ChIVPP (Chlorambucil, vinBLAStine, Procarbazine[i], prednisoLONE) Therapy

INDICATIONS FOR USE:

INDICATION	ICD10	Regimen Code	HSE approved reimbursement status*
Treatment of patients with Hodgkin lymphoma who are unsuitable for anthracycline- or bleomycin-containing treatments or more intensive treatment	C81	00452a	N/A

* This applies to post 2012 indications

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.

Treatment is administered every 28 days for 6-8 cycles or until disease progression or unacceptable toxicity develops.

Facilities to treat anaphylaxis MUST be present when systemic anti-cancer therapy (SACT) is administered.

Day	Drug	Dose	Route	Diluent & Rate	Cycle
1-14	Chlorambucil[a, b]	6mg/m^2 (cap dose at 10mg)[c]	PO		Every 28 days for 6 to 8 cycles
1 and 8	vinBLAStine[d]	6mg/m^2 (cap dose at 10mg)	IV	50mL NaCl 0.9% over 15 minutes	Every 28 days for 6 to 8 cycles
1-14	Procarbazine[e]	100mg/m^2 (cap dose at 150mg)	PO		Every 28 days for 6 to 8 cycles
1-14	PrednisoLONE	40mg/m^2 (cap dose at 60mg)	PO		Every 28 days for 6 to 8 cycles
[a] Chlorambucil tablets should be taken on an empty stomach (one hour before a meal or 3 hours after).					
[b] Chlorambucil tablets should be stored in their original container between 2^{0}C and 8^{0}C.					
[c] For patients who are frail or have significant co-morbidities, consider 50% dose reduction of chlorambucil on Cycle 1 to assess tolerability.					
[d] vinBLAStine is a neurotoxic chemotherapeutic agent. **Refer to NCCP Guidance on the Safe Use of Neurotoxic drugs (including Vinca Alkaloids) in the treatment of cancer** **Available on the NCCP website**					
[e] Procarbazine is an unlicensed drug. If the drug is not to be dispensed by the hospital, then the hospital should ensure communication with the patient's community pharmacy to ensure there is no interruption in treatment. Procarbazine is available as 50mg capsules, round dose to nearest 50mg.					

Note: Administration volumes and fluids have been standardised to facilitate electronic prescribing system builds.

ELIGIBILITY:

- Indication as above

EXCLUSIONS:

- Hypersensitivity to chlorambucil , vinBLAStine, procarbazine, prednisoLONE or to any of the excipients
- Pregnancy or breast feeding

PRESCRIPTIVE AUTHORITY:

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

TESTS:

Baseline tests:

- FBC, renal and liver profile
- Uric acid, LDH
- Blood glucose
- Neurotoxicity assessment
- Virology screen - hepatitis B virus (HBV) serology [HBV sAg, HBV sAb, HBV cAb], hepatitis C virus (HCV) serology, human immunodeficiency virus (HIV) serology, human T-lymphotropic virus type 1 and human T-lymphotropic virus type 2 (HTLV-1 and HTLV-2), cytomegalovirus (CMV) serology [IgG], and additional screening as clinically indicated *(Reference Regimen Specific Complications for information on Hepatitis B reactivation)

Regular tests:

- FBC (on Day 1 and Day 8 of each cycle), renal and liver profile
- Uric acid, LDH
- Blood glucose
- Neurotoxicity assessment

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 on Day 1

ANC x 10^9/L		Platelets x 10^9/L	
≥1.5	and	≥100	100%
<1.5	and/or	<100	Delay treatment for 1 week until recovery

Table 2: Recommended dose modification for haematological toxicity on Day 8

ANC x 10^9/L		Platelets x 10^9/L	Chlorambucil	vinBLAStine	Procarbazine
≥1.0		≥80	100% dose	100% dose	100% dose
0.5-0.99	and	50-79	50% dose	50% dose	Discontinue
<0.5	and/or	<50	Discontinue	Omit	Discontinue

Renal and Hepatic Impairment:

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

<table>
<tr><th>Drug</th><th colspan="2">Renal impairment</th><th>Hepatic impairment</th></tr>
<tr><td>Chlorambucil[a]</td><td colspan="2">Renal impairment: no dose adjustment is needed
Haemodialysis: no need for dose adjustment is expected</td><td>Mild and moderate: no need for dose adjustment is expected
Severe: not recommended</td></tr>
<tr><td>vinBLAStine[b]</td><td colspan="2">Renal impairment: no dose adjustment is needed
Haemodialysis: no need for dose adjustment is expected</td><td>Bilirubin > 51 µmol/L: 50% of the original dose</td></tr>
<tr><td rowspan="3">Procarbazine[c]</td><td>CrCl (mL/min)</td><td>Dose</td><td rowspan="3">Hepatic impairment: No need for dose adjustments is expected</td></tr>
<tr><td>≥10</td><td>No dose adjustment is needed</td></tr>
<tr><td><10</td><td>Not recommended</td></tr>
<tr><td colspan="4">[a] Chlorambucil: Renal and hepatic – Giraud et al 2023
[b] vinBLAStine: Renal and hepatic – Giraud et al 2023
[c] Procarbazine: Renal and hepatic – Giraud et al 2023</td></tr>
</table>

Management of adverse events:

Table 3: Dose modification of vinBLAStine based on adverse events

Drug	Adverse Event	Dose Modification
vinBLAStine	Peripheral neuropathy Grade ≥ 2	Dose reduction of vinBLAStine may be required at the discretion of the prescribing consultant

SUPPORTIVE CARE:

EMETOGENIC POTENTIAL:

- As outlined in NCCP Classification Document for Systemic AntiCancer Therapy (SACT) Induced Nausea and Vomiting - Available on NCCP website

Chlorambucil: Minimal to low **(Refer to local policy).**
vinBLAStine: Minimal **(Refer to local policy).**
Procarbazine: Moderate to High **(Refer to local policy).**

For information:
Within NCIS regimens, antiemetics have been standardised by the Medical Oncologists and Haemato-oncologists and information is available in the following documents:

- NCCP Supportive Care Antiemetic Medicines for **Inclusion in NCIS** (Medical Oncology) – Available on NCCP website
- NCCP Supportive Care Antiemetic Medicines for **Inclusion in NCIS** (Haemato-oncology) – Available on NCCP website

PREMEDICATIONS: None

OTHER SUPPORTIVE CARE:

- All patients should receive irradiated blood products
- 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)**
- Proton Pump Inhibitor **(Refer to local policy)**
- Mouth care prophylaxis **(Refer to local policy)**
- Prophylactic regimen against vinBLAStine-induced constipation is recommended **(Refer to local policy)**

ADVERSE EFFECTS:

- Please refer to the relevant Summary of Product Characteristics (SmPC) for details.

REGIMEN SPECIFIC COMPLICATIONS:

- **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:

- Current SmPC and drug interaction databases should be consulted for information.

REFERENCES:

1. Selby, P., P. Patel, S. Milan, et al. 1990. "ChlVPP combination chemotherapy for Hodgkin's disease: long-term results." Br.J.Cancer. 62(2):279-285.
2. Vinca alkaloids + Azoles. Stockley's Drug Interactions 11th Edition
3. Giraud E L, Lijster B D, et al. Dose recommendations for anticancer drugs in patients with renal or hepatic impairment: an update. Available at: https://pubmed.ncbi.nlm.nih.gov/37269847/
4. NCCP Classification Document for Systemic Anti-Cancer Therapy (SACT) Induced Nausea and Vomiting. V5 2023. Available at: https://www.hse.ie/eng/services/list/5/cancer/profinfo/chemoprotocols/nccp-classification-document-for-systemic-anti-cancer-therapy-sact-induced-nausea-and-vomiting.pdf
5. Chlorambucil (Leukeran®) Summary of Product Characteristics. Last updated 30/06/2022. Accessed July 2024. Available at: https://www.hpra.ie/img/uploaded/swedocuments/Licence_PA1691-007-001_30062022103832.pdf
6. Procarbazine 50mg capsules. Summary of Product Characteristics. Accessed July 2024. Available at: http://www.medicines.org.uk/emc/medicine/386/SPC
7. vinBLAStine Sulfate 1mg/ml Solution for Injection or Infusion. Summary of Product Characteristics. Last update 13/10/2023. Accessed July 2024. Available at: https://www.hpra.ie/img/uploaded/swedocuments/Licence_PA0822-208-001_06122024145749.pdf

Version	Date	Amendment	Approved By
1	15/11/2024		Dr Liam Smyth

Comments and feedback welcome at oncologydrugs@cancercontrol.ie.

[i] This is an unlicensed indication for the use of procarbazine in Ireland. Patients should be informed of this and consented to treatment in line with the hospital's policy on the use of unlicensed medication and unlicensed or "off label" indications. Prescribers should be fully aware of their responsibility in communicating any relevant information to the patient and also ensuring that the unlicensed or "off label" indication has been acknowledged by the hospital's Drugs and Therapeutics Committee, or equivalent, in line with hospital policy