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

Liposomal vincristine (Marqibo) is a liposomal form of generic vincristine sulfate. It is an intravenous chemotherapy used to treat a specific type of leukemia. This policy and the coverage criteria below do not apply to generic vincristine sulfate. Generic vincristine sulfate does not require prior authorization.
Policy/Criteria

I. Most contracts require prior authorization approval of liposomal vincristine (Marqibo) prior to coverage. Liposomal vincristine (Marqibo) may be considered medically necessary when both criteria A and B below are met.

A. A diagnosis of Philadelphia chromosome negative (Ph-negative) acute lymphoblastic leukemia (ALL)

AND

B. Disease has progressed after at least two prior regimens including at least one induction/maintenance and one relapsed/refractory regimen (see Appendix 1)

II. Administration, Quantity Limitations, and Authorization Period

A. OmedaRx does not consider liposomal vincristine (Marqibo) to be a self-administered medication.

B. Authorization may be reviewed at least annually to confirm that current medical necessity criteria are met and that the medication is effective.

III. Liposomal vincristine (Marqibo) is considered investigational when used for all other conditions, including but not limited to:

A. Treatment-naïve acute lymphoblastic leukemia

B. Non-Hodgkin lymphomas (NHLs), including diffuse large B-cell lymphoma (DLBCL) and mantle cell lymphoma (MCL)

C. Hodgkin lymphoma

D. Metastatic melanoma

E. Pediatric cancers

F. Retinoblastoma

G. Ependymoma

H. Wilms’ Tumor

I. Sarcoma, including rhabdomyosarcoma

Position Statement

- Liposomal vincristine (Marqibo) is generic vincristine sulfate, a vinca alkaloid chemotherapy agent, encapsulated in a fatty vehicle.

- Because liposomal vincristine (Marqibo) is a unique formulation of generic vincristine sulfate, there may be interest in using liposomal vincristine (Marqibo) in indications where generic vincristine sulfate has been shown to be effective. To date, there is a lack of evidence to determine the relative clinical benefit of liposomal vincristine (Marqibo) compared to generic vincristine sulfate.
Like generic vincristine sulfate, liposomal vincristine (Marqibo) is contraindicated for intrathecal administration and in patients with demyelinating conditions. They are also both associated with serious adverse effects including neuropathy, myelosuppression, severe constipation and/or paralytic ileus, and tissue injury due to extravasation.

**Clinical Efficacy**

**Acute Lymphoblastic Leukemia**

- Liposomal vincristine (Marqibo) has not been shown to provide additional clinical benefit compared to currently existing therapies used in the treatment of ALL.

- Liposomal vincristine (Marqibo) was approved based on one unpublished phase II, single-arm study in 65 patients with Ph-negative ALL that had progressed following two or more anti-leukemia therapies. [1]
  
  * The primary endpoint evaluated in this study was complete response plus complete response without full platelet recovery.
  
  * Ten (15.4%) subjects achieved the combined primary endpoint. Three (4.6%) subjects achieved complete response, while seven (10.8%) achieved complete response without full platelet recovery.

- One additional published phase II study evaluated overall response rate in 16 patients with refractory ALL. [2]
  
  * Treatment with liposomal vincristine (Marqibo) was the first salvage attempt in 11 patients, the second salvage attempt in 3 patients, and the third salvage attempt in 2 patients.
  
  * The overall response rate in the fourteen evaluable patients was 14% (1 complete responder; 1 partial responder).

- Liposomal vincristine (Marqibo) has not been studied in treatment-naïve ALL.

- The National Comprehensive Cancer Network (NCCN) ALL guideline lists blinatumomab as a category 1 recommendation for treatment of refractory Philadelphia chromosome-negative ALL. Generic vincristine sulfate (as augmented hyper-CVAD), cytarabine, alkylator combinations, and liposomal vincristine (Marqibo) are all listed among their category 2A recommendations in this treatment space. [3]

**Non-Hodgkin Lymphoma (NHL)**

- Liposomal vincristine (Marqibo) has not been shown to provide additional clinical benefit compared to currently existing therapies used in the treatment of NHLs.

- Two preliminary, early-phase studies were identified that evaluate liposomal vincristine (Marqibo) in refractory NHL, including large B-cell lymphoma and mantle cell lymphoma. The studies are small, uncontrolled, and evaluated tumor response. No clinical benefit has been demonstrated to date in these populations. [4, 5]

- The NCCN does not list liposomal vincristine (Marqibo) among the treatment options for relapsed/refractory NHLs. [6]
Other Uses

- Liposomal vincristine (Marqibo) is currently being studied in a variety of other cancers including Hodgkin lymphoma, metastatic melanoma, non-Hodgkin’s lymphomas (including diffuse large B-cell lymphoma and mantle cell lymphoma), acute myeloid leukemia (AML), and several pediatric cancers. [7]
- Liposomal vincristine (Marqibo) is considered investigational in the above mentioned cancers due to the low level of available evidence in these settings.

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

Safety [1]

- The safety profile for liposomal vincristine (Marqibo) appears similar to generic vincristine sulfate.
- Boxed warnings for liposomal vincristine (Marqibo) include potential death with intrathecal use and potential overdose if confused with generic vincristine as the dosing recommendations are different.
- Additional warnings include neuropathy, myelosuppression, tumor lysis syndrome, severe constipation and/or paralytic ileus, severe fatigue, hepatotoxicity, embryofetal toxicity, and tissue injury due to extravasation.
- Liposomal vincristine (Marqibo) is contraindicated in patients with demyelinating conditions including Charcot-Marie-Tooth syndrome.
- The most commonly reported adverse reactions (incidence ≥ 30%) in clinical studies include constipation, nausea, pyrexia, fatigue, peripheral neuropathy, febrile neutropenia, diarrhea, anemia, decreased appetite, and insomnia.

Dosing and Administration [1]

- Liposomal vincristine (Marqibo) is administered at a dose of 2.25 mg/m² intravenously over 1 hour once every 7 days.
- Liposomal vincristine (Marqibo) may be fatal if administered intrathecally.
- Dosing recommendations for liposomal vincristine (Marqibo) are different from those for generic vincristine; therefore, the drug name and dose should be verified prior to preparation and administration.
- Liposomal vincristine (Marqibo) requires approximately 60 to 90 minutes of preparation time and must be done according to aseptic technique in a biological safety cabinet.
- Dosing modification is recommended for patients who experience liposomal vincristine (Marqibo)-related peripheral neuropathy.
Appendix 1: Therapies/Treatment Regimens for Philadelphia Chromosome Negative Acute Lymphoblastic Leukemia [Ph (-) ALL] [3]

### Commonly used induction regimens

- Other recommended regimens:
  - anthracycline (daunorubicin/doxorubicin)
  - generic vincristine sulfate
  - steroid (prednisone/dexamethasone)
  - asparaginase or rituximab (Rituxan)
  - other (e.g. cyclophosphamide, cytarabine, 6-mercaptopurine)

### Maintenance regimens

- methotrexate + 6-mercaptopurine + generic vincristine sulfate/prednisone pulses

### Relapsed/refractory regimens

- Clinical trial
  - blinatumomab (Blincyto)
- clofarabine (Clolar)
- cytarabine-containing regimens
- alkylator combination regimens (e.g. etoposide + ifosfamide + mitoxantrone)
- nelarabine (Arranon) [T ALL only]
- cyclophosphamide + generic vincristine sulfate + doxorubicin + dexamethasone + asparaginase + cytarabine/methotrexate (augmented hyper-CVAD)
- liposomal vincristine (Marqibo)

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**a** Systemic regimens, not including intrathecal (IT) CNS prophylaxis.

**b** Variable, based on age and underlying patient characteristics.
References


Revision History

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<thead>
<tr>
<th>Revision Date</th>
<th>Revision Summary</th>
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<tr>
<td>9/8/2017</td>
<td>The list of conditions considered investigational uses was updated.</td>
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<tr>
<td>8/12/2016</td>
<td>No changes with this annual update.</td>
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