Clinical Policy: Chlorambucil (Leukeran)

Reference Number: CP.PHAR.554
Effective Date: 12.01.21
Last Review Date: 11.26
Line of Business: HIM/ICHRA, Medicaid

Revision Log

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

Description

Chlorambucil (Leukeran®) is an aromatic nitrogen mustard derivative and an alkylating agent.

FDA Approved Indication(s)

Leukeran is indicated for the treatment of chronic lymphatic (lymphocytic) leukemia, malignant lymphomas including lymphosarcoma, giant follicular lymphoma, and Hodgkin's disease.

Limitation(s) of use: Leukeran is not curative in any of these disorders but may produce clinically useful palliation.

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 Leukeran is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Lymphoma (must meet all)**:**

1. Diagnosis of one of the following (a, b, c, d, or e):
   a. Giant follicular lymphoma;
   b. Chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL);
   c. Mycosis fungoides (MF)/Sezary syndrome (SS);
   d. Hodgkin's disease;
   e. Malignant lymphomas including lymphosarcoma;
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age ≥ 18 years;
4. For brand name Leukeran requests, member must use generic chlorambucil, if available, unless contraindicated or clinically significant adverse effects are experienced;
5. For CLL/SLL: Prescribed in combination with Gazyva®;
6. For MF/SS: Prescribed as a single agent as subsequent treatment;
7. Request meets one of the following (a, b, or c):*
   a. Daily dosing (all indications, including CLL/SLL) (i or ii):
      i. Dose does not exceed 0.2 mg/kg per day for up to 6 weeks;
      ii. Dose does not exceed 0.1 mg/kg per day after 6 weeks;

b. Intermittent dosing (CLL/SLL), including biweekly or monthly dosing: Dose does not exceed a 0.4 mg/kg initial dose or dose increases of 0.1 mg/kg until response/toxicity is observed;
c. 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/ICHRA) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: HIM.PA.33 for health insurance marketplace/ICHRA and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace/ICHRA) or PDL (Medicaid), the non-formulary policy for the relevant line of business: HIM.PA.103 for health insurance marketplace/ICHRA 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: HIM.PA.154 for health insurance marketplace/ICHRA and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. All Indications in Section I (must meet all)**:**

1. Currently receiving medication via Centene benefit, or documentation supports that member is currently receiving Leukeran for a covered indication and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. For brand name Leukeran requests, member must use generic chlorambucil, if available, unless contraindicated or clinically significant adverse effects are experienced;
4. If request is for a dose increase, request meets one of the following (a, b, or c):*
   a. Daily dosing (all indications, including CLL/SLL) (i or ii):
      i. If member has received ≤ 6 weeks of therapy for the current treatment course: New dose does not exceed 0.2 mg/kg per day for up to a total of 6 weeks per treatment course;
      ii. If member has received > 6 weeks of therapy for the current treatment course: New dose does not exceed 0.1 mg/kg per day;
   b. Intermittent dosing (CLL/SLL), including biweekly or monthly dosing: New dose does not exceed a 0.4 mg/kg initial dose or dose increases of 0.1 mg/kg until response/toxicity is observed;

c. 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/ICHRA) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: HIM.PA.33 for health insurance marketplace/ICHRA and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace/ICHRA) or PDL (Medicaid), the non-formulary policy for the relevant line of business: HIM.PA.103 for health insurance marketplace/ICHRA 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: HIM.PA.154 for health insurance marketplace/ICHRA 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 – HIM.PA.154 for health insurance marketplace/ICHRA and CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

CLL: chronic lymphocytic leukemia
FDA: Food and Drug Administration
NCCN: National Comprehensive Cancer Network
SLL: small lymphocytic lymphoma

Appendix B: Therapeutic Alternatives

Not applicable

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s):
  - Disease has demonstrated prior resistance to Leukeran
  - Hypersensitivity to Leukeran
- Boxed warning(s):
  - Bone marrow suppression
  - Carcinogen
  - Mutagenic and teratogenic in humans

- Produces human infertility

Appendix D: General Information

- Leukeran use in the treatment of Hodgkin lymphoma, follicular lymphoma, and marginal zone lymphoma is no longer supported by NCCN – prescribers are encouraged to consult the respective NCCN treatment guidelines for recommended therapy options.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Malignant lymphomas including lymphosarcoma, follicular lymphoma, and Hodgkin's disease	Daily dosage: The usual oral dosage is 0.1 to 0.2 mg/kg body weight PO daily for 3 to 6 weeks as required. If maintenance dosage is used, it should not exceed 0.1 mg/kg daily.	0.2 mg/kg/day daily dosing 0.1 mg/kg/day if maintenance dosing
Chronic lymphatic (lymphocytic) leukemia	Daily dosage: The usual oral dosage is 0.1 to 0.2 mg/kg body weight PO daily for 3 to 6 weeks as required. If maintenance dosage is used, it should not exceed 0.1 mg/kg daily. Intermittent dosing: Alternate schedules for the treatment of chronic lymphocytic leukemia employing intermittent, biweekly, or once-monthly pulse doses of chlorambucil have been reported. Intermittent schedules of chlorambucil begin with an initial single dose of 0.4 mg/kg. Doses are generally increased by 0.1 mg/kg until control of lymphocytosis or toxicity is observed.	0.2 mg/kg/day dailiy dosing 0.4 mg/kg/day or higher if itermittent, biweekly, or once-monthly pulse dosing

VI. Product Availability

Tablet: 2 mg

VII. References

1. Leukeran Prescribing Information. Wixom, MI: Waylis Therapeutics LLC; January 2025. Available at: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=58a3c995-5ad6-465d-8437-5970c9088213. Accessed July 13, 2026.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed July 27, 2026.
3. National Comprehensive Cancer Network. Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma Version 2.2026. Available at: https://www.nccn.org/professionals/physician_gls/pdf/cll.pdf. Accessed July 27, 2026.

4. National Comprehensive Cancer Network. Cutaneous Lymphomas Version 2.2026. Available at: https://www.nccn.org/professionals/physician_gls/pdf/cutaneous_lymphomas.pdf. Accessed July 27, 2026.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
4Q 2022 annual review: no significant changes; added previously P&T-approved template language re: redirection to generic equivalents, if available; references reviewed and updated. Template changes applied to other diagnoses/indications.	07.07.22	11.22
4Q 2023 annual review: no significant changes; references reviewed and updated.	08.11.23	11.23
4Q 2024 annual review: clarified follicular lymphoma is classic; for MF/SS, added requirement for use as a single agent and as subsequent treatment per NCCN; for CLL/SLL, added requirement for combination use per NCCN; references reviewed and updated.	08.07.24	11.24
4Q 2025 annual review: added use in Hodgkin's disease per PI (removed from Section III); for all indications, extended initial approval duration from 6 months to 12 months for this maintenance medication for a chronic condition; references reviewed and updated.	07.17.25	11.25
4Q 2026 annual review: removed off-label use in marginal zone lymphomas as this is no longer NCCN supported; revised "classic" follicular lymphoma to "giant" follicular lymphoma to align with FDA labeling as this use is no longer NCCN supported; added use in malignant lymphomas including lymphosarcoma in line with FDA labeling; added ICHRA line of business; references reviewed and updated.	07.28.26	11.26

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.

©2021 Centene Corporation. All rights reserved. All materials are exclusively owned by Centene Corporation and are protected by United States copyright law and international copyright law. No part of this publication may be reproduced, copied, modified, distributed, displayed, stored in a retrieval system, transmitted in any form or by any means, or otherwise published without the prior written permission of Centene Corporation. You may not alter or remove any trademark, copyright or other notice contained herein. Centene® and Centene Corporation® are registered trademarks exclusively owned by Centene Corporation.