Medication Policy Manual

**Policy No:** dru388

**Topic:** Blincyto®, blinatumomab

**Date of Origin:** March 13, 2015

**Committee Approval Date:** September 8, 2017

**Next Review Date:** September 2018

**Effective Date:** October 1, 2017

**IMPORTANT REMINDER**

This Medication Policy has been developed through consideration of medical necessity, generally accepted standards of medical practice, and review of medical literature and government approval status.

*Benefit determinations should be based in all cases on the applicable contract language.* To the extent there are any conflicts between these guidelines and the contract language, the contract language will control.

The purpose of Medication Policy is to provide a guide to coverage. Medication Policy is not intended to dictate to providers how to practice medicine. Providers are expected to exercise their medical judgment in providing the most appropriate care.

**Description**

Blinatumomab (Blincyto) is an immunotherapy used in the treatment of B-cell precursor acute lymphoblastic leukemia (ALL) when the disease recurs after, or does not respond to front-line therapies. It is given via continuous intravenous infusion over 28 days in six-week cycles. Hospitalization is recommended when starting the infusion to monitor for severe adverse effects.
Policy/Criteria

I. Most contracts require prior authorization approval of blinatumomab (Blincyto) prior to coverage. Blinatumomab (Blincyto) may be considered medically necessary when criteria A, B, and C below are met.

A. Documentation of a diagnosis of relapsed or refractory B-cell precursor acute lymphoblastic leukemia (ALL).

AND

B. At least one prior ALL therapy has been ineffective.

AND

C. Blinatumomab (Blincyto) will be used as monotherapy.

II. Administration, Quantity Limitations, and Authorization Period

A. OmedaRx does not consider blinatumomab (Blincyto) to be a self-administered medication.

B. When prior authorization is approved, blinatumomab (Blincyto) may be authorized in the following quantities:

1. **Initial Authorization:** Five, 28-day infusions (induction and consolidation).

2. **Reauthorization:** If remission is achieved with the initial induction and consolidation cycles, up to four additional, 28-day infusions (maintenance) may be authorized.

C. No additional treatment courses will be authorized beyond nine, 28-day infusions.

III. Blinatumomab (Blincyto) is considered investigational when used concomitantly with any other ALL medication.

IV. Blinatumomab (Blincyto) is considered investigational when used for all other conditions, including but not limited to diffuse large B-cell lymphoma.
Position Statement

- Blinatumomab (Blincyto) is an immunotherapy that targets CD-19-positive B-cells (precursor B-cells). It is indicated for the treatment of Philadelphia chromosome (Ph)-negative, relapsed or refractory B-cell precursor acute lymphoblastic leukemia (ALL).

- It is not indicated for mature B-cell (CD-20-positive) ALL. Other therapies are used in treating this ALL subtype.

- Blinatumomab (Blincyto) improved median overall survival (OS) relative to chemotherapy in patients with Philadelphia chromosome-negative B-cell precursor ALL who were refractory to or relapsed after prior ALL therapies. Although a survival difference was demonstrated early in therapy, survival rates in the two treatment groups were similar around 15 months which indicates that there may be a lack of long-term benefit with this therapy.

- In a small, single-arm, open-label study, blinatumomab (Blincyto) was shown to induce complete remission in 36% of patients with relapsed or refractory Philadelphia chromosome-positive B-cell precursor ALL. It is unknown if blinatumomab (Blincyto) improves OS in this subpopulation.

- Concomitant use of blinatumomab (Blincyto) with other ALL therapies has not been studied.

- Based on its mechanism of action, there is interest in using blinatumomab (Blincyto) in other cancers; however, there is currently no evidence supporting its safety and effectiveness in any other condition.

- Potentially serious and life-threatening reactions including Cytokine Release Syndrome and neurological toxicities have been reported with blinatumomab (Blincyto).

- Blinatumomab (Blincyto) is given as a continuous intravenous infusion for 28 days (one cycle). A minimum of a 2-week treatment-free interval is recommended between cycles. If remission is achieved after two cycles of therapy, an additional 3 cycles (consolidation) may be administered. Hospitalization is recommended when initiating the first two cycles to monitor for potentially life-threatening adverse effects.
Clinical Efficacy

Philadelphia chromosome-negative B-cell precursor ALL

In a multicenter, open-label randomized controlled trial, blinatumomab (Blincyto) demonstrated improved overall survival (OS) relative to investigator’s choice of chemotherapy in patients with relapsed or refractory Philadelphia chromosome-negative B-cell precursor ALL. Although an early survival advantage was apparent, there appeared to be little difference in survival between groups at 15 months which indicates the potential lack of a long-term benefit. [1]

- Subjects in the trial had disease in one of the following stages: refractory to primary induction or to salvage with intensive combination therapy, first relapse with first remission lasting fewer than 12 months, second or greater relapse, or relapse at any time after an autologous hematopoietic stem cell transplant.
- Median OS was 7.7 months in the blinatumomab (Blincyto) treatment arm and 4.0 months in the chemotherapy treatment arm (HR 0.71; 95% CI [0.55, 0.93]; p = 0.01. The median duration of follow up was 11.7 months.
- Because the survival curves converged by 15 to 18 months, there is some uncertainty regarding long-term benefits of this therapy.

Philadelphia chromosome-positive B-cell precursor ALL

A small, single-arm trial evaluated complete remission rates achieved with blinatumomab (Blincyto) in patients with relapsed or refractory Philadelphia chromosome-positive B-cell precursor ALL. The design of this study is not suitable for evaluating efficacy because it lacks a comparator and employs an unvalidated surrogate endpoint. [2]

- All subjects in the trial had prior therapy with TKIs directed against the Philadelphia chromosome [imatinib (Gleevec), dasatinib (Sprycel), nilotinib (Tasigna), or ponatinib (Pomalyst)].
- Complete remissions were achieved in approximately 36% of subjects after induction with two cycles of blinatumomab (Blincyto).
- Although disease remission is one of the goals of treatment in ALL, this endpoint has not been validated to correlate with clinical outcomes such as improved symptom control, quality of life, or survival.

Treatment guidelines

The National Comprehensive Cancer Network (NCCN) ALL guideline lists multi-agent chemotherapy regimens as standard front-line therapies for Ph-negative ALL. Bone marrow transplant is an option for patients who achieve remission and have sufficient performance status. Blinatumomab (Blincyto) is listed as a category 1 recommendation for patients with relapsed/refractory Ph-negative, B-cell precursor ALL; and as a category 2A recommendation for patients with relapsed/refractory Ph-positive, B-cell precursor ALL. [3]

OmedaRx performs independent analyses of oncology medications. The OmedaRx analysis and coverage policy may differ from NCCN clinical practice guidelines.
OTHER CANCER SETTINGS AND CONDITIONS

There is interest in using blinatumomab (Blincyto) in other B-cell-mediated cancers; however, there is currently no good evidence to support its safety and effectiveness outside of the Ph-negative B-cell precursor ALL setting.

- A small, preliminary, observational trial evaluated response rates with blinatumomab (Blincyto) in 21 subjects with relapsed or refractory diffuse large B-cell lymphoma (DLBCL). Further studies are needed to determine the optimal treatment strategy in this population. [4]

Safety [5]
- Package labeling for blinatumomab (Blincyto) includes a boxed warning for serious and potentially life-threatening or fatal Cytokine Release Syndrome (CRS) and neurological toxicity.
- The most common adverse effects (incidence of 20% or greater) reported with blinatumomab (Blincyto) in clinical trials included pyrexia, headache, peripheral edema, febrile neutropenia, nausea, hypokalemia, tremor, rash, and constipation.
- There is a Risk Evaluation and Mitigation Strategy (REMS) communication plan for blinatumomab (Blincyto) to inform healthcare providers of the following risks: Cytokine Release Syndrome, neurological toxicities, and preparation and administration errors.

Dosing [5]
- Blinatumomab (Blincyto) is administered as a continuous intravenous infusion over 28 days (one cycle). Each cycle is followed by a 2-week treatment-free interval.
- A treatment course consists of up to two cycles for induction, followed by three additional cycles for consolidation, and then up to four additional cycles of continued therapy (maintenance).
- Dosing (for patients who weigh at least 45 kg):
  * Cycle 1: 9 mcg/day on days 1 through 7, and 28 mcg/day on days 8 through 28.
  * Cycles 2 through 9: 28 mcg/day on days 1 through 28.
- Premedication with dexamethasone is recommended prior to each cycle. Blinatumomab (Blincyto) package labeling recommends that the first 9 days of the first cycle, and the first 2 days of the second cycle be administered in a hospital setting.
Cross References

Marqibo®, vincristine sulfate liposome injection, Medication Policy Manual, Policy No. 278

Codes

<table>
<thead>
<tr>
<th>Codes</th>
<th>Number</th>
<th>Description</th>
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<tbody>
<tr>
<td>HCPCS</td>
<td>J9039</td>
<td>Injection, Blinatumomab, 1 microgram</td>
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References


Revision History

<table>
<thead>
<tr>
<th>Revision Date</th>
<th>Revision Summary</th>
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<tr>
<td>9/8/2017</td>
<td>- Coverage of blinatumomab (Blincyto) was expanded to include patients with relapsed or refractory Philadelphia chromosome-positive B-cell precursor ALL based on new evidence in this population (it is now covered regardless of Philadelphia chromosome status). - Dosing limitations were updated to reflect new dosing recommendations (added maintenance cycles).</td>
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<td>9/9/2016</td>
<td>Added diffuse B-cell lymphoma as an investigational condition.</td>
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