et al. Targeted therapy with the T-cell-engaging antibody blinatumomab of chemotherapy-refractory minimal residual disease in B-lineage acute lymphoblastic leukemia patients results in high response rate and prolonged leukemia-free survival. *J Clin Oncol.* 2011;29(18):2493-2498. doi:10.1200/JCO.2010.32.7270.
- 9e. Foà R, Bassan R, Vitale A, et al. Dasatinib-Blinatumomab for Ph-Positive Acute Lymphoblastic Leukemia in Adults. *N Engl J Med.* 2020 Oct 22;383(17):1613-1623.
- 10e. Litzow MR, Sun Z, Paletta E, et al. Consolidation therapy with blinatumomab improves overall survival in newly diagnosed adult patients with B-Lineage acute lymphoblastic leukemia in measurable residual disease negative remission: results from the ECOG-ACRIN E1910 randomized Phase III National Cooperative Clinical Trials Network Trial. *Blood.* 2022;140(suppl 2):LBA-1. doi:10.1182/blood-2022-171751.
- 11e. Jabbour E, Sasaki K, Short NJ, et al. Long-term follow-up of salvage therapy using a combination of inotuzumab ozogamicin and mini-hyper-CVD with or without blinatumomab in relapsed/refractory Philadelphia chromosome-negative acute lymphoblastic leukemia. *Cancer.* 2021 Jun 15;127(12):2025-2038. doi: 10.1002/encr.33469.
- 12e. Van Der Sluis IM, De Lorenzo P, Kotecha RS, et al. A Phase 2 Study to Test the Feasibility, Safety and Efficacy 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.
- 13e. Jabbour E, Short NJ, Jain N, et al. Hyper-CVAD and sequential blinatumomab for newly diagnosed Philadelphia chromosome-negative B-cell acute lymphocytic leukaemia: a single-arm, single-centre, phase 2 trial. *Lancet Haematol* 2022;9:e878-e885.
- 14e. Jabbour E, Short NJ, Senapati J, et al. Mini-hyper-CVD plus inotuzumab ozogamicin, with or without blinatumomab, in the subgroup of older patients with newly diagnosed Philadelphia chromosome-negative B-cell acute lymphocytic leukaemia: long-term results of an open-label phase 2 trial. *Lancet Haematol* 2023;10:e433-e444.
- 15e. Martinelli G, Boissel N, Chevallier P, et al. Complete hematologic and molecular response in adult patients with relapsed/refractory Philadelphia chromosomepositive B-precursor acute lymphoblastic leukemia following treatment with blinatumomab: Results from a phase II, single-arm, multicenter study. *J Clin Oncol* 2017;35:1795-1802.
- 16e. Magellan Rx Management. Blincyto Clinical Literature Review Analysis. Last updated February 2024. Accessed February 2024.

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)

The preceding information is intended for non-Medicare coverage determinations. 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 Determinations (NCDs) and/or Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. Local Coverage Articles (LCAs) may also exist for claims payment purposes or to clarify benefit eligibility under Part B for drugs which may be self-administered. The following link may be used to search for NCD, LCD, or LCA documents: <https://www.cms.gov/medicare-coverage-database/search.aspx>. Additional indications, including any preceding information, may be applied 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		
Jurisdiction	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, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
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.

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	Applicable State/US Territory	Contractor
J (10)	TN, GA, AL	Palmetto GBA
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC