ChIVPP

Indication
Treatment of Hodgkins disease for patients who cannot tolerate ABVD/AVD.

ICD-10 codes
Codes with a prefix C81.

Regimen details

Day	Drug	Dose	Route
1-14	Chlorambucil	6mg/m^2 OD*	PO
1 and 8	Vinblastine	6mg/m^2 (max. 10mg)	IV infusion
1-14	Procarbazine	100mg/m^2 OD (max 200mg)	PO
1-14	Prednisolone	40mg/m^2 OM (max. 60mg)	PO

*For patients over 60 years of age, consider a 50% starting dose.

Cycle frequency
Every 28 days

Number of cycles
Maximum 6-8 cycles

Administration
Chlorambucil is available as 2mg tablets. Tablets should be taken on an empty stomach, at least 1 hour before or 3 hours after a meal.

Vinblastine is administered as an intravenous infusion in 50mL sodium chloride 0.9% over 10 minutes, as per national guidance. The nurse should remain with the patient throughout the infusion.

Procarbazine is available as 50mg capsules. Procarbazine should be swallowed whole with water. Patients should be advised to avoid alcohol and tyramine containing foods.

Prednisolone is available as 5mg and 25 mg tablets. The dose should be taken in the morning, with or after food.

Pre-medication
For patients with bulky disease consider pre-hydration with at least 1000mL sodium chloride 0.9% IV infusion as necessary. Ensure good oral fluid intake where possible.

Emetogenicity
This regimen has moderate emetogenic potential (days 1-14).

Additional supportive medication
Allopurinol 300mg (100mg if creatinine clearance <20mL/min) OD for the first cycle if required.
H_2 antagonist or PPI if required.
Antiemetics as per local policy.
Antifungal, antiviral and PCP prophylaxis as per local policy.

Extravasation

Vinblastine is a vesicant (Group 5).

Investigations – pre first cycle

Investigation	**Validity period** (or as per local policy)
FBC*	14 days
U+E (including creatinine)	14 days
LFT	14 days
LDH	14 days
Calcium	14 days
Magnesium	14 days
Glucose	14 days

ECG and Echocardiogram if suspected cardiac dysfunction.
* and day 8.

Investigations –pre subsequent cycles

Investigation	**Validity period** (or as per local policy)
FBC	96 hours (and within 24 hours of day 8 – at consultants discretion)
U+E (including creatinine)	7 days
LFT	7 days

Standard limits for administration to go ahead

If blood results not within range, authorisation to administer **must** be given by prescriber/ consultant.

Investigation	**Limit**
Neutrophil count	≥ 1.0 x 10^9/L
Platelet count	≥ 100 x 10^9/L
Creatinine clearance	≥ 45 mL/min
Bilirubin	≤ 1.5 x ULN
AST/ALT	< ULN

Dose modifications

- **Haematological toxicity**

Day 1:
If neutrophils < 1.0 x 10^9/L **or** platelets < 100 x 10^9/L delay by 1 week or until count recovery. If counts recovered within 2 weeks resume at full dose, otherwise consider dose reduction.

Day 8 FBC should be performed on cycle 1 and then at consultants discretion for subsequent cycles.

Day 8:

Neutrophils (x 10^9/L)		**Platelets** (x 10^9/L)	**Chlorambucil dose**	**Vinblastine dose**	**Procarbazine dose**
≥ 1	and	≥ 100	100%	100%	100%
≥ 1	and	80-99	50%	50%	50%
0.5-< 1.0	or	50-79	50%	50%	Stop
<0.5	or	<50	Stop	Omit	Stop

- **Renal impairment**

CrCl (mL/min)	**Chlorambucil dose**	**Vinblastine dose**	**Procarbazine dose**
≥ 45	100%	100%	100%
30-44	Monitor for myelosuppression	100%	Consider 50% dose reduction
<30		Discuss with consultant	Discontinue

- **Hepatic impairment**

Bilirubin (x ULN)		**ALT/AST** (x ULN)	**Vinblastine dose**	**Procarbazine dose**
≤ 1.5	and	< ULN	100%	100%
1.5 – 3	or	1-3	50%	100%
> 3	and	< ULN	50%	Consider dose reduction
> 3	and	> 3	Omit	Contra-indicated

Chlorambucil should be dose reduced in severe hepatic impairment and the dose further modified based on response and degree of myelosuppression.

- **Other toxicities**

Toxicity	**Definition**	**Dose adjustment**
Neuropathy	Grade 2 (moderate symptoms)	Reduce procarbazine to 75% dose Reduce vinblastine dose or omit, consultant decision.
	Grade 3+ (severe symptoms, limiting self-care)	Discontinue treatment

Adverse effects - for full details consult product literature/ reference texts

- **Serious side effects**

Myelosuppression
Stevens-Johnson syndrome (chlorambucil)
Hepatotoxicity
Pneumonitis / pulmonary fibrosis
Thromboembolism
Nephrotoxicity
Hypersensitivity and allergic reactions
Teratogenicity
Infertility

- **Frequently occurring side effects**

Nausea or vomiting
Fatigue, flu-like symptoms
Anorexia, weight loss
Constipation, diarrhoea
Neurotoxicity
Myelosuppression
Stomatitis/mucositis

- **Other side effects**

Rash, pigmentation, photosensitivity

Significant drug interactions – for full details consult product literature/ reference texts

Coumarin-derived anticoagulants such as warfarin: patients established on warfarin should either be changed to low molecular weight heparin or have weekly monitoring of INR. Patients who are initiated on anti-coagulation should remain on low molecular weight heparin until completion of the course of chemotherapy.

Vinblastine:
Erythromycin may increase toxicity of vinblastine.

Procarbazine:
Alcohol: Procarbazine has a weak disulfiram-like effect and can lead to alcohol intolerance.
MAO inhibition: Procarbazine is a weak inhibitor of MAO and can cause CNS side-effects. Care should be taken when co-prescribing antihypertensives, CNS depressants or tricyclic antidepressants.
Barbiturates: Phenobarbital can lead to a reduced anti-tumour effect of lomustine due to induction of hepatic enzymes and increased elimination. Barbiturates can cause increased CNS depression with procarbazine.

Additional comments

Haematological toxicity may be cumulative.
Patients should receive irradiated blood products.

References

- Summary of Product Characteristics Chlorambucil (Medac). Accessed 13 July 2016 via www.medicines.org.uk
- Summary of Product Characteristics Procarbazine (Medac). Accessed 13 July 2016 via www.medicines.org.uk
- Summary of Product Characteristics Vinblastine (Hospira). Accessed 13 July 16 via www.medicines.org.uk
- Johnson PW, Radford JA, Cullen MH, Sydes MR, Walewski J, Jack AS, MacLennan KA, Stenning SP, Clawson S, Smith P, Ryder D, Hancock BW; United Kingdom Lymphoma Group LY09 Trial. Comparison of ABVD and alternating or hybrid multidrug regimens for the treatment of advanced Hodgkin's lymphoma: results of the United Kingdom Lymphoma Group LY09 Trial J Clin Oncol. 2005 Dec 20;23(36):9208-1

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