Clinical Policy: Chlorambucil (Leukeran)

Reference Number: HIM.PA.SP59
Effective Date: 08.28.18
Last Review Date: 11.18 Revision Log
Line of Business: HIM

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. Chronic Lymphatic (Lymphocytic) Leukemia (must meet all)**:**
1. Diagnosis of chronic lymphatic (lymphocytic) leukemia;
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age ≥ 18 years;
4. Dose does not exceed 0.4 mg per kg per day.

Approval duration: 6 months

B. Malignant Lymphomas (must meet all)**:**
1. Diagnosis of malignant lymphoma;
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age ≥ 18 years;
4. Request meets one of the following (a or b):
   a. Dose does not exceed 0.2 mg per kg per day;
   b. 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

C. Follicular Lymphomas (must meet all)**:**
1. Diagnosis of follicular lymphoma;

2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age ≥ 18 years;
4. Request meets one of the following (a or b):
   a. Dose does not exceed 0.2 mg per kg per day;
   b. 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

D. Hodgkin Disease (Lymphoma):
1. Diagnosis of Hodgkin disease;
2. Prescribed by or in consultation with an oncologist or hematologist;
3. The use of Leukeran in the treatment of Hodgkin lymphoma is no longer supported by NCCN – prescribers are encouraged to consult NCCN treatment guidelines for Hodgkin lymphoma for information on recommended treatment regimens *(see Appendix B below for examples of NCCN-recommended regimens).*

E. 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 Except Hodgkin Disease (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. If request is for a dose increase, request meets one of the following (a or b):
   a. New dose does not exceed any of the following (i or ii):
      i. Chronic lymphocytic (lymphatic) leukemia: 0.4 mg/kg/day;
      ii. Follicular lymphoma, malignant lymphomas including lymphosarcoma: 0.1 mg/kg/day;
   b. 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. Hodgkin Disease:
1. Diagnosis of Hodgkin disease;
2. Prescribed by or in consultation with an oncologist or hematologist;
3. The use of Leukeran in the treatment of Hodgkin lymphoma is no longer supported by NCCN – prescribers are encouraged to consult NCCN treatment guidelines for Hodgkin lymphoma for information on recommended treatment regimens *(see Appendix B below for examples of NCCN-recommended regimens).*

C. 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.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
FDA: Food and Drug Administration

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
Doxorubicin, bleomycin, vinblastine, dacarbazine (ABVD)	Hodgkin's Lymphoma Varies per protocol and patient tolerance	Varies
Doxorubicin, vinblastine, mechlorethamine, etoposide, vincristine, bleomycin, prednisone (Stanford V)	Hodgkin's Lymphoma Varies per protocol and patient tolerance	Varies
Bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, prednisone (Escalated BEACOPP)	Hodgkin's Lymphoma Varies per protocol and patient tolerance	Varies
Brentuximab vedotin, doxorubicin, vinblastine, dacarbazine (Adcetris® + AVD)	Hodgkin's Lymphoma Varies per protocol and patient tolerance	Varies
Cyclophosphamide, doxorubicin, vincristine, prednisone,	Hodgkin's Lymphoma Varies per protocol and patient tolerance	Varies

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
rituximab (CVP + Rituxan®)		
Rituximab (Rituxan®)	Hodgkin's Lymphoma Varies per protocol and patient tolerance	Varies

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 whose disease has demonstrated a prior resistance to Leukeran;
  - Patients who have demonstrated 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
Chronic lymphatic (lymphocytic) leukemia	0.1 mg/kg PO QD Intermittent schedules of Leukeran begin with an initial single dose of 0.4 mg/kg PO QD. Doses are generally increased by 0.1 mg/kg until control of lymphocytosis or toxicity is observed. Subsequent doses are modified to produce mild hematologic toxicity.	0.4 mg/kg/day
Malignant lymphomas including lymphosarcoma, follicular lymphoma	0.1 mg/kg PO QD	0.1 mg/kg/day
Hodgkin disease	The use of Leukeran in the treatment of Hodgkin lymphoma is no longer supported by NCCN – prescribers are encouraged to consult NCCN treatment guidelines for Hodgkin lymphoma for information	Not applicable

Indication	Dosing Regimen	Maximum Dose
	on recommended treatment regimens.	

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 August 21, 2018.
2. Micromedex® Healthcare Series [Internet database]. Greenwood Village, Colo: Thomson Healthcare. Updated periodically. Accessed August 21, 2018.
3. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed August 22, 2018.
4. National Comprehensive Cancer Network. Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma Version 1.2019. Available at: https://www.nccn.org/professionals/physician_gls/pdf/cll.pdf. Accessed August 22, 2018.
5. National Comprehensive Cancer Network. B-Cell Lymphomas Version 4.2018. Available at: https://www.nccn.org/professionals/physician_gls/pdf/b-cell.pdf. Accessed August 22, 2018.
6. National Comprehensive Cancer Network. Hodgkin Lymphoma Version 3.2018. Available at: https://www.nccn.org/professionals/physician_gls/pdf/hodgkins.pdf. Accessed August 22, 2018.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	08.22.18	10.18

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 Health Insurance Marketplace members, when applicable, this policy applies only when the prescribed agent is on your health plan approved formulary. Request for non-formulary drugs must be reviewed using the non-formulary policy; HIM.PA.103.