Prior Authorization Review Panel

CHC-MCO Policy Submission

A separate copy of this form must accompany each policy submitted for review.
Policies submitted without this form will not be considered for review.

Plan: PA Health & Wellness	**Submission Date: 11/01/2025**
Policy Number: PA.CP.PHAR.554	**Effective Date: 10/2021** **Revision Date: 10/2025**
Policy Name: Chlorambucil (Leukeran)	

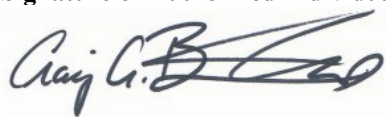
Type of Submission – Check all that apply:

- ☐ **New Policy**
- ✓ **Revised Policy***
- ☐ **Annual Review - No Revisions**
- ☐ **Statewide PDL -** *Select this box when submitting policies for Statewide PDL implementation and when submitting policies for drug classes included on the Statewide PDL.*

***All revisions to the policy must be highlighted using track changes throughout the document.**

Please provide any changes or clarifying information for the policy below:

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.

Name of Authorized Individual (Please type or print): **Craig A. Butler, MD MBA**	**Signature of Authorized Individual:** 

Clinical Policy: Chlorambucil (Leukeran)

Reference Number: PA.CP.PHAR.554
Effective Date: 10/2021
Last Review Date: 10/2025

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 PA Health & Wellness® 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-e):
   a. Marginal zone lymphoma (MZL) (i, ii, or iii):
      i. Splenic MZL;
      ii. Nodal MZL;
      iii. Extranodal mucosa-associated lymphoid tissues (MALT) (1 or 2):
         1) Gastric MALT lymphoma;
         2) Nongastric MALT lymphoma;
   b. Classic follicular lymphoma;
   c. Chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL);
   d. Mycosis fungoides (MF) or Sezary syndrome (SS);
   e. Hodgkin's disease;
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)*.

Approval duration: 12 months

B. Other diagnoses/indications

1. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

II. Continued Therapy

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

1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.PHARM.01) applies;
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)*.

   Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.PHARM.01) applies .
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

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 – PA.CP.PMN.53;

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

CLL: chronic lymphocytic leukemia
FDA: Food and Drug Administration
MALT: mucosa-associated lymphoid tissues
MZL: marginal zone lymphoma
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 is no longer supported by NCCN – prescribers are encouraged to consult NCCN treatment guidelines for Hodgkin lymphoma therapies.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Malignant lymphomas including lymphosarcoma and follicular lymphoma, 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.	0.2 mg/kg/day dailiy dosing 0.4 mg/kg/day or higher if itermittent, biweekly, or once-monthly pulse dosing

Indication	Dosing Regimen	Maximum Dose
	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.	

VI. Product Availability

Tablet: 2 mg

VII. References

1. Leukeran Prescribing Information. Wixon, MI: Waylis Therapeutics LLC; January 2025. Available at: https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=58a3c995-5ad6-465d-8437-5970c9088213. Accessed July 17, 2025.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed July 17, 2025.
3. National Comprehensive Cancer Network. B-Cell Lymphomas Version 2.2025. Available at: https://www.nccn.org/professionals/physician_gls/pdf/b-cell.pdf. Accessed July 17, 2024.
4. National Comprehensive Cancer Network. Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma Version 3.2025. Available at: https://www.nccn.org/professionals/physician_gls/pdf/cll.pdf. Accessed July 17, 2025.
5. National Comprehensive Cancer Network. Primary Cutaneous Lymphomas Version 3.2025. Available at: https://www.nccn.org/professionals/physician_gls/pdf/primary_cutaneous.pdf. Accessed July 17, 2024.

Reviews, Revisions, and Approvals	Date
Policy created	10/2021
4Q 2022 annual review: no significant changes; references reviewed and updated.	10/2022
4Q 2023 annual review: no significant changes; references reviewed and updated.	10/2023
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.	10/2024
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.	10/2025