Clinical Policy: Blinatumomab (Blincyto)

Reference Number: ERX.SPA.241
Effective Date: 09.01.18
Last Review Date: 08.18

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 that binds to CD19 (expressed on cells of B-lineage origin) and CD3 (expressed on T cells).

FDA Approved Indication(s)
Blincyto is indicated for:

- MRD-positive B-cell precursor ALL
  - Treatment of B-cell precursor acute lymphoblastic leukemia (ALL) in first or second complete remission with minimal residual disease (MRD) greater than or equal to 0.1% in adults and children. 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-cell precursor ALL
  - Treatment of relapsed or refractory B-cell precursor acute lymphoblastic leukemia (ALL) in adults and children.

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 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-cell precursor acute lymphoblastic leukemia (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 positive for minimal residual disease (MRD+);
   b. Relapsed or refractory B-ALL (i and ii):
      i. Philadelphia chromosome-negative (Ph-) disease;
      ii. Philadelphia chromosome-positive (Ph+) disease and intolerant or refractory to at least one second-generation or later tyrosine kinase inhibitor (TKI; i.e., Sprycel®, Tasigna®, Bosulif®, Iclusig®);
      **Prior authorization is (or may be) required for these agents*
4. Dose does not exceed 28 mcg/day.

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, new dose does not exceed 28 mcg/day.
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+: positive 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 and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Sprycel® (dasatinib)	140 mg PO QD (adults*)	180 mg/day
Iclusig® (ponatinib)	45 mg PO QD (adults*)	45 mg/day
Tasigna® (nilotinib)	400 mg PO BID (off-label use; adults* - as referenced in Kim, et al., 2015; see also Appendix D)	800 mg/day
Bosulif® (bosutinib)	500 to 600 mg PO QD (off-label use; adults* - as referenced in Gambacroti-Passerini, et al., 2015; see also Appendix D).	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.
**Sprycel and Iclusig are FDA approved for Ph+ ALL in adults; however, all four listed TKIs are NCCN recommended (category 2A) for Ph+ ALL in both adults and adolescents/young adults.*

Appendix C: Contraindications

Not applicable

Appendix D: General Information

- MRD-positive B-cell precursor ALL
  - In 2018, Blincyto received FDA approval for MRD+ 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-cell precursor 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 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 (MRD+ in remission)	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 o Induction cycle 1 ▪ Days 1-28: 28 mcg/day ▪ Days 29-42: 14-day treatment-free interval o 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) o 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 o 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 o Induction cycle 1 ▪ Days 1-7: 9 mcg/day ▪ Days 8-28: 28 mcg/day ▪ Days 29-42: 14-day treatment-free interval o Induction cycle 2 ▪ Days 1-28: 28 mcg/day ▪ Days 29-42: 14-day treatment-free interval o Consolidation cycles 3-5 ▪ Days 1-28: 28 mcg/day ▪ Days 29-42: 14-day treatment-free interval o 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) o 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 o Induction cycle 2 ▪ Days 1-28: 15 mcg/m2/day ▪ Days 29-42: 14-day treatment-free interval o Consolidation cycles 3-5 ▪ Days 1-28: 15 mcg/m2/day ▪ Days 29-42: 14-day treatment-free interval o Continued therapy cycles 6-9 ▪ Days 1-28: 15 mcg/m2/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 2018. Available at: http://pi.amgen.com/~/media/amgen/repositorysites/pi-amgen-com/blincyto/blincyto_pi_hcp_english.ashx. Accessed April 2018.
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4. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2018. 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.
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7. Kim DY, Joo YD, Lim SN, et al. Nilotinib combined with multiagent chemotherapy for newly diagnosed Philadelphia-positive acute lymphoblastic leukemia. Blood 2015; 126: 746-756.
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Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created.	05.08.18	08.18

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.

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