Clinical Policy: Chlorambucil (Leukeran)

Reference Number: PA.CP.PHAR.554
Effective Date: 10/2021
Last Review Date: 10/2022

Revision Log

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. Hodgkin Lymphoma, Non-Hodgkin Lymphoma, or Chronic Lymphocytic Leukemia (must meet all)**:**

1. One of the following diagnoses (a, b, c, or d):
   a. Marginal zone lymphoma (i, ii, or iii):
      i. Splenic marginal zone lymphoma;
      ii. Nodal marginal zone lymphoma;
      iii. Extranodal marginal zone lymphoma (a or b):
         a) Gastric MALT lymphoma;
         b) Nongastric MALT lymphoma;
   b. Follicular lymphoma;
   c. Chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL);
   d. Mycosis fungoides or Sezary syndrome;
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. 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: 6 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.LTSS.PHAR.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.LTSS.PHAR.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;

B. Hodgkin lymphoma: 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.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
CLL/SLL: chronic lymphocytic leukemia/small lymphocytic lymphoma
FDA: Food and Drug Administration
NCCN: National Comprehensive Cancer Network

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

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Malignant lymphomas including lymphosarcoma and follicular lymphoma	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	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
	control of lymphocytosis or toxicity is observed.	

VI. Product Availability

Tablet: 2 mg

VII. References

1. Leukeran Prescribing Information. Research Park Triangle, NC: GlaxoSmithKline; October 2011. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2011/010669s032lbl.pdf. Accessed July 7, 2022.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed July 7, 2022.
3. National Comprehensive Cancer Network. B-Cell Lymphomas Version 4.2022. Available at: https://www.nccn.org/professionals/physician_gls/pdf/b-cell.pdf. Accessed July 7, 2022.
4. National Comprehensive Cancer Network. Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma Version 3.2022. Available at: https://www.nccn.org/professionals/physician_gls/pdf/cll.pdf. Accessed July 7, 2022.
5. National Comprehensive Cancer Network. Primary Cutaneous Lymphomas Version 2.2022. Available at: https://www.nccn.org. Accessed July 7, 2022.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	10/2021	
4Q 2022 annual review: no significant changes; references reviewed and updated.	10/2022	