Clinical Policy: Blinatumomab (Blincyto)

Reference Number: CP.PHAR.312
Effective Date: 02.01.17
Last Review Date: 08.24
Line of Business: Commercial, HIM, Medicaid

Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

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

FDA Approved Indication(s)

Blincyto is indicated in adult and pediatric patients one month and older 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

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® 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. Age ≥ 1 month;
4. Requested as treatment for (a, b, c, d, or e):
   a. B-ALL in remission but MRD-positive;
   b. Philadelphia chromosome-positive (Ph+) 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, consolidation therapy, or relapsed or refractory disease;
      ii. As a single agent for relapsed or refractory disease or for consolidation therapy for MRD-positive disease;
   c. Ph- disease, and prescribed in one of the following ways (i, ii, iii, or iv):
      i. As consolidation therapy as a single agent or alternating with multiagent therapy;
      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);
iv. For pediatric disease only: As single agent therapy after consolidation therapy;

d. Ph-like pediatric ALL, and prescribed as single agent therapy after consolidation therapy;
e. Infant ALL, and both of the following (i and ii):
i. KMT2A status (11q23 rearranged);
ii. Prescribed in combination with an Interfant regimen (prednisone, dexamethasone, vincristine, cytarabine, daunorubicin, pegaspargase/ calaspargase, methotrexate; intrathecal therapy: cytarabine, prednisone (if initial central nervous system involvement, methotrexate, prednisone);

5. 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).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration: 6 months

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. B-Cell Acute Lymphoblastic Leukemia (must meet all)**:**
1. Currently receiving medication via Centene benefit, or documentation supports that member is currently receiving Blincyto for a covered indication and has received this medication for at least 30 days;
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).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration: 12 months

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

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. 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

V. 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 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
	  ○ 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
		28 mcg/day

Indication	Dosing Regimen	Maximum Dose
	○ 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

VI. Product Availability

Single-dose vial for reconstitution: 35 mcg

VII. 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 June 20, 2024.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at nccn.org. Accessed June 24, 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 June 20, 2024.
4. National Comprehensive Cancer Network Guidelines. Pediatric Acute Lymphoblastic Leukemia Version 5.2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/ped_all.pdf. Accessed June 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	P&T Approval Date
3Q 2020 annual review: no significant changes; HIM line of business added; references reviewed and updated.	05.12.20	08.20

Reviews, Revisions, and Approvals	Date	P&T Approval Date
RT4: updated FDA-indication to clarify B-ALL is CD19-positive.	03.24.21	
3Q 2021 annual review: no significant changes; updated reference for HIM off-label use to HIM.PA.154 (replaces HIM.PHAR.21); references reviewed and updated.	03.29.21	08.21
3Q 2022 annual review: no significant changes; references reviewed and updated.	05.02.22	08.22
Template changes applied to other diagnoses/indications.	09.21.22	
3Q 2023 annual review: added pathways for use in Ph+ B-ALL in combination with TKI and for use in infant ALL per NCCN; RT4: updated FDA Approved Indication(s) section to reflect conversion from accelerated to full approval for MRD-positive ALL indication; references reviewed and updated.	04.14.23	08.23
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; references reviewed and updated. 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.	06.24.24	08.24

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage

decisions and the administration of benefits are subject to all terms, conditions, exclusions, and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members, and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in 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.