Chemotherapy Protocol

LYMPHOMA

BRENTUXIMAB VEDOTIN-DACARBAZINE-DOXORUBICIN-VINBLASTINE

(B- AVD)

Regimen

- Lymphoma – Brentuximab vedotin - Dacarbazine-Doxorubicin-Vinblastine

Indication

- Previously untreated stage III or IV CD30 positive Hodgkins lymphoma in adult patients

Toxicity

Drug	Adverse Effect
Brentuximab vedotin	Peripheral sensory neuropathy, cough, diarrhoea, infusion related reactions, upper respiratory tract infections, progressive multifocal leukoencephalopathy
Dacarbazine	Fatigue, facial flushing, rash, flu-like syndrome, photosensitivity
Doxorubicin	Cardiotoxicity, urinary discolouration (red)
Vinblastine	Peripheral neuropathy, constipation, jaw pain, ileus

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

Patients diagnosed 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.

Monitoring

Drugs

- FBC, LFTs and U&Es prior to day one and fifteen of treatment
- Ensure adequate cardiac function before starting therapy. Baseline LVEF should be measured in patients with a history of cardiac problems, cardiac risk factors or in the elderly. Discontinue doxorubicin if cardiac failure develops.

Dose Modifications

The dose modifications listed are for haematological, liver and renal function and some limited 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

Deliver on time and at full dose regardless of haematological counts unless there is an overriding clinical reason not to do so. Any dose modifications or delays must be discussed and approved by the responsible consultant.

Prophylactic filgrastim was not mandated on the Echelon-1 clinical trial but should be considered in patients felt to be at higher risk of febrile neutropenia, at the discretion of the treating clinician.

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.**

Hepatic Impairment

If abnormal liver function tests are lymphoma related proceed with treatment at full dose unless there is an overriding clinical reason not to do so.

Drug	Bilirubin µmol/L		AST/ALT units/L	Dose (% of original dose)
Brentuximab vedotin	Child Pugh score A,B or C			The recommended starting dose in patients with hepatic impairment is 0.9 mg/kg. Patients with hepatic impairment should be closely monitored for adverse events
Dacarbazine				Activated and metabolised in the liver. Can be hepatotoxic. Consider dose reduction or omission in severe hepatic impairment
Doxorubicin	less than *30	and	2-3xULN	75%
	*22-50	and/or	more than 3xULN	50%
	51-86		N/A	25%
	more than 86 or Child-Pugh C		N/A	Omit
Vinblastine	*22-51			75%
	more than 51			50%

* Limits reflect local practice and may vary from published sources

Renal Impairment

Drug	Creatinine Clearance (ml/min)	Dose (% of original dose)
Brentuximab vedotin	<30mL/min	The recommended starting dose in patients with severe renal impairment is 0.9 mg/kg. Patients with renal impairment should be closely monitored for adverse events
Dacarbazine	45-60	80%
	30-44	75%
	less than 30	70%
Doxorubicin	less than10	Consider dose reduction in severe renal failure
Vinblastine	N/A	No dose adjustment needed

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.

Brentuximab vedotin

Brentuximab vedotin can cause peripheral sensor or motor neuropathy, if a NCI-CTC grade 2 occurs reduce Brentuximab vedotin dose to 0.9mg/kg up to a maximum of 90mg every two weeks. If grade 3 occurs then withhold Brentuximab vedotin until toxicity is at grade 2 then reduce Brentuximab vedotin dose to 0.9mg/kg up to a maximum of 90mg every two weeks

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.

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 vedotin must be permanently discontinued

Doxorubicin

Discontinue doxorubicin if cardiac failure develops.

Vinblastine

Reduce the vinblastine dose to 3mg/m^2 if a NCI-CTC grade 2 motor or a NCI-CTC grade 3 sensory neurological toxicity occurs. For higher toxicity grades or if toxicity increases despite dose reduction stop the vinblastine.

Regimen

28 day cycle

6 cycles will be set in Aria

Drug	Dose	Days	Administration
Dacarbazine	375mg/m^2	1 & 15	Intravenous infusion in 500ml sodium chloride 0.9% over 60 minutes
Doxorubicin	25mg/m^2	1 & 15	Intravenous bolus over 10 minutes
Vinblastine	6mg/m^2	1 & 15	Intravenous bolus in 50ml sodium chloride 0.9% over 10 minutes
Brentuximab vedotin	1.2mg/kg (max 120mg)	1 & 15	In 100 mL sodium chloride 0.9% over 30 minutes. Must be administered after completion of AVD, starting approximately 1 hour after the end of dacarbazine infusion.

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 120mg
- Dacarbazine will dose banded according to national dose bands
- Doxorubicin will dose banded according to the national dose bands
- The maximum lifetime cumulative dose of doxorubicin is 450mg/m². However prior radiotherapy to mediastinal / pericardial area should receive a lifetime cumulative doxorubicin dose of no more than 400mg/m².
- Vinblastine dose will be rounded to the nearest 1mg (up if halfway)
- There is no maximum dose of vinblastine in this protocol

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Administration Information

Extravasation

- Brentuximab vedotin - neutral
- Dacarbazine – vesicant
- Doxorubicin - vesicant
- Vinblastine - vesicant

Other

- Dacarbazine can cause considerable pain at the infusion site. This may be helped by adjusting the infusion time or infusion volume and protecting the infusion from light.

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

- Loperamide 4mg initially then 2mg after each loose stool when required for diarrhoea.

- Antiemetics

  15-30 minutes prior to chemotherapy

    - Aprepitant 125mg D1 and D15
    - dexamethasone 8mg oral or equivalent intravenous dose
    - ondansetron 8mg oral or intravenous

  As take home medication

    - Aprepitant 80mg D2 and D3, D16 and 17
    - domperidone 10mg three times a day when required oral
    - ondansetron 8mg twice a day for three days oral

- Anti-infective prophylaxis as follows:

    - co-trimoxazole 960mg once a day on Monday, Wednesday and Friday only
    - aciclovir 400mg TWICE a day

Co-trimoxazole and Aciclovir should continue for three months after final dose of BV-AVD

- Allopurinol 300mg once a day oral for the first cycle only

- Mouthwashes according to local or national policy on the treatment of mucositis

- Gastric protection with a proton pump inhibitor or a H_2 antagonist may be considered in patients considered at high risk of GI ulceration or bleed.

- Growth factors may be considered at the discretion of the treating clinician

Additional Information

- The National Patient Safety Agency report NPSA/2008/RRR04 must be followed in relation to intravenous administration of vinca alkaloids.

References
1. Ansell SM, Straus DJ, Connors JM, Jurczak W, Kim WS, Gallamini A, Ramchandren R, Friedberg JW, Advani RH, Hutchings M, Evens AM. Seven-year overall survival analysis from ECHELON-1 study of A plus AVD versus ABVD in patients with previously untreated stage III/IV classical Hodgkin lymphoma. JCO 2024 Jun 1;42(16).
2. Ansell SM, Radford J, Connors JM, Długosz-Danecka M, Kim WS, Gallamini A, Ramchandren R, Friedberg JW, Advani R, Hutchings M, Evens AM. Overall survival with Brentuximab vedotin vedotin in stage III or IV Hodgkin's lymphoma. New England Journal of Medicine. 2022 Jul 28;387(4):310-20.
3. NICE. Brentuximab vedotin vedotin in combination for untreated stage 3 or 4 CD30-positive Hodgkin lymphoma [TA1059]. Technology appraisal guidance. Published 7 May 2025. Last updated 7 May 2025. Available at https://www.nice.org.uk/guidance/ta1059
4. Takeda UK Ltd. Adcetris® (Brentuximab vedotin vedotin) 50 mg powder for concentrate for solution for infusion. Summary of Product Characteristics (SmPCs). Last updated 20/03/2025. Available online at https://www.medicines.org.uk/emc/
5. Medac GmbH. Doxorubicin hydrochloride 2mg/ml solution for infusion. Summary of Product Characteristics (SmPC). Last updated 05/09/2024. Available at https://www.medicines.org.uk/emc/
6. Hospira UK Ltd. Vinblastine Sulfate 1 mg/ml solution for injection. Summary of Product Characteristics (SmPC). Last updated 29/08/2024. Available at https://www.medicines.org.uk/emc/
7. Medac GmbH. Dacarbazine 100 mg powder for solution for injection/infusion. Summary of Product Characteristics (SmPC). Last updated 18/01/2024. Available at https://www.medicines.org.uk/emc/ 8. Giraud EL, de Lijster B, Krens SD, Desar IME, Boerrigter E, van Erp NP. Dose recommendations for anticancer drugs in patients with renal or hepatic impairment: an update. Lancet Oncol 2023; 24: e229

REGIMEN SUMMARY

B-AVD – Brentuximab vedotin-Dacarbazine-Doxorubicin-Vinblastine

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. Aprepitant 125mg oral

3. Dexamethasone 4mg oral or equivalent intravenous dose

4. Ondansetron 8mg oral or intravenous

5. Dacarbazine 375mg/m^2 intravenous infusion in 500ml sodium chloride 0.9% over 60 minutes

6. Doxorubicin 25mg/m^2 intravenous bolus over 10 minutes

7. Vinblastine 6mg/m^2 intravenous bolus in 50ml sodium chloride 0.9% over 10 minutes

8. Brentuximab vedotin 1.2mg/kg intravenous infusion in 100mL Sodium Chloride 0.9% over 30 minutes
   Administration instruction
   Must be administered after completion of AVD, starting approximately 1 hour after the end of dacarbazine infusion

9. Hydrocortisone 100mg intravenous once only when required for the relief of brentuximab vedotin infusion related reactions

10. Salbutamol 2.5mg nebule once only when required for the relief of brentuximab vedotin related bronchospasm

11. 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

Take Home Medicines

12. Aprepitant 80mg oral once a day on days 2,3, 16 and 17

13. Dexamethasone 4mg once a day on days 2,3 16 and 17

14. Domperidone 10mg three times a day when required oral
    Administration Instructions
    Please supply sufficient for day 1 and 15 (30 tablets or nearest whole pack equivalent)

15. Ondansetron 8mg twice a day oral for 3 days to start on the evening of the day of chemotherapy administration (day 1 and 15)
    Administration Instructions
    Please supply sufficient for day 1 and 15 (12 tablets or nearest whole pack equivalent)

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

17. Aciclovir 400mg twice a day oral for 28 days

18. Co-trimoxazole 960mg once a day on Monday, Wednesday and Friday oral for 28 days

Cycle 1 Day 15

19. Aprepitant 125mg

20. Dexamethasone 4mg oral or equivalent intravenous dose

21. Ondansetron 8mg oral or intravenous

22. Dacarbazine 375mg/m^2 intravenous infusion in 500ml sodium chloride 0.9% over 60 minutes

23. Doxorubicin 25mg/m^2 intravenous bolus over 10 minutes

24. Vinblastine 6mg/m^2 intravenous bolus in 50ml sodium chloride 0.9% over 10 minutes

25. Brentuximab vedotin 1.2mg/kg intravenous infusion in 100mL Sodium Chloride 0.9% over 30 minutes
    Administration instruction
    Must be administered after completion of AVD, starting approximately 1 hour after the end of dacarbazine infusion

26. Hydrocortisone 100mg intravenous once only when required for the relief of brentuximab vedotin infusion related reactions

27. Salbutamol 2.5mg nebule once only when required for the relief of brentuximab vedotin related bronchospasm

28. 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

Cycle 2 - 6

Day 1

29. 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.

30. Aprepitant 125mg oral

31. Dexamethasone 4mg oral or equivalent intravenous dose

32. Ondansetron 8mg oral or intravenous

33. Dacarbazine 375mg/m^2 intravenous infusion in 500ml sodium chloride 0.9% over 60 minutes

34. Doxorubicin 25mg/m^2 intravenous bolus over 10 minutes

35. Vinblastine 6mg/m^2 intravenous bolus in 50ml sodium chloride 0.9% over 10 minutes

36. Brentuximab vedotin 1.2mg/kg intravenous infusion in 100mL Sodium Chloride 0.9% over 30 minutes
    Administration instruction
    Must be administered after completion of AVD, starting approximately 1 hour after the end of dacarbazine infusion

37. Hydrocortisone 100mg intravenous once only when required for the relief of brentuximab vedotin infusion related reactions

38. Salbutamol 2.5mg nebule once only when required for the relief of brentuximab vedotin related bronchospasm

39. 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

Take Home Medicines

40. Aprepitant 80mg oral on days 2,3, 16 and 17

41. Dexamethasone 4mg on days 2,3 16 and 17

42. Domperidone 10mg three times a day when required oral
    Administration Instructions
    Please supply sufficient for day 1 and 15 (30 tablets or nearest whole pack equivalent)

43. Ondansetron 8mg twice a day oral for 3 days to start on the evening of the day of chemotherapy administration (day 1 and 15)
    Administration Instructions
    Please supply sufficient for day 1 and 15 (12 tablets or nearest whole pack equivalent)

44. Aciclovir 400mg twice a day oral for 28 days

45. Co-trimoxazole 960mg once a day on Monday, Wednesday and Friday oral for 28 days

Cycle 2 - 6

Day 15

46. Aprepitant 125mg

47. Dexamethasone 4mg oral or equivalent intravenous dose

48. Ondansetron 8mg oral or intravenous

49. Dacarbazine 375mg/m^2 intravenous infusion in 500ml sodium chloride 0.9% over 60 minutes

50. Doxorubicin 25mg/m^2 intravenous bolus over 10 minutes

51. Vinblastine 6mg/m^2 intravenous bolus in 50ml sodium chloride 0.9% over 10 minutes

52. Brentuximab vedotin 1.2mg/kg intravenous infusion in 100mL Sodium Chloride 0.9% over 30 minutes
    Administration instruction
    Must be administered after completion of AVD, starting approximately 1 hour after the end of dacarbazine infusion

53. Hydrocortisone 100mg intravenous once only when required for the relief of brentuximab vedotin infusion related reactions

54. Salbutamol 2.5mg nebule once only when required for the relief of brentuximab vedotin related bronchospasm

55. 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

DOCUMENT CONTROL

Version	Date	Amendment	Written By	Approved By
1	June 2025	New regimen	Nanda Basker Pharmacist	Robert Lown Consultant

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.