Regimen Monograph

A - Regimen Name

ALEM Regimen
Alemtuzumab

ALEM(IV) Regimen
Alemtuzumab

Disease Site	Hematologic - Leukemia - Chronic Lymphocytic (CLL)
Intent	Palliative
Regimen Category	**Evidence-Informed :** Regimen is considered appropriate as part of the standard care of patients; meaningfully improves outcomes (survival, quality of life), tolerability or costs compared to alternatives (recommended by the Disease Site Team and national consensus body e.g. pan-Canadian Oncology Drug Review, pCODR). Recommendation is based on an appropriately conducted phase III clinical trial relevant to the Canadian context OR (where phase III trials are not feasible) an appropriately sized phase II trial. Regimens where one or more drugs are not approved by Health Canada for any indication will be identified under Rationale and Use.

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B - Drug Regimen

Week 1:

alemtuzumab[a, b, c]	3 mg	IV / Subcut *	(first dose)
alemtuzumab[a, b, c]	10 mg	IV / Subcut *	(second dose)
alemtuzumab[a, b, c]	30 mg	IV / Subcut *	(third dose)

(This drug is not publicly funded. Universal compassionate access program is available.)

Weeks 2 to 13:

alemtuzumab[a, b, c]	30 mg	IV / Subcut *	3 times per week

(This drug is not publicly funded. Universal compassionate access program is available.)

*Use ALEM(IV) in T-Cell Prolymphocytic Leukemia

a. Although not approved by Health Canada, alemtuzumab has been given subcutaneously instead of intravenously; the incidence of infusion reactions may be lower. (Note: intravenous should be used for T-cell prolymphocytic leukemia)

b. Gradual dose escalation is required at the initiation of therapy and after treatment interruptions of 7 days or more. In most patients, escalation to 30mg can be accomplished in 3-7 days. Initial doses can be administered in various ways; sequentially (daily on days 1 to 3) and on alternate days (i.e. days 1, 3, and 5). Both schedules were used in clinical trials.

c. Single doses of alemtuzumab greater than 30 mg or cumulative weekly doses of greater than 90 mg should not be administered since higher doses are associated with an increased incidence of pancytopenia.

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C - Cycle Frequency

For a usual total of 13 weeks (1 week dose escalation, 12 weeks maintenance), unless disease progression or unacceptable toxicity occurs. There is no data available to support re-treatment with alemtuzumab; however, Rai et al. has considered re-treatment in appropriate patients who relapsed more than 1 year after initial treatment.

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D - Premedication and Supportive Measures

Antiemetic Regimen: Minimal

Premedication (prophylaxis for infusion reactions):

Administer 30 minutes prior to IV/SC alemtuzumab*:

- H1-receptor antagonist (e.g. diphenhydramine 50 mg IV)
- Acetaminophen 650 mg PO

*Can consider corticosteroids (methylprednisolone 1g) on the first 3 days

Other Supportive Care:

- Trimethoprim/sulfamethoxazole DS twice daily three times per week and famciclovir (or equivalent) 250mg bid during treatment and for 2 months after or until CD4+ count ≥ 200 cell/uL
- Allopurinol and hydration to reduce the risk of tumour lysis syndrome are recommended.
- Irradiated blood products should be used

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E - Dose Modifications

Doses should be modified according to the protocol by which the patient is being treated.

Dosage with toxicity

Toxicity (grade or 10^9)	**1st Occurrence**	**2nd Occurrence**	**3rd Occurrence**
ANC < 0.25 and/or platelet ≤ 25	Hold, restart at same dose when ANC ≥ 0.5 and platelets ≥ 50	Hold, restart at 10mg when ANC ≥ 0.5 and platelets ≥ 50	Discontinue

If baseline ANC ≤ 0.25, and/or platelet ≤ 25 and ↓ 50%	Hold, restart at same dose when ≥ baseline	Hold, restart at 10mg when ≥ baseline	Discontinue
≥ Grade 3 non-hematologic toxicity, including serious infections and CMV viremia	Hold until ≤ grade 2. Consider dose modification		
Autoimmune disorders	Discontinue		
PML, autoimmune anemia or thrombocytopenia	Discontinue		
If delay between dosing is ≥ 7 days, must re-escalate starting from 3mg Do not modify dose for lymphopenia			

Management of Infusion-Related Reactions:

Also refer to the CCO guideline for detailed description of Management of Cancer Medication-Related Infusion Reactions.

Grade	Management	Re-challenge
1-2	• Stop or slow the infusion rate • Manage the symptoms Restart: • Once symptoms resolve, the infusion can be restarted at a slower rate with pre-medications, unless a serious reaction occurred	No specific recommendations can be made at this time. If reaction was with IV route, switch to SC if possible
3-4	• Stop treatment • Aggressively manage symptoms Restart: • Once symptoms resolve, the	

	infusion can be restarted at a slower rate with pre-medications, unless a serious reaction occurred	

Hepatic Impairment

No information found.

Renal Impairment

No information found.

Dosage in the Elderly

No dosage adjustment required. Limited experience in this population.

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F - Adverse Effects

Refer to alemtuzumab drug monograph(s) for additional details of adverse effects

Very common (≥ 50%)	Less common (10-24%)	Uncommon (< 10%), but may be severe or life-threatening
• Myelosuppression +/- infection and bleeding (may be severe) • Atypical infections • Hypersensitivity (may be severe)	• Nausea, vomiting • Rash	• Arrhythmia • Cardiotoxicity • Tumor lysis syndrome • Arterial or venous thromboembolism • Nephrotoxicity • GI obstruction or perforation

		• Disseminated intravascular coagulation (DIC) • Cholecystitis • Pancreatitis • Pneumonitis • Secondary malignancy • Autoimmune disorders • Transfusion associated GVHD

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G - Interactions

Refer to alemtuzumab drug monograph(s) for additional details

- Additive effects with medications that can increase risk of bleeding
- Additive effects with medications that can cause hypotension (especially at time of infusion)

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H - Drug Administration and Special Precautions

Refer to alemtuzumab drug monograph(s) for additional details

Administration

- See the Product Monograph for full details of preparation and administration.
- Full resuscitation facilities and experienced personnel should be available.
- Do not administer as an intravenous push or bolus.
- Mix in 100mL IV bag (5% Dextrose or Normal Saline). Gently invert the bag to mix the solution. Infuse the admixture over 2 hours.
- Other drug substances should not be added or simultaneously infused through the same intravenous line
- Infusion reactions with subcutaneous alemtuzumab are much milder (off-label route of administration) than IV. Consider subcutaneous administration (except in patients with T-PLL).

Also refer to the CCO guideline for detailed description of Management of Cancer Medication-Related Infusion Reactions.

Contraindications

- Patients who have or have had PML, have active and/or severe infections, active hepatitis B, or severely immunocompromised (e.g. AIDS patients with very low CD4 or CD8 counts), or active secondary malignancies
- Avoid the use of live vaccine

Other warnings/precautions

- Gradual dose escalation of alemtuzumab to the recommended maintenance dose is required at the initiation of therapy and after interruption of therapy for more than 7 days. Alemtuzumab can result in serious and even fatal infusion reactions.
- Single doses of alemtuzumab greater than 30mg or cumulative doses of more than 90mg per week should not be administered, as they are associated with a higher incidence of pancytopenia.
- Exercise caution in patients with a history of recurring or chronic infections or with underlying conditions which may further predispose patients to serious infection.
- Anti-viral and anti-Pneumocystis carinii pneumonia prophylaxis are strongly recommended
- Use with caution in patients with pre-existing cardiac disease
- alemtuzumab should be given to pregnant women only if the benefits outweigh the risks to the mother and fetus; rituximab should not be used during pregnancy. Women of childbearing potential and men of reproductive potential should use effective contraceptive methods during treatment and for a minimum of six months following alemtuzumab therapy.
- IgG is secreted in human milk; therefore, breastfeeding should be discontinued for at least three months after cessation of therapy.

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I - Recommended Clinical Monitoring

Treating physicians may decide to monitor more or less frequently for individual patients but should always consider recommendations from the product monograph.

Recommended Clinical Monitoring

- CBC and platelets; Weekly and as needed
- Infusion reactions; during infusion and for at least 2 hours after IV infusion
- Clinical toxicity assessment for infusion reactions, respiratory and cardiac events, auto-immune disorders, bleeding and infection

- Grade toxicity using the current NCI-CTCAE (Common Terminology Criteria for Adverse Events) version

Suggested Clinical Monitoring

- CD4+ counts should be assessed after treatment until recovery to ≥ 200 cells/μL
- Consider CMV monitoring.

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J - Administrative Information

Approximate Patient Visit

ALEM	IV: 3 hours; SC: 1 hour

Pharmacy Workload **(average time per visit)**

ALEM	8.334 minutes
ALEM(IV)	8.334 minutes

Nursing Workload **(average time per visit)**

ALEM	32.33 minutes
ALEM(IV)	59.167 minutes

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K - References

Alemtuzumab drug monograph, Cancer Care Ontario.

Hillmen P, Skotnicki AB, Robak T. Alemtuzumab compared with chlorambucil as first-line therapy for chronic lymphocytic leukemia. JCO 2007; 25(35): 5616-23.

Keating MJ, Flinn I, Jain V, et al. Therapeutic role of alemtuzumab (Campath-1H) in patients who have failed fludarabine: results of a large international study. Blood 2002; 99: 3554-3561.

Lundin J, Kimby E, Bjorkholm M, et al. Phase II trial of subcutaneous anti-CD52 monoclonal antibody alemtuzumab (Campath-1H) as first-line treatment for patients with B-cell chronic lymphocytic leukemia (B-CLL). Blood 2002; 100: 768-773.

Osterborg A, Dyer MJS, Bunjes D, et al. Phase II multicentre study of human CD52 antibody in previously treated chronic lymphocytic leukemia. J Clin Oncol 1997; 15: 1567-74.

Rai K, Freter CE, Mercier RJ, et al. Alemtuzumab in previously treated Chronic Lymphocytic Leukemia Patients who had also received fludarabine. Journal of Clinical Oncology 2002; 20: 3891-97.

Stilgenbauer S, Winkler D, Krober A, et al. Subcutaneous campath-1H (alemtuzumab) in fludarabine-refractory CLL: interim analysis of the CLL2h study of the German CLL Study Group (GCLLSG). [abstract]. Blood 2004; 104(11): A487.

November 2019 Updated infusion reaction information in Premedication and Supportive Measures, Dose Modifications, Drug Administration and Monitoring sections

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M - Disclaimer

Regimen Abstracts

A Regimen Abstract is an abbreviated version of a Regimen Monograph and contains only top level information on usage, dosing, schedule, cycle length and special notes (if available). It is intended for healthcare providers and is to be used for informational purposes only. It is not intended to constitute or be a substitute for medical advice, and all uses of the Regimen Abstract are subject to clinical judgment. Such information is provided on an "as-is" basis, without any representation, warranty, or condition, whether express, or implied, statutory or otherwise, as to the information's quality, accuracy, currency, completeness, or reliability, and Cancer Care Ontario disclaims all liability for the use of this information, and for any claims, actions, demands or suits that arise from such use.

Information in regimen abstracts is accurate to the extent of the ST-QBP regimen master listings, and has not undergone the full review process of a regimen monograph. Full regimen monographs will be published for each ST-QBP regimen as they are developed.

Regimen Monographs

Refer to the New Drug Funding Program or Ontario Public Drug Programs websites for the most up-to-date public funding information.

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