Clinical Policy: Blinatumomab (Blincyto)

Reference Number: CP.PHAR.312
Effective Date: 02.01.17
Last Review Date: 08.19
Line of Business: Commercial, Medicaid, HIM-Medical Benefit

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 adults and children for the treatment of:

- B-cell precursor acute lymphoblastic leukemia (B-ALL) in first or second complete remission with minimal residual disease (MRD) ≥ 0.1%.*
  **This indication is approved under accelerated approval based on MRD response rate and hematological relapse-free survival. Continued approval for this indication may be contingent upon verification and description of clinical benefit in the confirmatory trials.*
- Relapsed or refractory B-ALL.

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. 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 or b):
   a. B-ALL in remission but MRD-positive;
   b. Relapsed or refractory B-ALL (i or ii):
      i. Philadelphia chromosome-negative (Ph-) disease;
      ii. Philadelphia chromosome-positive (Ph+) disease and intolerant or refractory to at least one second- or subsequent-generation tyrosine kinase inhibitor* (TKI; i.e., Sprycel®, Tasigna®, Bosulif®, Iclusig®);
      **Prior authorization may be required for these agents.*
4. 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: 6 months

B. Other diagnoses/indications

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial and CP.PMN.53 for Medicaid and HIM-Medical Benefit.

II. Continued Therapy

A. 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).

Approval duration: 12 months

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

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial and CP.PMN.53 for Medicaid and HIM-Medical Benefit.

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 and CP.PMN.53 for Medicaid and HIM-Medical Benefit or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

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

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen*	Dose Limit/ Maximum Dose
Sprycel (dasatinib)	Ph+ ALL: Labeled use Adults: 140 mg PO QD Children: PO QD weight-based	Adults: 180 mg/day Children: 100 mg/day
Iclusig (ponatinib)	Ph+ ALL: Labeled use Adults: 45 mg PO QD *Also NCCN reccommended (category 2A) for Ph+ ALL in adolescents/young adults.*	45 mg/day
Tasigna (nilotinib)	Ph+ ALL: Off-label use: Adults: 400 mg PO BID (Kim, 2015; see also Appendix D) *Also NCCN reccommended (category 2A) for Ph+ ALL in adults and adolescents/young adults.*	800 mg/day
Bosulif (bosutinib)	Ph+ ALL: Off-label use: Adults: 500 to 600 mg PO QD (Gambacroti-Passerini, 2015; see also Appendix D) *Also NCCN reccommended (category 2A) for Ph+ ALL in adults and adolescents/young adults.*	600 mg/day

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

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

Appendix D: General Information

- MRD-positive B-ALL
  - In 2018, Blincyto received FDA approval for MRD-positive B-ALL in remission based on a single-arm, open label study (BLAST) showing complete MRD response in a majority of adults undergoing Blincyto therapy; the new FDA indication includes both children and adults based on this pivotal trial.
- Relapsed or refractory B-ALL
  - In 2017, blinatumomab's labeled use was expanded from treatment of Ph- relapsed/refractory B-ALL to treatment of Ph+ disease based on a single-arm, open label study (ALCANTARAA) showing complete remission (CR), or CR with partial hematologic recovery, after disease progression on at least one second- or thid-generation TKI. FDA approved second- and third-generation TKIs for Ph+ ALL in adults include Sprycel (and children) and Iclusig. NCCN recommended (category 2A) TKIs for Ph+ ALL in adults and adolescents/young adults include Sprycel, Iclusig, Tasigna and Bosulif.

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/m2/day
	  ▪ Days 29-42: 14-day treatment-free interval
	  ○ Consolidation cycles 2-4
	  ▪ Days 1-28: 15 mcg/m2/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/m2/day
	  ▪ Days 8-28: 15 mcg/m2/day
	  ▪ Days 29-42: 14-day treatment-free interval
	  ○ Induction cycle 2
	  ▪ Days 1-28: 15 mcg/m2/day
	  ▪ Days 29-42: 14-day treatment-free interval
	  ○ Consolidation cycles 3-5
	  ▪ Days 1-28: 15 mcg/m2/day
		28 mcg/day

Indication	Dosing Regimen	Maximum Dose
	▪ Days 29-42: 14-day treatment-free interval ○ Continued therapy cycles 6-9 ▪ Days 1-28: 15 mcg/m2/day ▪ Days 29-84: 56-day treatment-free interval	

VI. Product Availability

Single-dose vial for reconstitution: 35 mcg

VII. References

1. Blincyto Prescribing Information. Thousand Oaks, CA: Amgen, Inc.; April 2019. Available at: http://pi.amgen.com/~/media/amgen/repositorysites/pi-amgen-com/blincyto/blincyto_pi_hcp_english.ashx. Accessed May 1, 2019.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at nccn.org. Accessed May 1, 2019.
3. National Comprehensive Cancer Network Guidelines. Acute Lymphoblastic Leukemia Version 1.2019. Available at nccn.org. Accessed May 1, 2019.
4. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2019. Available at http://www.clinicalpharmacology-ip.com/.
5. Gökbuget N, Dombret H, Bonifacio M, et al. Blinatumomab for minimal residual disease in adults with B-precursor acute lymphoblastic leukemia. Blood 2018; doi: https://doi.org/10.1182/blood-2017-08-798322.
6. 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.

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
Policy split from CP.PHAR.182.Excellus Oncology. NCCN recommended uses added.	01.01.17	02.17
Dosing added. Safety information removed. NCCN recommended uses added separately.	09.05.17	11.17

Reviews, Revisions, and Approvals	Date	P&T Approval Date
3Q 2018 annual review: policies combined for Commercial (new), HIM - Medical Benefit (new), Medicaid; 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.	05.08.18	08.18
3Q 2019 annual review: induction cycle 1 dosing updated per PI for MDR-positive ALL (lower dose on days 1 through 7 is replaced by same dose as days 8 through 28); references reviewed and updated.	05.14.19	08.19

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.

For Health Insurance Marketplace members, when applicable, this policy applies only when the prescribed agent is on your health plan approved formulary. Request for non-formulary drugs must be reviewed using the formulary exception policy.