Cladribine 0.14mg/kg Day 1 to 5 Therapy

INDICATIONS FOR USE:

INDICATION	ICD10	Regimen Code	Reimbursement Status
First line treatment for adult patients with Hairy Cell Leukaemia	C91	00402a	Hospital

TREATMENT:

The starting dose of the drugs detailed below may be adjusted downward by the prescribing clinician, using their independent medical judgement, to consider each patient's individual clinical circumstances.

Cladribine is usually administered for 1 cycle only. There is no dose reduction for haematological counts for this first cycle. If repeated, it should be given after recovery of blood counts to baseline.

Facilities to treat anaphylaxis MUST be present when the chemotherapy is administered.

Day	Drug	Dose	Route	Diluent & Rate
1-5	Cladribine	0.14mg/kg	SC	n/a

ELIGIBILTY:

- Indications as above

EXCLUSIONS:

- Hypersensitivity to cladribine or any of the excipients.
- Creatinine Clearance ≤ 50ml/min
- Moderate to severe hepatic impairment (Child–Pugh Score >6)
- Pregnancy
- Lactation

PRESCRIPTIVE AUTHORITY:

The treatment plan must be initiated by a Consultant Haematologist working in the area of haematological malignancies.

TESTS:

Baseline tests:

- FBC, renal and liver profile
- LDH, Uric acid
- Virology screen - Hepatitis B (HBsAg, HBcoreAb) & C, HIV CMV, EBV, VZV and HSV.
  *See Adverse Effects/Regimen Specific Complications re Hepatitis B Reactivation

Regular tests:

- FBC weekly during treatment and for up to 8 weeks after therapy
- Renal and liver profile and LDH as clinically indicated
- Creatinine clearance using Cockroft Gault equation

Disease monitoring:

Disease monitoring should be in line with the patient's treatment plan and any other test/s, as directed by the supervising Consultant.

Bone marrow reassessment post cladribine treatment should generally be delayed for 4 to 6 months to allow for delayed marrow recovery that can be associated with cladribine.

DOSE MODIFICATIONS:

- Any dose modification should be discussed with a Consultant

Renal and Hepatic Impairment:

Table 1: Dose modifications based on renal and hepatic impairment

Renal impairment	Hepatic impairment
Contraindicated in patients with moderate to severe renal impairment (creatinine clearance ≤ 50 ml/min)	Contraindicated in patients moderate to severe hepatic impairment (Child-Pugh score > 6)

SUPPORTIVE CARE:

EMETOGENIC POTENTIAL: Minimal (**Refer to local policy).**

PREMEDICATIONS: None

OTHER SUPPORTIVE CARE:

- Tumour lysis syndrome prophylaxis **(Refer to local policy)**
- PJP prophylaxis **(Refer to local policy)***
- Anti-viral prophylaxis **(Refer to local policy)***
- Anti-fungal prophylaxis **(Refer to local policy)**
- All patients being treated with cladribine should receive irradiated blood products **(Refer to local policy)**
- Contraceptive measures for women of child-bearing potential during therapy and for at least 6 months after cessation of therapy.

***Note :** Recommended that the use of concomitant drugs should be minimised during cladribine infusions as patients often develop rashes. Co-trimoxazole and aciclovir should be started once treatment is completed

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS

The adverse effects listed are not exhaustive. Please refer to the relevant Summary of Product Characteristics for full details.

Cladribine is an antineoplastic and immunosuppressive substance that can induce considerable toxic adverse reactions, such as myelo- and immunosuppression, long-lasting lymphocytopenia, and opportunistic infections. Patients undergoing treatment with cladribine should be closely monitored for signs of haematological and non-haematological toxicities.

- **Progressive multifocal leukoencephalopathy (PML):** Cases of PML, including fatal cases, have been reported with cladribine. PML diagnosis has been reported 6 months to several years after treatment with cladribine. An association between cladribine and prolonged lymphopenia was reported in several of these cases. Consider PML in the differential diagnosis for patients with new or worsening neurological, cognitive or behavioural signs or symptoms. If PML is suspected, the patients should not receive further treatment with cladribine (7).
- **Secondary malignancies:** Like other nucleoside analogues, treatment with cladribine is associated with the occurrence of second malignancies. Therefore, regular monitoring of patients treated with cladribine is required.
- **Haematological toxicity:** During the first month following treatment, myelosuppression is most notable and red blood cell or platelet transfusions may be required. An increased incidence of opportunistic infections is expected during and for 6 months following therapy with cladribine. Careful and regular monitoring of peripheral blood counts is essential during and for 2 to 4 months following treatment with cladribine.
- **Fever** of unknown origin frequently occurs in patients treated for hairy cell leukaemia and is manifested predominantly during the first 4 weeks of therapy.
- **Fertility**: Men being treated with cladribine should be advised not to father a child up to 6 months after treatment Women of childbearing potential must use effective contraception during treatment with cladribine and for 6 months after the last cladribine dose.
- **Hepatitis B Reactivation:** Patients should be tested for both HBsAg and HBcoreAb as per local policy. If either test is positive, such patients should be treated with anti-viral therapy. **(Refer to local infectious disease policy**). These patients should be considered for assessment by hepatology.

DRUG INTERACTIONS:

- Due to a potential increase of haematological toxicity and bone marrow suppression, cladribine must not be used concomitantly with other myelosuppressive medicinal products.
- Corticosteroids have been shown to enhance the risk of severe infections when used in combination with cladribine and should not be given concomitantly with cladribine.
- Current drug interaction databases should be consulted for more information including potential for interactions with CYP3AR inhibitors/inducers.

ATC CODE:

Cladribine L01BB04

REFERENCES:

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2. Jones G et al. Revised guidelines for the diagnosis and management of hairy cell leukaemia and hairy cell leukaemia variant. British Journal of Haematology 2011: 156: 186-195.
3. Piro LD, Carrera CJ, Carson DA and Beutler E. Lasting remissions in hairy cell leukemia induced by a single infusion of 2-chlorodeoxyadenosine. New Engl J Med 1990;322:1117-21.
4. Robak T, Błasińska-Morawiec M, et al. 2-chlorodeoxyadenosine (2-CdA) in 2-hour versus 24-hour intravenous infusion in the treatment of patients with hairy cell leukemia. Leuk Lymphoma. 1996;22(1-2):107.
5. Robak T, Jamroziak K, et al. Cladribine in a weekly versus daily schedule for untreated active hairy cell leukemia: final report from the Polish Adult Leukemia Group (PALG) of a prospective, randomized, multicenter trial. Blood. 2007;109(9):3672.
6. Lauria F, Bocchia M et al. Weekly administration of 2-chlorodeoxyadenosine in patients with hairy-cell leukemia is effective and reduces infectious complications. Haematologica 1999; 84(1):22-25.
7. Safety Notices Litak (Cladribine) - Important Safety Information from LIPOMED GmbH as approved by the HPRA Monday, December 4, 2017 http://www.hpra.ie/homepage/medicines/safety-notices/item?t=/litak-(cladribine)---important-safety-information-from-lipomed-gmbh-as-approved-by-the-hpra&id=90390a26-9782-6eee-9b55-ff00008c97d0
8. LITAK® Summary of Product Characteristics Accessed April 2020. Available at: https://www.ema.europa.eu/en/documents/product-information/litak-epar-product-information_en.pdf

Version	Date	Amendment	Approved By
1	27/04/2018		Dr Hilary O'Leary
2	14/10/2020	Regimen review Updated recommended management of hepatitis B reactivation	Dr Hilary O'Leary

Comments and feedback welcome at oncologydrugs@cancercontrol.ie.