Clinical Policy: Blinatumomab (Blincyto)

Reference Number: PA.CP.PHAR.312
Effective Date: 01/2018
Last Review Date: 07/2025

Description
Blinatumomab (Blincyto®) is a bispecific CD19-directed CD3 T-cell engager.

FDA Approved Indication(s)
Blincyto is indicated in adults and children for the treatment of:

- CD19-positive B-cell precursor acute lymphoblastic leukemia (B-ALL) in first or second complete remission with minimal residual disease (MRD) ≥ 0.1%.
- Relapsed or refractory CD19-positive B-ALL.
- CD19-positive Philadelphia chromosome-negative (Ph-) B-ALL in the consolidation phase of multiphase chemotherapy

Policy/Criteria
It is the policy of PA Health & Wellness ® that Blincyto is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. B-Cell Acute Lymphoblastic Leukemia (must meet all):

1. Diagnosis of B-ALL;
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Requested as treatment for (a- f):
   a. B-ALL in remission but positive for minimal residual disease (MRD+);
   b. Philadelphia chromosome (Ph)-positive (*adults*) or BCR::ABL1-positive (*pediatrics*) disease, and prescribed in one of the following ways (i or ii):
      i. In combination with a tyrosine kinase inhibitor (TKI; e.g., imatinib, Sprycel®, Tasigna®, Bosulif®, Iclusig®) for induction therapy (*adults only*), consolidation therapy, or relapsed or refractory disease;
      ii. As a single agent for relapsed or refractory disease or for consolidation therapy (if request is for adult consolidation therapy, disease must be MRD-positive);
   c. Ph-negative (*adults*) or BCR::ABL1-negative (*pediatrics*) disease, and prescribed in one of the following ways (i, ii, or iii):
      i. As consolidation therapy as a single agent, alternating with multiagent therapy (*adults only*), or combination therapy (*pediatrics only*);
      ii. For relapsed or refractory disease as a single agent;
      iii. For adult disease only: As maintenance therapy for MRD-negative or unavailable disease, alternating with POMP (mercaptopurine, vincristine, methotrexate, prednisone);
   d. BCR::ABL1-like pediatric ALL, and prescribed as consolidation therapy as a single agent therapy after consolidation therapy;
   e. Infant ALL, and one of the following (i or ii):
      i. KMT2A status (11q23 rearranged):

Commented [NMN1]: Is this NCCN compendium rec represented by this? "Single-agent therapy for Ph-negative or Ph-like B-ALL that is minimal residual disease positive (MRD+) after consolidation therapy"

"After consolidation" is different than "as consolidation therapy"?

Commented [NVB2R1]: I initially thought it was since the recommendation looked like it was under consolidation - but looking at it again, the rec is more in between the consolidation column and maintenance column of the NCCN algorithm. So just in case, I've added 4.c.iv as well as 4.d

1) Prescribed in combination with an Interfant regimen (e.g., prednisone, dexamethasone, vincristine, cytarabine, daunorubicin, pegaspargase/ calaspargase, methotrexate; intrathecal therapy: cytarabine, prednisone (if initial central nervous system involvement, methotrexate, prednisone);

ii. KMT2A status (11q23) not rearranged (standard risk):

1) Prescribed as a single agent incorporated into frontline consolidation therapy;

f. Other category 1, 2A, or 2B NCCN-recommended uses not listed;

4. Request meets one of the following (a or b):
   a. Dose does not exceed 28 mcg per day;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

Approval duration: 6 months

B. Other diagnoses/indications: Refer to PA.CP.PMN.53

II. Continued Approval

A. Acute Lymphoblastic Leukemia (must meet all)**:**

1. Currently receiving medication via PA Health & Wellness benefit or member has previously met all initial approval criteria or the Continuity of Care policy (PA.PHARM.01) applies;;
2. Member is responding positively to therapy;
3. If request is for a dose increase, request meets one of the following (a or b):
   a. New dose does not exceed 28 mcg per day;
   b. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.PHARM.01) applies; or
2. Refer to PA.CP.PMN.53

III. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

B-ALL: B-cell precursor acute lymphoblastic leukemia
CR: complete remission
FDA: Food and Drug Administration
MRD: minimal residual disease
NCCN: National Comprehensive Cancer Network
TKI: tyrosine kinase inhibitor

Appendix B: Therapeutic Alternatives
Not applicable

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): known hypersensitivity to blinatumomab or to any component of the product formulation
- Boxed warning(s): cytokine release syndrome (CRS); neurological toxicities including immune effector cell-associated neurotoxicity syndrome

IV. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose

B-ALL (in remission and MRD-positive)	Treatment course: 1 cycle of Blincyto IV for induction followed by up to 3 additional cycles for consolidation.
	• Patients ≥ 45 kg receive a fixed dose
	  ○ Induction cycle 1
	  ▪ Days 1-28: 28 mcg/day
	  ▪ Days 29-42: 14-day treatment-free interval
	  ○ Consolidation cycles 2-4
	  ▪ Days 1-28: 28 mcg/day
	  ▪ Days 29-42: 14-day treatment-free interval
	• Patients < 45 kg based on body surface area (BSA)
	  ○ Induction cycle 1
	  ▪ Days 1-28: 15 mcg/m^2/day
	  ▪ Days 29-42: 14-day treatment-free interval
	  ○ Consolidation cycles 2-4
	  ▪ Days 1-28: 15 mcg/m^2/day
	  ▪ Days 29-42: 14-day treatment-free interval
		28 mcg/day

B-ALL (relapsed or refractory)	Treatment course: 2 cycles of Blincyto IV for induction followed by 3 cycles for consolidation and up to 4 cycles of continued therapy.
	• Patients ≥ 45 kg receive a fixed dose
	  ○ Induction cycle 1
	  ▪ Days 1-7: 9 mcg/day
	  ▪ Days 8-28: 28 mcg/day
	  ▪ Days 29-42: 14-day treatment-free interval
	  ○ Induction cycle 2
	  ▪ Days 1-28: 28 mcg/day
	  ▪ Days 29-42: 14-day treatment-free interval
	  ○ Consolidation cycles 3-5
	  ▪ Days 1-28: 28 mcg/day
	  ▪ Days 29-42: 14-day treatment-free interval
	  ○ Continued therapy cycles 6-9
	  ▪ Days 1-28: 28 mcg/day
	  ▪ Days 29-84: 56-day treatment-free interval
	• Patients < 45 kg based on body surface area (BSA)
	  ○ Induction cycle 1
	  ▪ Days 1-7: 5 mcg/m^2/day
	  ▪ Days 8-28: 15 mcg/m^2/day
	  ▪ Days 29-42: 14-day treatment-free interval
		28 mcg/day

Indication	Dosing Regimen	Maximum Dose
	○ Induction cycle 2 ▪ Days 1-28: 15 mcg/m^2/day ▪ Days 29-42: 14-day treatment-free interval ○ Consolidation cycles 3-5 ▪ Days 1-28: 15 mcg/m^2/day ▪ Days 29-42: 14-day treatment-free interval ○ Continued therapy cycles 6-9 ▪ Days 1-28: 15 mcg/m^2/day ▪ Days 29-84: 56-day treatment-free interval	
B-ALL (in the consolidation phase)	Treatment course: 1 cycle of Blincyto IV • Patients ≥ 45 kg receive a fixed dose ○ Consolidation cycle ▪ Days 1-28: 28 mcg/day ▪ Days 29-42: 14-day treatment-free interval • Patients < 45 kg based on BSA ○ Consolidation cycle ▪ Days 1-28: 15 mcg/m^2/day ▪ Days 29-42: 14-day treatment-free interval	28 mcg/day

V. Product Availability

Single-dose vial for reconstitution: 35 mcg

VI. References

1. Blincyto Prescribing Information. Thousand Oaks, CA: Amgen, Inc.; June 2024. Available at: http://pi.amgen.com/~/media/amgen/repositorysites/pi-amgen-com/blincyto/blincyto_pi_hcp_english.ashx. Accessed October 2, 2024.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at nccn.org. Accessed May 15, 2024.
3. National Comprehensive Cancer Network Guidelines. Acute Lymphoblastic Leukemia Version 1.2024. Available at https://www.nccn.org/professionals/physician_gls/pdf/all.pdf.. Accessed May 20, 2024.
4. National Comprehensive Cancer Network Guidelines. Pediatrics Acute Lymphoblastic Leukemia Version 5.2024. Available at https://www.nccn.org/professionals/physician_gls/pdf/ped_all.pdf. Accessed May 20, 2024.
5. Clinical Pharmacology [database online]. Elsevier, Inc.; 2024. Available at https://www.clinicalkey.com/pharmacology/. Accessed May 20, 2024.

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J9039	Injection, blinatumomab, 1 microgram

Reviews, Revisions, and Approvals	Date
3Q 2018 annual review: new indication for MRD+ B-ALL added; summarized NCCN and FDA-approved uses for improved clarity (TKI requirement reduced from 2 to 1 for Ph+ disease); added specialist involvement in care; references reviewed and updated.	05/2018
3Q 2019 annual review: No changes per Statewide PDL implementation 01-01-2020	07/2019
3Q 2020 annual review: Addition of dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence); references reviewed and updated.	07/2020
3Q 2021 annual review: updated FDA-indication to clarify B-ALL is CD19-positive; references reviewed and updated.	07/2021
3Q 2022 annual review: no significant changes; references reviewed and updated.	07/2022
3Q 2023 annual review: added pathways for use in Ph+ B-ALL in combination with TKI and for use in infant ALL per NCCN; references reviewed and updated.	07/2023
3Q 2024 annual review: specified that infant ALL must have KMT2A status (11q23 rearranged) and added pathway for use as frontline consolidation therapy per NCCN; revised boxed warning in Appendix C per updated prescribing information; RT4: added new FDA approved indication for Ph-B-ALL as consolidation therapy and added age restriction of at least 1 month per updated prescribing information; rearranged criteria into Ph+ vs Ph- disease, added pathway for use as induction therapy for Ph+ disease, removed requirement that relapsed or refractory Ph+ disease must be refractory to TKIs, added pathway for use as maintenance therapy for Ph- disease, added pathway for use after consolidation therapy and for Ph-like disease for pediatric members, and specified how Blincyto should be prescribed for all uses per NCCN.references reviewed and updated.	07/2024