

CHLORAMBUCIL:

Class: Antineoplastic Agent, Alkylating Agent

Indications: - Chronic lymphocytic leukemia (CLL) - Hodgkin lymphoma
- Non-Hodgkin's lymphomas (NHL) - Waldenström's macroglobulinemia

Available dosage form in the hospital: 2mg Tab

Trade Names: Leukeran, Chloraminophene (FR)

Dosage: Note: With bone marrow lymphocytic infiltration involvement (in CLL, Hodgkin lymphoma, or NHL), the maximum dose is 0.1 mg/kg/day. While short treatment courses are preferred, if maintenance therapy is required, the maximum dose is 0.1 mg/kg/day.

-Chronic lymphocytic leukemia (CLL): Oral:

- U.S. labeling:* 0.1 mg/kg/day for 3-6 weeks or 0.4 mg/kg pulsed doses administered intermittently, biweekly, or monthly (increased by 0.1 mg/kg/dose until response/toxicity observed)
- Canadian labeling:* Initial: 0.15 mg/kg/day until WBC is 10,000/mm³; interrupt treatment for 4 weeks, then may resume at 0.1 mg/kg/day until response (generally ~2 years)/toxicity observed
- Unlabeled dosing for CLL:* 0.4 mg/kg day 1 every 2 weeks; if tolerated may increase by 0.1 mg/kg with each treatment course to a maximum dose of 0.8 mg/kg and maximum of 24 cycles (Eichhorst, 2009) or 30 mg/m² day 1 every 2 weeks (in combination with prednisone) (Raphael, 1991) or 40 mg/m² day 1 every 4 weeks until disease progression or complete remission or response plateau for up to a maximum of 12 cycles (Rai, 2000)

-Hodgkin lymphoma: Oral:

- U.S. labeling:* 0.2 mg/kg/day for 3-6 weeks
- Canadian labeling:* 0.2 mg/kg/day for 4-8 weeks

-Non-Hodgkin's lymphomas (NHL): Oral

- U.S. labeling:* 0.1 mg/kg/day for 3-6 weeks
- Canadian labeling:* Initial: 0.1-0.2 mg/kg/day for 4-8 weeks; for maintenance treatment, reduce dose or administer intermittently

-Waldenström's macroglobulinemia (U.S. unlabeled use): Oral: 0.1 mg/kg/day (continuously) for at least 6 months or 0.3 mg/kg/day for 7 days every 6 weeks for at least 6 months (Kyle, 2000)

Geriatric

Refer to adult dosing. Begin at the lower end of dosing range(s)

Renal Impairment:

No dosage adjustment provided in manufacturer's labeling; however, renal elimination of unchanged chlorambucil and active metabolite (phenylacetic acid mustard) is minimal and renal impairment is not likely to affect elimination. The following adjustments have been recommended: Adults:

Aronoff, 2007:

- $Cl_{cr} > 50$ mL/minute: No adjustment necessary.
- $Cl_{cr} 10-50$ mL/minute: Administer 75% of dose.
- $Cl_{cr} < 10$ mL/minute: Administer 50% of dose.

-Peritoneal dialysis (PD): Administer 50% of dose.

-Kintzel, 1995: Based on the pharmacokinetics, dosage adjustment is not indicated

Hepatic Impairment:

Chlorambucil undergoes extensive hepatic metabolism. Although dosage reduction should be considered in patients with hepatic impairment, no dosage adjustment is provided in the manufacturer's labeling (data is insufficient).

Dosing: Obesity

ASCO Guidelines for appropriate chemotherapy dosing in obese adults with cancer: Utilize patient's actual body weight (full weight) for calculation of body surface area- or weight-based dosing, particularly when the intent of therapy is curative; manage regimen-related toxicities in the same manner as for nonobese patients; if a dose reduction is utilized due to toxicity, consider resumption of full weight-based dosing with subsequent cycles, especially if cause of toxicity (eg, hepatic or renal impairment) is resolved (Griggs, 2012). **Note:** The manufacturer recommends the maximum dose should not exceed 0.1 mg/kg/day if maintenance therapy is required and with bone marrow infiltration.

Dosing: Adjustment for Toxicity

-Skin reactions: Discontinue treatment

-Hematologic:

- WBC or platelets below normal: Reduce dose.
- Severely depressed WBC or platelet counts: Discontinue.
- Persistently low neutrophil or platelet counts or peripheral lymphocytosis: May be suggestive of bone marrow infiltration; if infiltration confirmed, do not exceed 0.1 mg/kg/day.

-Concurrent or within 4 weeks (before or after) of chemotherapy/radiotherapy: Initiate treatment cautiously; reduce dose; monitor closely.

Common side effect:

central nervous system: Agitation (rare), ataxia (rare), confusion (rare), drug fever, fever, focal/generalized seizure (rare), hallucinations (rare)

Dermatologic: Angioneurotic edema, erythema multiforme (rare), rash, skin hypersensitivity, Stevens-Johnson syndrome (rare), toxic epidermal necrolysis (rare), urticaria

Endocrine & metabolic: Amenorrhea, infertility, SIADH (rare)

Gastrointestinal: Diarrhea (infrequent), nausea (infrequent), oral ulceration (infrequent), vomiting (infrequent)

Genitourinary: Azoospermia, cystitis (sterile)

Hematologic: Neutropenia (onset: 3 weeks; recovery: 10 days after last dose), bone marrow failure (irreversible), bone marrow suppression, anemia, leukemia (secondary), leukopenia, lymphopenia, pancytopenia, thrombocytopenia

Hepatic: Hepatotoxicity, jaundice

Neuromuscular & skeletal: Flaccid paresis (rare), muscular twitching (rare), myoclonia (rare), peripheral neuropathy, tremor (rare)

Respiratory: Interstitial pneumonia, pulmonary fibrosis

Miscellaneous: Allergic reactions, malignancies (secondary)

Pregnancy Risk Factor: D