Clinical Policy: Vincristine Sulfate Liposome Injection (Marqibo)

Reference Number: CP.PHAR.315
Effective Date: 02.17
Last Review Date: 11.22
Line of Business: Commercial, HIM, Medicaid

Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Vincristine sulfate liposome injection (Marqibo®) is a vinca alkaloid.

FDA Approved Indication(s)

Marqibo is indicated for the treatment of adult patients with Philadelphia chromosome-negative (Ph-) acute lymphoblastic leukemia (ALL) in second or greater relapse or whose disease has progressed following two or more anti-leukemia therapies.*

This indication is approved under accelerated approval based on overall response rate. Continued approval for this indication may be continegent upon verification and description of clinical benefit in confirmatory trials.

* On May 2, 2022, the FDA has withdrawn approval of Marqibo after a postmarking clinical trial failed to verify the clinical benefit of the drug. The most updated NCCN guidance (Acute Lymphoblastic Leukemia v1.2022) still supports usage.

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 Centene Corporation® that Marqibo is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Acute Lymphoblastic Leukemia (off-label NCCN recommended use) (must meet all)**:**

1. Diagnosis of ALL;
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age ≥ 18 years;
4. One of the following (a or b):*
   a. For members with Ph- ALL, disease has relapsed ≥ 2 times or has progressed following ≥ 2 anti-leukemia therapies (*see Appendix B for examples*);
   b. For members with Philadelphia chromosome-positive (Ph+) ALL, disease is refractory to tyrosine kinase inhibitor therapy (e.g., imatinib [Gleevec®], Sprycel®, Tasigna®, Bosulif®, Iclusig®);

   **Prior authorization may be required.*
5. Prescribed as a single agent;
6. Request meets one of the following (a or b):*
   a. Dose does not exceed 2.25 mg/m^2 every 7 days;

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 (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Acute Lymphoblastic Leukemia (off-label NCCN recommended use) (must meet all)**:**

1. Currently receiving medication via Centene benefit, or documentation supports that member is currently receiving Marqibo 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 2.25 mg/m^2 every 7 days;
   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. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or

b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or

2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

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 policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid or evidence of coverage documents;

B. Patients with the demyelinating form of Charcot-Marie-Tooth syndrome.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

ALL: acute lymphoblastic leukemia
FDA: Food and Drug Administration
NCCN: National Comprehensive Cancer Network

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 for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Examples of Ph- ALL anti-leukemia therapies		
• CALGB 8811 Larson regimen: daunorubicin, vincristine, prednisone, pegaspargase, cyclophosphamide • Single agent therapies such as blinatumomab, inotuzumab ozogamicin	Varies	Varies
Ph+ ALL tyrosine kinase inhibitor therapy		
imatinib (Gleevec)	600 mg PO QD	600 mg/day
Sprycel (dasatinib)	140 mg PO QD	180 mg/day
Tasigna (nilotinib)	400 mg PO BID	800 mg/day
Bosulif (bosutinib)	400-500 mg PO QD	600 mg/day
Iclusig (ponatinib)	45 mg PO QD	45 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.

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s):
  - Patients with demyelinating conditions including Charcot-Marie-Tooth syndrome
  - Hypersensitivity to vincristine sulfate or any of the other components of Marqibo (vinCRIStine sulfate LIPOSOME injection)
  - Intrathecal administration
- Boxed warning(s): for intravenous use only – fatal if given by other routes; dosage recommendations differ from vincristine sulfate, verify drug name and dose to avoid overdosage

Appendix D: General Information

On May 2, 2022, the FDA withdrew approval of Marqibo after a postmarking clinical trial failed to verify the clinical benefit of the drug. The manufacturer voluntarily withdrew its new drug application and drug approval was subsequently withdrawn.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
ALL (off-label)	2.25 mg/m^2 IV over 1 hour once every 7 days	See dosing regimen

VI. Product Availability

Marqibo Kit containing the following:

- Vial: vincristine sulfate injection, USP 5 mg/5 mL (1 mg/mL)
- Vial: sphingomyelin/cholesterol liposome injection 103 mg/mL
- Vial: sodium phosphate injection 355 mg/25 mL (14.2 mg/mL)

VII. References

1. Marqibo Prescribing Information. East Windsor, NJ: Acrotech Biopharma, LLC; March 2022. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/202497Orig1s013lbl.pdf . Accessed August 2, 2022.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: www.nccn.org. Accessed August 2, 2022.
3. National Comprehensive Cancer Network. Acute Lymphoblastic Leukemia Version 1.2022. Available at: www.nccn.org. Accessed August 2, 2022.
4. Food and Drug Administration, HHS. Acrotech Biopharm LLC; Withdrawal of approval of new drug application for marqibo (vincristine sulfate liposome injection), 5 miligrams/ 5 milliliters. Fderal Register. May 2, 2022. Available at: https://www.federalregister.gov/documents/2022/05/02/2022-09235/acrotech-biopharma-llc-withdrawal-of-approval-of-new-drug-application-for-marqibo-vincristine. Accessed August 2, 2022.

Coding Implications
Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J9371	Injection, vincristine sulfate liposome, 1 mg

Reviews, Revisions, and Approvals	Date	P&T Approval Date
4Q 2018 annual review: no significant changes; added Commercial line of business and HIM-Medical; added age and prescriber restrictions; references reviewed and updated.	07.16.18	11.18
4Q 2019 annual review: Ph- anti-leukemia therapy examples added to Appendix B; FDA/NCCN dosing limitation added; references reviewed and updated.	08.27.19	11.19
4Q 2020 annual review: no significant changes; references reviewed and updated.	08.11.20	11.20
4Q 2021 annual review: revised HIM-Medical Benefit to HIM; added requirement for use as a single agent per NCCN and pivotal trial; updated Appendix C to include hypersensitivity contraindication; references reviewed and updated.	06.28.21	11.21
4Q 2022 annual review: changed to off-label usage for ALL due to FDA withdrawal but still supported by NCCN; references reviewed and updated. Template changes applied to other diagnoses/indications.	08.02.22	11.22

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. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering

benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. 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. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.