

Chemotherapy Protocol

LYMPHOMA

BRENTUXIMAB VEDOTIN

This protocol may require funding

Regimen

- Lymphoma – Brentuximab vedotin

Indication

- Hodgkin's lymphoma
- Systemic anaplastic large cell lymphoma
- CD30 positive T cell lymphoma

Toxicity

Drug	Adverse Effect
Brentuximab vedotin	Peripheral sensory neuropathy, cough, diarrhoea, infusion related reactions, upper respiratory tract infections, progressive multifocal leukoencephalopathy

Patients with Hodgkin's lymphoma carry a lifelong risk of transfusion associated graft versus host disease (TA-GVHD). Where blood products are required these patients must receive only irradiated blood products for life. Local blood transfusion departments must be notified as soon as a diagnosis is made and the patient must be issued with an alert card to carry with them at all times.

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

Monitoring

Drugs

- FBC, LFTs and U&Es prior to day one of treatment

Dose Modifications

The dose modifications listed are for haematological, liver and renal function and some drug specific toxicities only. Dose adjustments may be necessary for other toxicities as well.

In principle all dose reductions due to adverse drug reactions should not be re-escalated in subsequent cycles without consultant approval. It is also a general rule for chemotherapy that if a third dose reduction is necessary treatment should be stopped.

Please discuss all dose reductions / delays with the relevant consultant before prescribing, if appropriate. The approach may be different depending on the clinical circumstances.

Haematological

Dose modifications for haematological toxicity in the table below are for general guidance only. Always refer to the responsible consultant as any dose reductions or delays will be dependent on clinical circumstances and treatment intent. Low counts can be a consequence of bone marrow infiltration as well as drug toxicity.

Consider blood transfusion if patient symptomatic of anaemia or has a haemoglobin of less than 8g/dL. **Irradiated blood products must be used in Hodgkin's Lymphoma patients.**

Neutrophils (x10 ⁹ /L)	Dose Modifications
1 or greater	100%
Less than 1	1 st occurrence Delay until recovery to 1x10 ⁹ /L or above then continue at full dose. Consider growth factor support for all subsequent cycles. 2 nd occurrence Delay until recovery to 1x10 ⁹ /L or above then continue at a dose of 1.2mg/kg with growth factor support or discontinue as appropriate.
Platelets (x10 ⁹ /L)	Dose Modifications
50 or greater	100%
Less than 50	1 st occurrence Delay until recovery to 50x10 ⁹ /L or above then continue at full dose. 2 nd occurrence Delay until recovery to 50x10 ⁹ /L or above then continue at a dose of 1.2mg/kg or discontinue as appropriate.

Hepatic Impairment

Please note that the approach may be different where abnormal liver function tests are due to disease involvement.

Drug	Child Pugh Score	Dose (% of original dose)
Brentuximab vedotin	A, B or C	The recommended starting dose in patients with hepatic impairment is 1.2 mg/kg. Patients with hepatic impairment should be closely monitored for adverse events

Renal Impairment

Drug	Creatinine Clearance (ml/min)	Dose (% of original dose)
Brentuximab vedotin	<30	The recommended starting dose in patients with severe renal impairment is 1.2 mg/kg. Patients with renal impairment should be closely monitored for adverse events

Other

Dose reductions or interruptions in therapy are not necessary for those toxicities that are considered unlikely to be serious or life threatening. For example, alopecia, altered taste or nail changes.

Skin

Cases of Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis have been reported in patients who received brentuximab vedotin. If patients experience any skin reactions during treatment, they should be monitored closely and, in the case of any suspicion of the skin reaction evolving to a serious muco-cutaneous reaction, treatment with brentuximab vedotin should be withheld until complete resolution of the event or discontinued. Other potential causes of skin toxicity should be evaluated and suspected agents discontinued accordingly.

Lung

The concomitant use of bleomycin is contra-indicated because of the increased risk of pulmonary toxicity

Peripheral Neuropathy

For new or worsening NCI-CTC grade 2 or 3 peripheral neuropathy delay brentuximab until symptoms have resolved to grade 1 or baseline and restart at 1.2mg/kg. For grade 4 peripheral neuropathy discontinue brentuximab vedotin.

Infusion reactions

Infusion related adverse reactions, including anaphylaxis, have been observed in patients treated with brentuximab vedotin.

If anaphylaxis occurs, immediately and permanently discontinue brentuximab vedotin and administer appropriate medical therapy.

For other infusion related reactions including chills, nausea, dyspnoea, pruritus, pyrexia and cough interrupt the infusion and institute appropriate medical management.

Give pre-medication consisting of chlorphenamine, hydrocortisone and paracetamol for all subsequent infusions.

Progressive multifocal leukoencephalopathy

Use of brentuximab vedotin has been associated with an increased risk of progressive multifocal leukoencephalopathy (PML). Patients must be monitored at regular intervals for any new or worsening neurological, cognitive or psychiatric symptoms that may be suggestive of PML. If PML is suspected, further dosing must be suspended until PML has been excluded. If PML is confirmed the brentuximab must be permanently discontinued.

Regimen

21 day cycle for up to 16 cycles (8 cycles will be set in Aria)

Drug	Dose	Days	Administration
Brentuximab vedotin	1.8mg/kg (max 180mg)	1	Intravenous infusion in 250ml sodium chloride 0.9% over 30 minutes

[Dose Information](#)

- Brentuximab vedotin will be dose banded according to the national dose bands 50mg/10ml)
- The dose of brentuximab vedotin will be capped at 180mg

[Administration Information](#)

Extravasation

- Brentuximab vedotin - neutral

Other

- Brentuximab doses below 100mg should be diluted in 100ml sodium chloride 0.9%.

[Additional Therapy](#)

- When required for the treatment of brentuximab vedotin infusion related reactions
 - chlorphenamine 10mg intravenous
 - hydrocortisone 100mg intravenous
 - paracetamol 1000mg oral
- When required for the relief of brentuximab vedotin related bronchospasm
 - salbutamol 2.5mg nebule
- Allopurinol 300mg once a day oral for cycle 1 only
- Loperamide 4mg initially then 2mg after each loose stool when required for diarrhoea.
- Mouthwashes according to local or national policy on the treatment of mucositis
- Gastric protection with a proton pump inhibitor or a H₂ antagonist may be considered in patients considered at high risk of GI ulceration or bleed.

[Additional Information](#)

- Brentuximab is metabolised by CYP3A isoenzyme. Always check for interactions

[Coding \(OPCS 4.6\)](#)

- Procurement – X71.5
- Delivery – X72.3

[References](#)

1. Adcetris prescribing information. Seattle Genetics Inc. January 2012
2. Pro B, Advani R, Brice P et al. Brentuximab Vedotin (SGN-35) in Patients With Relapsed or Refractory Systemic Anaplastic Large-Cell Lymphoma: Results of a Phase II Study. JCO (2012); 30 (18): 2190-2196
3. Younes A, Gopal A, Smith S et al. Results of a Pivotal Phase II Study of Brentuximab Vedotin for Patients With Relapsed or Refractory Hodgkin's Lymphoma. JCO (2012); 30 (18): 2183-2189

REGIMEN SUMMARY

Brentuximab vedotin

Cycle 1 Day 1

1. **Warning –Check blood transfusion status**
Administration Instructions
Patients with HODGKIN'S lymphoma carry a lifelong risk of transfusion associated graft versus host disease. Where blood products are required these patients must receive ONLY IRRADIATED BLOOD PRODUCTS for life. Ensure transfusion departments are notified and the patient has been issued with an alert card to carry with them at all times.
2. Brentuximab vedotin 1.8mg/kg (max 180mg) intravenous infusion in 250ml sodium chloride 0.9% over 30 minutes
3. Chlorphenamine 10mg intravenous when required for the treatment of brentuximab vedotin infusion related reactions
4. Hydrocortisone 100mg intravenous when required for the treatment of brentuximab vedotin infusion related reactions
5. Paracetamol 1000mg oral when required for the treatment of brentuximab vedotin infusion related reactions
Administration Instructions
Please check if the patient has taken paracetamol. The maximum dose is 4g/24hours
6. Salbutamol 2.5mg nebule when required for the relief of brentuximab vedotin related bronchospasm

Take home medicines

7. Allopurinol 300mg once a day oral for 21 days

Cycles 2, 3, 4, 5, 6, 7 and 8 Day 1

1. Brentuximab vedotin 1.8mg/kg (max 180mg) intravenous infusion in 250ml sodium chloride 0.9% over 30 minutes
2. Chlorphenamine 10mg intravenous when required for the treatment of brentuximab vedotin infusion related reactions
3. Hydrocortisone 100mg intravenous when required for the treatment of brentuximab vedotin infusion related reactions
4. Paracetamol 1000mg oral when required for the treatment of brentuximab vedotin infusion related reactions
Administration Instructions
Please check if the patient has taken paracetamol. The maximum dose is 4g/24hours
5. Salbutamol 2.5mg nebule when required for the relief of brentuximab vedotin related bronchospasm

DOCUMENT CONTROL

Version	Date	Amendment	Written By	Approved By
1.3	Aug 2018	Dose adjusted according to national dose bands Administration instructions added to paracetamol	Donna Kimber Pharmacy Technician	Dr Deborah Wright Pharmacist
1.2	Jan 2015	Header changed Hepatic and renal impairment tables updated Bolus removed from intravenous bolus throughout text Irradiated blood product statement updated in dose modification section. Mucositis recommendation changed OPCS code updated "Warning-Check blood transfusion status" added to cycle 1. Disclaimer added	Donna Kimber Pharmacy Technician	Rebecca Wills Pharmacist
1.1	Feb 2013	Volume of administration changed to 250ml in regimen and regimen summary. "Brentuximab vedotin doses below 100mg should be diluted in 100ml sodium chloride 0.9%." added to administration information. "prevention or" removed from chlorphenamine, hydrocortisone and paracetamol entries	Rebecca Wills Pharmacist	Dr Deborah Wright Pharmacist
1	July 2012	None	Rebecca Wills Pharmacist Dr Deborah Wright Pharmacist	Dr Andrew Davies Consultant Medical Oncologist Dr Alison Milne Consultant Haematologist

This chemotherapy protocol has been developed as part of the chemotherapy electronic prescribing project. This was and remains a collaborative project that originated from the former CSCCN. These documents have been approved on behalf of the following Trusts;

Hampshire Hospitals NHS Foundation Trust
 NHS Isle of Wight
 Portsmouth Hospitals NHS Trust
 Salisbury Hospitals NHS Foundation Trust
 University Hospital Southampton NHS Foundation Trust
 Western Sussex Hospitals NHS Foundation Trust

All actions have been taken to ensure these protocols are correct. However, no responsibility can be taken for errors which occur as a result of following these guidelines.