

**Acute Lymphoblastic Leukemia, Single Agent Therapies**  
**Besponsa (inotuzumab ozogamicin)**  
**Blincyto (blinatumomab)**  
 Effective 06/05/2023

<b>Plan</b>	<input checked="" type="checkbox"/> MassHealth UPPL <input type="checkbox"/> Commercial/Exchange	<b>Program Type</b>	<input checked="" type="checkbox"/> Prior Authorization <input type="checkbox"/> Quantity Limit <input type="checkbox"/> Step Therapy
<b>Benefit</b>	<input type="checkbox"/> Pharmacy Benefit <input checked="" type="checkbox"/> Medical Benefit (NLX)		
<b>Specialty Limitations</b>			
<b>Contact Information</b>	<b>Specialty Medications</b>		
	All Plans	Phone: 866-814-5506	Fax: 866-249-6155
	<b>Non-Specialty Medications</b>		
	MassHealth	Phone: 877-433-7643	Fax: 866-255-7569
	Commercial	Phone: 800-294-5979	Fax: 888-836-0730
	Exchange	Phone: 855-582-2022	Fax: 855-245-2134
	<b>Medical Specialty Medications (NLX)</b>		
	All Plans	Phone: 844-345-2803	Fax: 844-851-0882
<b>Exceptions</b>			

### Overview

Besponsa (inotuzumab ozogamicin) is a CD22-directed antibody-drug conjugate (ADC) indicated for the treatment of relapsed or refractory B-cell precursor acute lymphoblastic leukemia (B-ALL) in adults.

Blincyto (blinatumomab) is a bispecific CD19-directed CD3 T-cell engager indicated for the treatment of relapsed or refractory B-ALL in adults and children.

No PA	Drug that require PA
Alkylator-containing regimens	Besponsa <sup>®</sup> (inotuzumab ozogamicin) <sup>MB</sup>
Augmented Hyper CVAD (cyclophosphamide, vincristine, doxorubicin, dexamethasone and pegaspargase) alternating with high-dose methotrexate and cytarabine	Blincyto <sup>®</sup> (blinatumomab) <sup>MB</sup>

MB This drug is available through the health care professional who administers the drug or in an outpatient or inpatient hospital setting. The plan does not pay for this drug to be dispensed through the retail pharmacy.

### Coverage Guidelines

Authorization may be reviewed on a case by case basis for members who are new to the plan currently receiving treatment with requested medication excluding when the product is obtained as samples or via manufacturer's patient assistance programs.

**OR**

Authorization may be granted for members when all the following criteria are met, and documentation is provided:

1. Diagnosis of Acute Lymphoblastic Leukemia (ALL)
2. Prescriber is an oncologist or hematologist
3. Appropriate dosing (weight is required)
4. If the request is for Besponsa®, member is ≥ 18 years of age
5. **ONE** of the following:
  - a. If the request is for Blincyto®, member with complete remission following initial treatment
  - b. **BOTH** of the following:
    - i. Philadelphia chromosome-positive
    - ii. Paid claims or physician documented inadequate response or adverse reaction to one tyrosine kinase inhibitor for the treatment of ALL (e.g., bosutinib, dasatinib, imatinib, ponatinib, nilotinib)
  - c. **ALL** of the following
    - i. Philadelphia chromosome-negative
    - ii. B-cell precursor ALL
    - iii. Paid claims or physician documents of prior therapy for the treatment of ALL with one prior systemic therapy (*see Appendix*)

#### **Continuation of Therapy**

Reauthorization by prescriber will infer a positive response to therapy.

#### **Limitations**

1. Initial approvals will be granted for 6 months.
2. Reauthorizations will be granted for 12 months.

#### **Appendix**

##### **Systemic Therapies for ALL**

Induction regimens for ALL noted by the NCCN are listed below. Please note that this list may not be all inclusive.

##### Philadelphia Chromosome Positive-ALL

EsPhALL: TKI plus (cyclophosphamide, vincristine, daunorubicin, dexamethasone, cytarabine, methotrexate, pegaspargase, and prednisone)

TKI + Hyper-CVAD: hyperfractionated cyclophosphamide, vincristine, doxorubicin and dexamethasone, alternating with high-dose methotrexate and cytarabine

TKI + multi-agent chemotherapy: daunorubicin, vincristine, prednisone and cyclophosphamide

TKI + corticosteroid

TKI

TKI + vincristine + dexamethasone

CALGB 10701 regimen: TKI + multiagent chemotherapy (dexamethasone, vincristine, daunorubicin, methotrexate, etoposide, and cytarabine)

Blinatumomab +/- TKI

##### Philadelphia Chromosome Negative-ALL

- CALGB 10403 regimen: daunorubicin, vincristine, prednisone and pegaspargase
- COG AALL0232 regimen: daunorubicin, vincristine, prednisone and pegaspargase
- COG AALL0434 with nelarabine (daunorubicin, vincristine, prednisone and pegaspargase)



- DFCI ALL regimen based on DFCI Protocol 00-01: doxorubicin, vincristine, prednisone, high-dose methotrexate and pegaspargase
- GRAALL-2005 regimen: daunorubicin, vincristine, prednisone, pegaspargase and cyclophosphamide
- PETHEMA ALL-96 regimen: daunorubicin, vincristine, prednisone, pegaspargase and cyclophosphamide
- Hyper-CVAD with or without rituximab: hyperfractionated cyclophosphamide, vincristine, doxorubicin and dexamethasone, alternating with high-dose methotrexate and cytarabine; with or without rituximab
- USC/MSKCC ALL regimen based on CCG-1882 regimen: daunorubicin, vincristine, prednisone and methotrexate with augmented pegaspargase
- Linker 4-drug regimen: daunorubicin, vincristine, prednisone and pegaspargase
- Blinatumomab
- CALGB 8811 Larson regimen: daunorubicin, vincristine, prednisone, pegaspargase and cyclophosphamide
- MRC UKALLXII/ECOG2993 regimen: daunorubicin, vincristine, prednisone and pegaspargase; and cyclophosphamide, cytarabine and 6-MP

## References

1. Besponsa® [prescribing information]. Philadelphia (PA): Wyeth Pharmaceuticals; 2018 Mar.
2. Kantarjian HM, DeAngelo DJ, Stelljes M, Martinelli G, Liedtke M, Stock W, et al. Inotuzumab Ozogamicin versus Standard Therapy for Acute Lymphoblastic Leukemia. *N Engl J Med*. 2016 Aug 25;375(8):740-53. doi: 10.1056/NEJMoa1509277. Epub 2016 Jun 12.
3. Blincyto® [package insert on the Internet]. Thousand Oaks, (CA): Amgen; 2021 Mar.
4. FDA granted accelerated approval to blinatumomab (Blincyto, Amgen Inc.) for the treatment of adult and pediatric patients with B-cell precursor acute lymphoblastic leukemia [press release on the Internet]. Food and Drug Administration: 2018 Mar 29 [cited 2021 Oct 12]. Available from: <https://www.fda.gov/drugs/resources-information-approved-drugs/fda-granted-accelerated-approval-blinatumomab-blincyto-amgen-inc-treatment-adult-and-pediatric>
5. Topp MS, Gökbuget N, Stein AS, Zugmaier G, O'Brien S, Bargou RC et al. Safety and activity of blinatumomab for adult patients with relapsed or refractory B-precursor acute lymphoblastic leukemia: a multicentre, single-arm, phase 2 study. *Lancet Oncol*. 2015 Jan;16(1):57-66. doi: 10.1016/S1470-2045(14)71170-2. Epub 2014 Dec 16.
6. Topp MS, Kufer P, Gökbuget N, Goebeler M, Klinger M, Neumann S, et al. Targeted therapy with the T-cell-engaging antibody blinatumomab of chemotherapy-refractory minimal residual disease in B-lineage acute lymphoblastic leukemia patients results in high response rate and prolonged leukemia-free survival. *J Clin Oncol*. 2011 Jun 20;29(18):2493-8. doi: 10.1200/JCO.2010.32.7270. Epub 2011 May 16.
7. Topp MS, Gökbuget N, Zugmaier G, Klappers P, Stelljes M, Neumann S, et al. Phase II trial of the anti-CD19 bispecific T cell-engager blinatumomab shows hematologic and molecular remissions in patients with relapsed or refractory B-precursor acute lymphoblastic leukemia. *J Clin Oncol*. 2014 Dec 20;32(36):4134-40. doi: 10.1200/JCO.2014.56.3247. Epub 2014 Nov 10.
8. National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology. Acute Lymphoblastic Leukemia Version 2.2021 [guideline on the Internet]. [Cited 2021 Oct 12]. Available from: [https://www.nccn.org/professionals/physician\\_gls/pdf/all.pdf](https://www.nccn.org/professionals/physician_gls/pdf/all.pdf).
9. Amgen slaps record-breaking \$178K price on rare leukemia drug Blincyto [press release on the Internet]. Fierce Pharma: 2014 Dec 18 [cited 2021 Oct 19]. Available from: <http://www.fiercepharmamarketing.com/story/amgen-slaps-record-breaking-178k-price-rare-leukemia-drug-blincyto/2014-12-18>.
10. Goebeler ME, Knop S, Viardot A, Kufer P, Topp MS, Einsele H, et al. Bispecific T-Cell Engager (BiTE) Antibody Construct Blinatumomab for the Treatment of Patients With Relapsed/Refractory Non-Hodgkin Lymphoma:



Final Results From a Phase I Study. J Clin Oncol. 2016 Apr 1;34(10):1104-11. doi: 10.1200/JCO.2014.59.1586. Epub 2016 Feb 16.

11. Cyle L, Morley NJ, Rambaldi A, Mason KD, Verhoef G, Furness CL et al. Open-Label, phase 2 study of blinatumomab as second salvage therapy in adults with relapsed/refractory aggressive B-cell non-Hodgkin lymphoma. 2020 Sep;61(9):2103-2112.

### **Review History**

09/21/22 – Reviewed and Created for Sept P&T; matched MH UPPL. Effective 01/01/2023

05/10/23 – Reviewed and updated for P&T. Criteria update to align Blincyto criteria with NCCN guideline by removing requirement the member be MDR positive. Updated references and appendix. Effective 6/5/23.

