Chlorambucil 10mg/m^2 Therapy

INDICATIONS FOR USE:

INDICATION	ICD10	Regimen Code	*Reimbursement Status
Treatment of patients with low grade lymphoma	C85	00411a	CDS
Treatment of patients with Chronic Lymphocytic Leukaemia	C91	00411b	CDS

If the reimbursement status is not defined[i], the indication has yet to be assessed through the formal HSE reimbursement process.

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 patients individual clinical circumstances.

Chlorambucil is administered on days 1-7 of a 28 day cycle for up to 6 cycles until disease control is achieved or disease progression/ unacceptable toxicity develops.

Day	Drug	Dose	Route	Cycle
1-7	Chlorambucil	10mg/m^2	PO (one hour before a meal or 3 hours after)	Every 28 days
Chlorambucil is available as 2mg tablets Tablets must be swallowed whole Chlorambucil tablets should be stored in the fridge (2 to 8 degrees C)				

ELIGIBILTY:

- Indications as above

EXCLUSIONS:

- Hypersensitivity to chlorambucil or any of the excipients

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
- Uric acid
- Virology screen -Hepatitis B (HBsAg, HBcoreAb)) & C, HIV

Regular tests:

- FBC, renal and liver profile weekly for the first month of treatment and then before every course of therapy

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.

DOSE MODIFICATIONS:

- Any dose modification should be discussed with a Consultant

Haematological:

Table 1: Recommended dose modification for haematological toxicity unless due to bone marrow infiltration

ANC x 10^9/L		Platelets x 10^9/L	Dose modification
<1	and/or	<75	Delay next cycle for one week If a delay > 2 weeks is required reduce dose of chlorambucil by 50%
<0.5	and/or	<50	Consider both delaying the next cycle and a dose reduction

Renal and Hepatic Impairment:

Table 2: Recommended dose modifications of chlorambucil in patients with renal or hepatic impairment

Renal impairment	Hepatic impairment
No dose reductions necessary, however, monitor patients carefully, as they are more prone to myelosuppression.	Dose reduce in patients with gross hepatic dysfunction. Modify dose according to response. Once the tolerance is established after the first month of therapy the dosage should be modified according to response e.g. level of haematological suppression

SUPPORTIVE CARE:

EMETOGENIC POTENTIAL: Low (**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)**

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS

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

- **Myelosuppression**: Since chlorambucil is capable of producing irreversible bone marrow suppression, blood counts should be closely monitored in patients undergoing treatment.
- **Rash:** Continued treatment with chlorambucil should be assessed if a rash develops since there have been reports of Stevens-Johnson Syndrome in patients receiving chlorambucil.

- **Seizures:** Chlorambucil is epileptogenic. Patients with a history of seizures or head trauma, or on other epileptogenic medications may be at increased risk of seizures with chlorambucil.
- **Hepatitis B Reactivation:** All patients should be tested for both HBsAg and HBcoreAb as per local policy. If either test is positive, such patients should be treated with lamivudine 100 mg/day orally, for the entire duration of chemotherapy and for six months afterwards. Such patients should also be monitored with frequent liver function tests and hepatitis B virus DNA at least every two months. If the hepatitis B virus DNA level rises during this monitoring, management should be reviewed with an appropriate specialist with experience managing hepatitis and consideration given to stopping chemotherapy.

DRUG INTERACTIONS:

- No specific clinically significant drug-drug interactions
- Current drug interaction databases should be consulted for more information eg

ATC CODE:

Chlorambucil L01AA02

REFERENCES:

1. Catovsky D, Richards S, Matutes E. et al. Assessment of fludarabine plus cyclophosphamide for patients with chronic lymphocytic leukaemia (the LRF CLL4 Trial): a randomised controlled trial. Lancet 2007; 370(9583):230-239.
2. CLL Trialists' Collaborative Group. Chemotherapeutic options in chronic lymphocytic leukemia: a metaanalysis of the randomized trials. CLL Trialists' Collaborative Group J.Natl.Cancer Inst. 1999;91(10):861-868.
3. Hillmen P, Gribben JG, Follows GA. et al. Rituximab plus chlorambucil as firstline treatment for chronic lymphocytic leukemia: Final analysis of an openlabel phase II study. J Clin Oncol 2014;32(12):1236-1241.
4. Dosage Adjustment for Cytotoxics in Renal Impairment January 2009; North London Cancer Network. Available at http://londoncancer.org/media/65600/renal-impairment-dosage-adjustment-for-cytotoxics.pdf
5. Dosage Adjustment for Cytotoxics in Hepatic Impairment January 2009;North London Cancer Network. Available at http://londoncancer.org/media/65594/hepatic-impairment-dosage-adjustment-for-cytotoxics.pdf
6. Leukeran® Summary of Product Characteristics Accessed Feb 2018 Available at: http://www.hpra.ie/img/uploaded/swedocuments/LicenseSPC_PA1691-007-001_16022016100039.pdf

Version	Date	Amendment	Approved By
1	24/04/2018		Dr Ruth Clifford

Comments and feedback welcome at oncologydrugs@cancercontrol.ie.

[i] ODMS – Oncology Drug Management System
CDS – Community Drug Schemes (CDS) including the High Tech arrangements of the PCRS community drug schemes
Further details on the Cancer Drug Management Programme is available at;
http://www.hse.ie/eng/services/list/5/cancer/profinfo/medonc/cdmp/