Clinical Policy: Blinatumomab (Blincyto)

Reference Number: ERX.SPA.241
Effective Date: 09.01.18
Last Review Date: 08.21
Line of Business: Commercial, Medicaid

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:

- CD19-positive 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 CD19-positive 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.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ 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., imatinib, Sprycel®, Tasigna®, Bosulif®, Iclusig®);
      **Prior authorization may be required for these agents.*
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*).

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

Approval duration: 6 months

B. Other diagnoses/indications

1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

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

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions, 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. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

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 policy – ERX.PA.01 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

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

Drug Name	Dosing Regimen*	Dose Limit/ Maximum Dose
Sprycel (dasatinib)	Ph+ ALL: Labeled use Adults: 140 mg PO QD *(resistance or intolerance to prior therapy)* Children and adolescents: PO QD weight-based *(newly diagnosed disease)*	Adults: 180 mg/day Children: 100 mg/day
Iclusig (ponatinib)	Ph+ ALL: Labeled use Adults: 45 mg PO QD *(T315I-positive disease or no other TKI is indicated)*	45 mg/day
Tasigna (nilotinib)	Ph+ ALL: Off-label use	Varies
Bosulif (bosutinib)	Ph+ ALL: Off-label use	Varies
imatinib (Gleevec®)	Ph+ ALL: Labeled use Adults: 600 mg PO once daily until disease progression	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.
**The above-referenced TKIs are NCCN recommended for PH+ ALL (category 1 or 2a).*

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

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 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
	  ○ 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
		28 mcg/day

VI. Product Availability

Single-dose vial for reconstitution: 35 mcg

VII. References

1. Blincyto Prescribing Information. Thousand Oaks, CA: Amgen, Inc.; March 2021. Available at: http://pi.amgen.com/~/media/amgen/repositorysites/pi-amgen-com/blincyto/blincyto_pi_hcp_english.ashx. Accessed March 24, 2021.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at nccn.org. Accessed March 15, 2021.
3. National Comprehensive Cancer Network Guidelines. Acute Lymphoblastic Leukemia Version 1.2021. Available at nccn.org. Accessed March 15, 2021.
4. National Comprehensive Cancer Network Guidelines. Pediatrics Acute Lymphoblastic Leukemia Version 2.2021. Available at nccn.org. Accessed March 15, 2021.
5. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2021. Available at http://www.clinicalpharmacology-ip.com/. Accessed March 15, 2021.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created.	05.08.18	08.18
3Q 2019 annual review: no significant changes; 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
3Q 2020 annual review: no significant changes; references reviewed and updated.	05.12.20	08.20
RT4: updated FDA-indication to clarify B-ALL is CD19-positive.	03.24.21	
3Q 2021 annual review: no significant changes; references reviewed and updated.	03.29.21	08.21

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.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. 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.