

Clinical Policy: Chlorambucil (Leukeran)

Reference Number: HIM.PA.SP59

Effective Date: 08.28.18

Last Review Date: 11.20

Line of Business: HIM

[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. Non-Hodgkin Lymphoma** (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. Primary cutaneous lymphoma (i or ii):
 - i. Primary cutaneous CD30+ T-cell lymphoproliferative disorder;
 - ii. Mycosis fungoides or Sezary syndrome;
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age \geq 18 years;
4. 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 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: 6 months

B. Other diagnoses/indications

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): HIM.PHAR.21 for health insurance marketplace.

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 daily dosing, member has received Leukeran for ≥ 6 weeks;
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. New dose does not exceed 0.2 mg/kg per day for up to 6 weeks;
 - ii. New dose does not exceed 0.1 mg/kg per day after 6 weeks;
 - 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 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. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.

Approval duration: Duration of request or 6 months (whichever is less); or

2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): HIM.PHAR.21 for health insurance marketplace.

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.PHAR.21 for health insurance marketplace or evidence of coverage documents;
- B. 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	<u>Daily dosage:</u> 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	<u>Daily dosage:</u> 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. <u>Intermittent dosing:</u> 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 daily dosing 0.4 mg/kg/day or higher if intermittent, biweekly, or once-monthly pulse dosing

VI. Product Availability

Tablets: 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 24, 2020.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed July 24, 2019.
3. National Comprehensive Cancer Network. B-Cell Lymphomas Version 2.2020. Available at: https://www.nccn.org/professionals/physician_gls/pdf/b-cell.pdf. Accessed July 24, 2020.
4. National Comprehensive Cancer Network. Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma Version 4.2020. Available at: https://www.nccn.org/professionals/physician_gls/pdf/cll.pdf. Accessed July 24, 2020.
5. National Comprehensive Cancer Network. Primary Cutaneous Lymphomas Version 2.2020. Available at: <https://www.nccn.org>. Accessed July 24, 2020.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	08.22.18	10.18
4Q 2019 annual review: diagnoses are reorganized around NCCN recommendations (non-Hodgkin subtypes) given dated PI terminology; Leukeran use for Hodgkin lymphoma is not NCCN recommended and therefore not covered as noted in Section III; 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

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.

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