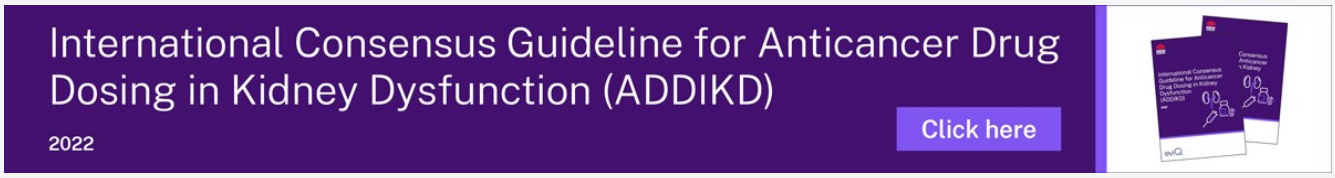
Hodgkin lymphoma ABVD (DOXOrubicin bleomycin vinBLASTine dacarbazine) advanced stage

ID: 56 v.6 **Endorsed** Essential Medicine List

Patients with lymphoma should be considered for inclusion into clinical trials. Link to ALLG website, ANZCTR website and Lymphoma Australia website.

The anticancer drug(s) in this protocol may have been included in the ADDIKD guideline. Dose recommendations in kidney dysfunction have yet to be updated to align with the ADDIKD guideline. Recommendations will be updated once the individual protocol has been evaluated by the reference committee. For further information refer to the ADDIKD guideline. To assist with calculations, use the eviQ Estimated Glomerular Filtration Rate (eGFR) calculator.



Related pages:

- Hodgkin lymphoma ABVD (DOXOrubicin bleomycin vinBLASTine dacarbazine) early stage
- Hodgkin lymphoma advanced-stage EBRT to involved sites

Treatment schedule - Overview

Cycle 1 to 6

Drug	Dose	Route	Day
DOXOrubicin	25 mg/m^2	IV	1 and 15
vinBLASTine	6 mg/m^2	IV	1 and 15
Dacarbazine	375 mg/m^2	IV infusion	1 and 15
Bleomycin	10,000 International Units/m^2	IV	1 and 15

Frequency: 28 days

Cycles: 6. Unless disease progression or unacceptable toxicity.

Notes:

- Do not delay treatment, irrespective of blood count as keeping to the protocol schedule and maintaining dose intensity is very important for treatment outcome.[1]
- DOSE EQUIVALENCE: 1,500 International Units of bleomycin are equivalent to 1.5 USP units and approximately equivalent to 1.5 mg (by potency) or 1 mg (by weight).[2]
- Protocols that give bleomycin in mg or mg/m^2 refer to mg potency **not** mg weight.[3]
- Growth factor support is not routinely required unless there are treatment delays (due to sepsis etc.), because it may increase the risk of bleomycin induced pulmonary toxicity. Monitor patients closely for signs of pulmonary toxicity if the combination is used.[4]
- Bleomycin can be omitted in patients who are PET 2 negative (at the discretion of the treating physician).[5]
- There is an increased risk of bleomycin toxicity in patients > 60yrs of age and careful monitoring and early cessation should be considered for this group.

Drug status: **Doxorubicin, bleomycin** and **vinblastine** are on the PBS general schedule

Dacarbazine is not TGA approved or PBS reimbursed.

eviQ are aware that there is a mismatch between dacarbazine product information and clinical use. Dacarbazine has an established place in the management of Hodgkin lymphoma.

Cost: ~ $460 per cycle, excluding dacarbazine.

Treatment schedule - Detail

The supportive therapies (e.g. antiemetics, premedications, etc.), infusion times, diluents, volumes and routes of administration, if included, are listed as defaults. They may vary between institutions and can be substituted to reflect individual institutional policy.

*Antiemetics if included in the treatment schedule are based upon recommendations from national and international guidelines. These are **defaults only** and may be substituted to reflect individual institutional policy. Select here for **recommended doses of alternative antiemetics**.*

Cycle 1 to 6

Day 1		
Netupitant	300 mg (PO)	60 minutes before chemotherapy (fixed dose preparation with palonosetron)
Palonosetron	0.5 mg (PO)	60 minutes before chemotherapy (fixed dose preparation with netupitant)
Dexamethasone	12 mg (PO)	60 minutes before chemotherapy
DOXOrubicin	25 mg/m^2 (IV)	over 5 to 15 minutes
vinBLASTine	6 mg/m^2 (IV)	in 50 mL sodium chloride 0.9% over 5 to 10 minutes
Dacarbazine	375 mg/m^2 (IV infusion)	in 500 mL sodium chloride 0.9% over 60 minutes
Bleomycin	10,000 International Units/m^2 (IV)	in 5 mL to 10 mL sodium chloride 0.9% over 10 minutes

Day 2 to 4		
Dexamethasone	8 mg (PO)	ONCE a day with or after food (or in divided doses). Note: dexamethasone 8mg doses may not be required and may be reduced or omitted at the clinician's discretion. *

Day 15		
Netupitant	300 mg (PO)	60 minutes before chemotherapy (fixed dose preparation with palonosetron)
Palonosetron	0.5 mg (PO)	60 minutes before chemotherapy (fixed dose preparation with netupitant)
Dexamethasone	12 mg (PO)	60 minutes before chemotherapy
DOXOrubicin	25 mg/m^2 (IV)	over 5 to 15 minutes
vinBLASTine	6 mg/m^2 (IV)	in 50 mL sodium chloride 0.9% over 5 to 10 minutes
Dacarbazine	375 mg/m^2 (IV infusion)	in 500 mL sodium chloride 0.9% over 60 minutes
Bleomycin	10,000 International Units/m^2 (IV)	in 5 mL to 10 mL sodium chloride 0.9% over 10 minutes

Day 16 to 18		
Dexamethasone	8 mg (PO)	ONCE a day with or after food (or in divided doses). Note: dexamethasone 8mg doses may not be required and may be reduced or omitted at the clinician's discretion. *

* Link to ID 7 Prevention of chemotherapy induced nausea and vomiting.

Notes:

- Do not delay treatment, irrespective of blood count as keeping to the protocol schedule and maintaining dose intensity is very important for treatment outcome.[1]
- DOSE EQUIVALENCE: 1,500 International Units of bleomycin are equivalent to 1.5 USP units and approximately equivalent to 1.5 mg (by potency) or 1 mg (by weight).[2]
- Protocols that give bleomycin in mg or mg/m^2 refer to mg potency **not** mg weight.[3]
- Growth factor support is not routinely required unless there are treatment delays (due to sepsis etc.), because it may increase the risk of bleomycin induced pulmonary toxicity. Monitor patients closely for signs of pulmonary toxicity if the combination is used.[4]
- Bleomycin can be omitted in patients who are PET 2 negative (at the discretion of the treating physician).[5]
- There is an increased risk of bleomycin toxicity in patients > 60yrs of age and careful monitoring and early cessation should be considered for this group.

Frequency: 28 days

Cycles: 6. Unless disease progression or unacceptable toxicity.

Indications and patient population

- Hodgkin lymphoma Stage IIb to Stage IV
  - Link to Lugano classification adapted from the Ann Arbor staging system with Cotswolds modifications
  - Link to International Prognostic Score (IPS)

Clinical information

Venous access required	IV cannula (IVC) or central venous access device (CVAD) is required to administer this treatment. Read more about central venous access device line selection
Hypersensitivity/infusion related reaction	High risk with bleomycin. Note: a hypersensitivity reaction can occur with any dose of bleomycin, regardless of whether a test dose has been performed. The manufacturer recommends a test dose of bleomycin 1,000 to 5,000 International Units prior to the first and second bleomycin doses in all lymphoma patients. Read more about Hypersensitivity reaction
Premedication	A corticosteroid may reduce severity of fever/chills related to bleomycin (note: dexamethasone/prednisolone is included as an antiemetic in this protocol); paracetamol may be used to reduce fever.
Emetogenicity HIGH	Suggested default antiemetics have been added to the treatment schedule, and may be substituted to reflect institutional policy. Ensure that patients also have sufficient antiemetics for breakthrough emesis: Metoclopramide 10 mg three times a day when necessary (maximum of 30 mg/24 hours, up to 5 days) OR Prochlorperazine 10 mg PO every 6 hours when necessary. Read more about preventing anti-cancer therapy induced nausea and vomiting

Cumulative lifetime dose of anthracyclines	Cumulative doses should take into account all previous anthracyclines received during a patient's lifetime (i.e. daunorubicin, doxorubicin, epirubicin, idarubicin and mitoxantrone). Criteria for reducing the total anthracycline cumulative lifetime dose include: • patient is elderly • prior mediastinal radiation • hypertensive cardiomegaly • concurrent therapy with high dose cyclophosphamide and some other cytotoxic drugs (e.g. bleomycin, dacarbazine, dactinomycin, etoposide, melphalan, mitomycin and vincristine). Baseline clinical assessments include echocardiogram (ECHO) or gated heart pool scan (GHPS) and electrocardiogram (ECG) evaluation. Patients with normal baseline cardiac function (left ventricular ejection fraction (LVEF) > 50%) and low risk patients require LVEF monitoring when greater than 70% of the anthracycline threshold is reached or if the patient displays symptoms of cardiac impairment. Post-treatment cardiac monitoring is recommended for patients who have received high levels of total cumulative doses of anthracyclines at the clinician's discretion. Read more about cardiac toxicity associated with anthracyclines
Pulmonary toxicity	Bleomycin has been associated with severe and life threatening respiratory complications. The total cumulative dose of bleomycin should NOT exceed 400,000 international units. The risk of pulmonary toxicity increases beyond a cumulative dose of 300,000 international units. Check the cumulative dose prior to each treatment. The approach to pulmonary screening with bleomycin is variable and inconsistent. The Haematology Reference Committee recommends baseline pulmonary function assessment, then monitor as clinically appropriate. Bleomycin should be stopped if there is clinical evidence of pulmonary toxicity (cough, dyspnoea, basal crepitation) or when the diffusing capacity for carbon monoxide (DLCO) is less than 30 to 35% of the pre-treatment value. Read more about pulmonary toxicity associated with anti-cancer drugs.
Growth factor support	Growth factor support is not routinely required unless there are treatment delays (due to sepsis etc.), because it may increase the risk of bleomycin induced pulmonary toxicity. Monitor patients closely for signs of pulmonary toxicity if the combination is used. G-CSF (short or long acting) is available on the PBS for chemotherapy induced neutropenia depending on patient factors and/or neutropenia risk. Access the PBS website
Peripheral neuropathy	Assess prior to each treatment. If a patient experiences grade 2 or greater peripheral neuropathy, a dose reduction, delay, or omission of treatment may be required; review by medical officer before commencing treatment. Read more about peripheral neuropathy Link to chemotherapy-induced peripheral neuropathy screening tool
Constipation	Prescribe prophylactic laxatives to prevent constipation related to the use of vinca alkaloids.
Tumour lysis risk	Assess patient for risk of developing tumour lysis syndrome. Read more about prevention and management of tumour lysis syndrome.
Pneumocystis jirovecii pneumonia (PJP) prophylaxis	Read more about prophylaxis of pneumocystis jiroveci (carinii) in cancer patients
Antiviral prophylaxis	Read more about antiviral prophylaxis drugs and doses
Irradiated blood components	The use of irradiated of blood components is recommended for patients receiving this treatment. Read more about the indications for the use of irradiated blood components
Blood tests	FBC, EUC, eGFR, calcium, magnesium, phosphate, LDH and LFTs at baseline, and prior to each treatment or as clinically indicated.

Hepatitis B screening and prophylaxis	Routine screening for HBsAg and anti-HBc is recommended prior to initiation of treatment. Prophylaxis should be determined according to individual institutional policy. Read more about hepatitis B screening and prophylaxis in cancer patients requiring cytotoxic and/or immunosuppressive therapy
Vaccinations	Live vaccines are contraindicated in cancer patients receiving immunosuppressive therapy and/or who have poorly controlled malignant disease. Refer to the recommended schedule of vaccination for immunocompromised patients, as outlined in the Australian Immunisation Handbook. Read more about COVID-19 vaccines and cancer.
Fertility, pregnancy and lactation	Cancer treatment can have harmful effects on fertility and this should be discussed with all patients of reproductive potential prior to commencing treatment. There is a risk of foetal harm in pregnant women. A pregnancy test should be considered prior to initiating treatment in females of reproductive potential if sexually active. It is important that all patients of reproductive potential use effective contraception whilst on therapy and after treatment finishes. Effective contraception methods and adequate contraception timeframe should be discussed with all patients of reproductive potential. Possibility of infant risk should be discussed with breastfeeding patients. Read more about the effect of cancer treatment on fertility

Dose modifications

Evidence for dose modifications is limited, and the recommendations made on eviQ are intended as a guide only. They are generally conservative with an emphasis on safety. Any dose modification should be based on clinical judgement, and the individual patient's situation including but not limited to treatment intent (curative vs palliative), the anti-cancer regimen (single versus combination therapy versus chemotherapy versus immunotherapy), biology of the cancer (site, size, mutations, metastases), other treatment related side effects, additional co-morbidities, performance status and patient preferences.Suggested dose modifications are based on clinical trial findings, product information, published guidelines and reference committee consensus . The dose reduction applies to each individual dose and not to the total number of days or duration of treatment cycle unless stated otherwise. Non-haematological gradings are based on Common Terminology Criteria for Adverse Events (CTCAE) unless otherwise specified. Renal and hepatic dose modifications have been standardised where possible. For more information see dosing considerations & disclaimer .

The dose recommendations in kidney dysfunction (i.e.renal impairment) displayed may not reflect those in the ADDIKD guideline and have been included for historical reference only. Recommendations will be updated once the individual protocol has been evaluated by the reference committee, with this version of the protocol then being archived. Clinicians are expected to refer to the ADDIKD guideline prior to prescribing in kidney dysfunction.
International Consensus Guideline for Anticancer Drug Dosing in Kidney Dysfunction (ADDIKD).

Note: All dose reductions are calculated as a percentage of the starting dose

Haematological toxicity	
ANC x 10^9/L (pre-treatment blood test)	
0.5 to less than 1.0	Grade 3 to 4 haematological toxicity or sepsis is not an indication for dose reduction. Keeping to the protocol schedule and maintaining dose intensity is very important for treatment outcome. Growth factor support is not routinely required unless there are treatment delays due to sepsis etc., only then consider support with G-CSF for subsequent cycles.
less than 0.5	

Renal impairment	
Creatinine clearance (mL/min)	

Renal impairment	
30 to 50	Reduce bleomycin by 25%
less than 30	Consider omitting bleomycin

Hepatic impairment	
Hepatic dysfunction	
Mild	Reduce doxorubicin and vinblastine by 25%
Moderate	Reduce doxorubicin and vinblastine by 50% : dose reduction of dacarbazine may be required
Severe	Omit doxorubicin, vinblastine and dacarbazine

Pulmonary toxicity
Bleomycin should be stopped if there is clinical evidence of pulmonary toxicity (cough, dyspnoea, basal crepitation) or when the DLCO is less than 30 to 35% of the pre-treatment value

Peripheral neuropathy	
Grade 2 or more which is present at the start of the next cycle	Dose reduce or omit vinblastine

Interactions

The drug interactions shown below are not an exhaustive list. For a more comprehensive list and for detailed information on specific drug interactions and clinical management, please refer to the specific drug product information and the following key resources:

- *MIMS - interactions tab (includes link to a CYP-450 table) (login required)*
- *Australian Medicines Handbook (AMH) – interactions tab (login required)*
- *Micromedex Drug Interactions (login required)*
- *Cancer Drug Interactions*
- *Cytochrome P450 Drug Interactions*

For more information see References & Disclaimer .

Bleomycin		
	Interaction	**Clinical management**
Nephrotoxic drugs (e.g. aminoglycosides, amphotericin, contrast dye, frusemide, NSAIDs)	Bleomycin toxicity may result from delayed clearance due to induced kidney dysfunction; including when low doses used	Avoid combination or monitor kidney function for increased bleomycin toxicity. Administer bleomycin before cisplatin in regimens using the combination
Oxygen during anaesthesia	Bleomycin causes sensitisation of lung tissue to oxygen	If oxygen is required, the use of low concentration (e.g. 25%) is recommended. Fluid replacement should be carefully monitored, with emphasis on administration of colloid rather than crystalloid, to avoid interstitial pulmonary oedema
Colony stimulating factors	May increase the risk of bleomycin induced pulmonary toxicity, especially at higher doses; this has not been confirmed in clinical trials	Monitor patients closely for signs of pulmonary toxicity if the combination is used

Dacarbazine		
	Interaction	**Clinical management**
CYP1A2 and 2E1 inducers (e.g. phenytoin, rifampicin etc.)	Increased toxicity of dacarbazine metabolite possible due to hastened and/or higher percentage of dacarbazine activation	Avoid combination or monitor closely for increased toxicity of dacarbazine metabolite
CYP1A2 and 2E1 inhibitors (e.g. abiraterone, amiodarone, ciprofloxacin, fluvoxamine, vemurafenib etc.)	Reduced efficacy of dacarbazine possible due to inhibition of the conversion of dacarbazine to its active metabolite (which may also result in reduced clearance of dacarbazine as the parent compound)	Avoid combination or monitor closely for decreased clinical response to dacarbazine; also, monitor for increased toxicity of dacarbazine as the parent compound
Sorafenib	Increased toxicity of dacarbazine metabolite possible due to increased serum concentration (mechanism uncertain)	Avoid combination or monitor closely for increased toxicity of dacarbazine metabolite
Fotemustine	Fatal adult respiratory distress syndrome (ARDS) if administered sequentially	An interval of one week should elapse between the last dose of fotemustine and the first day of dacarbazine treatment
Azathioprine, mercaptopurine	Increased toxicity of these drugs possible due to inhibition of xanthine oxidase by dacarbazine	Avoid combination or monitor closely for increased toxicity of azathioprine, mercaptopurine
Levodopa	Reduced response to levodopa in treating parkinsonism (mechanism unknown)	Adjust levodopa dose accordingly

Doxorubicin		
	Interaction	**Clinical management**
Cardiotoxic drugs (eg. bevacizumab, calcium channel blockers, propranolol, trastuzumab etc.)	Increased risk of doxorubicin-induced cardiotoxicity	Avoid combination or monitor closely for cardiotoxicity
Cyclophosphamide	Sensitises the heart to the cardiotoxic effects of doxorubicin; also, doxorubicin may exacerbate cyclophosphamide induced cystitis	Monitor closely for cardiotoxicity and ensure adequate prophylaxis for haemorrhagic cystitis when combination is used
Nephrotoxic drugs (e.g. aminoglycosides, amphotericin, contrast dye, frusemide, NSAIDs etc.)	Additive nephrotoxicity	Avoid combination or monitor kidney function closely
Glucosamine	Reduced efficacy of doxorubicin (due to induction of glucose-regulated stress proteins resulting in decreased expression of topoisomerase II *in vitro*)	The clinical effect of glucosamine taken orally is unknown. Avoid combination or monitor for decreased clinical response to doxorubicin
CYP2D6 inhibitors (e.g. SSRIs (esp. paroxetine), perhexiline, cinacalcet, doxepin, flecainide, quinine, terbinafine, ritonavir etc.)	Increased toxicity of doxorubicin possible due to reduced clearance	Monitor for doxorubicin toxicity
CYP3A4 inhibitors (e.g. aprepitant, azole antifungals, clarithromycin, erythromycin, grapefruit juice, ritonavir etc.)	Increased toxicity of doxorubicin possible due to reduced clearance	Monitor for doxorubicin toxicity
CYP3A4 inducers (e.g. carbamazepine, phenytoin, phenobarbitone, rifampicin, St John's wort etc.)	Reduced efficacy of doxorubicin possible due to increased clearance	Monitor for decreased clinical response to doxorubicin

NK-1 antagonist e.g. aprepitant, fosaprepitant, netupitant		
	Interaction	**Clinical management**
Dexamethasone	Increased effects/toxicity of dexamethasone due to inhibition of its metabolism via CYP3A4	Reduce dose of **antiemetic dexamethasone** by approximately 50% when adding a NK-1 antagonist. For protocols that already recommend a NK-1 antagonist, the dose reduction of **antiemetic dexamethasone** has already been taken into account. If **dexamethasone is part of the chemotherapy protocol**, dose reduction as per the product information is not routinely recommended in clinical practice and no additional dexamethasone is required for antiemetic cover.
Warfarin	Reduced anticoagulant efficacy of warfarin due to increased clearance (aprepitant induces CYP2C9). *Note interaction only applicable to aprepitant/ fosaprepitant	INR should be monitored in the 2 week period, particularly at 7 to 10 days following the administration of aprepitant/ fosaprepitant
Combined oral contraceptive	Reduced contraceptive efficacy due to increased clearance. *Note interaction only applicable to aprepitant/ fosaprepitant	Alternative non-hormonal methods should be used during and for 1 month after stopping aprepitant/ fosaprepitant
CYP3A4 inducers (e.g. carbamazepine, phenytoin, phenobarbitone, rifampicin, St John's wort etc.)	Reduced efficacy of NK-1 antagonist possible due to increased clearance	Avoid combination or monitor for decreased antiemetic effect. Consider using an alternative antiemetic regimen
CYP3A4 inhibitors (e.g. azole antifungals, clarithromycin, erythromycin, grapefruit juice, ritonavir etc.)	Increased toxicity of NK-1 antagonist possible due to reduced clearance	Avoid combination or monitor for increased adverse effects of NK-1 antagonist (e.g. headache, hiccups, constipation)
Drugs metabolised by CYP3A4 (e.g. etoposide, imatinib, irinotecan, midazolam, paclitaxel, vinblastine, vincristine etc.)	Increased effects/toxicity of these drugs possible due to inhibition of CYP3A4 by NK-1 antagonist	Avoid combination or monitor for increased toxicity especially with orally administered drugs

Vinblastine		
	Interaction	**Clinical management**
CYP3A4 and P-gp inhibitors (e.g. amiodarone, aprepitant, azole-antifungals, ritonavir, lapatinib, nilotinib, sorafenib, macrolides, ciclosporin, grapefruit juice etc.)	Increased toxicity of vinblastine possible due to reduced clearance	Monitor for vinblastine toxicity (esp. neurotoxicity, adynamic ileus)
CYP3A4 inducers (e.g. carbamazepine, phenytoin, phenobarbitone, rifampicin, St John's wort etc.)	Reduced efficacy of vinblastine possible due to increased clearance	Monitor for decreased clinical response to vinblastine
Drugs undergoing P-gp-mediated elimination (e.g. dabigatran, loperamide, phenytoin etc.)	Reduced efficacy of these drugs possible due to induction of P-gp by vinblastine resulting in increased clearance	Avoid combination or monitor for decreased clinical response to interacting drugs
Mitomycin	Increased risk of pulmonary toxicity when vinblastine administered following or concomitantly with mitomycin	Avoid combination or monitor closely for pulmonary toxicity (i.e. interstitial infiltrates, pleural effusion resulting in respiratory distress and cough)
Ototoxic drugs (e.g. cisplatin, aminoglycosides, frusemide, NSAIDs)	Additive ototoxicity (as reported with other vinca alkaloids)	Avoid combination or perform regular audiometric testing

General		
	Interaction	**Clinical management**
Warfarin	Anti-cancer drugs may alter the anticoagulant effect of warfarin.	Monitor INR regularly and adjust warfarin dosage as appropriate; consider alternative anticoagulant.
Direct oral anticoagulants (DOACs) e.g. apixaban, rivaroxaban, dabigatran	Interaction with both CYP3A4 and P-gp inhibitors /inducers. DOAC and anti-cancer drug levels may both be altered, possibly leading to loss of efficacy or toxicity (i.e. increased bleeding).	Apixaban: avoid concurrent use with strong CYP3A4 and P-gp inhibitors. If treating VTE, avoid use with strong CYP3A4 and P-gp inducers. Rivaroxaban: avoid concurrent use with strong CYP3A4 and P-gp inhibitors. Dabigatran: avoid combination with strong P-gp inducers and inhibitors. If concurrent use is unavoidable, monitor closely for efficacy/toxicity of both drugs.
Digoxin	Anti-cancer drugs can damage the lining of the intestine; affecting the absorption of digoxin.	Monitor digoxin serum levels; adjust digoxin dosage as appropriate.
Antiepileptics	Both altered antiepileptic and anti-cancer drug levels may occur, possibly leading to loss of efficacy or toxicity.	Where concurrent use of an enzyme-inducing antiepileptic cannot be avoided, monitor antiepileptic serum levels for toxicity, as well as seizure frequency for efficacy; adjust dosage as appropriate. Also monitor closely for efficacy of the anti-cancer therapy.
Antiplatelet agents and NSAIDs	Increased risk of bleeding due to treatment related thrombocytopenia.	Avoid or minimise combination. If combination deemed essential, (e.g. low dose aspirin for ischaemic heart disease) monitor for signs of bleeding.
Serotonergic drugs, including selective serotonin reuptake inhibitors (SSRIs e.g. paroxetine) and serotonin noradrenaline reuptake inhibitors (SNRIs e.g. venlafaxine)	Increased risk of serotonin syndrome with concurrent use of 5-HT3 receptor antagonists (e.g. palonosetron, ondansetron, granisetron, tropisetron, dolasetron, etc.)	Avoid combination. If combination is clinically warranted, monitor for signs and symptoms of serotonin syndrome (e.g. confusion, agitation, tachycardia, hyperreflexia). For more information link to TGA Medicines Safety Update
Vaccines	Diminished response to vaccines and increased risk of infection with live vaccines.	Live vaccines (e.g. BCG, MMR, zoster and varicella) are contraindicated in patients on immunosuppressive therapy. Use with caution in patients on non-immunosuppressive therapy. For more information; refer to the recommended schedule of vaccination for cancer patients, as outlined in the Australian Immunisation Handbook

Administration

eviQ provides safe and effective instructions on how to administer cancer treatments. However, eviQ does not provide every treatment delivery option, and is unable to provide a comprehensive list of cancer treatment agents and their required IV line giving set/filter. There may be alternative methods of treatment administration, and alternative supportive treatments that are also appropriate. Please refer to the individual

product information monographs via the TGA website for further information.

Day 1 and 15

Approximate treatment time: 3 hours

Safe handling and waste management

Safe administration

General patient assessment prior to each day of treatment.

Peripheral neuropathy assessment tool

Any toxicity grade 2 or greater may require dose reduction, delay or omission of treatment and review by medical officer before commencing treatment.

Prime IV line(s).

Insert IV cannula or access TIVAD or CVAD.

- weigh patient before each treatment

Hydration if prescribed.

Pre treatment medication

Verify antiemetics taken or administer as prescribed.

Chemotherapy - Time out

Doxorubicin

Administer doxorubicin (vesicant):

- over 5 to 15 minutes
  - via a minibag **OR**
  - by IV bolus via a side port of a freely flowing IV infusion
- ensure vein is patent and monitor for signs of extravasation throughout administration
- flush with ~150 mL of sodium chloride 0.9%
- potential for flare reaction during administration of doxorubicin (facial flushing and red streaking along the vein) stop infusion and exclude extravasation before continuing at a slower rate of infusion.

Although rare, cardiac arrhythmias may occur during or immediately after doxorubicin administration. If sudden onset of dyspnoea, palpitations or irregular pulse occurs, stop administration immediately and obtain urgent medical officer review.

Vinblastine

Administer vinblastine (vesicant):

- via a minibag over 5 to 10 minutes
- ensure vein is patent and monitor for signs of extravasation throughout administration
- flush with ~150 mL of sodium chloride 0.9%.

Dacarbazine

Administer dacarbazine (irritant):

- via IV infusion over 60 minutes
- protect from light
- flush with ~100 mL of sodium chloride 0.9%.

Too rapid an infusion of dacarbazine can lead to pain at the infusion site:

- stop the infusion
- ensure the drug has not extravasated
- when patency has been confirmed, continue infusion at a slower rate and commence a concurrent infusion of 500 mL of sodium chloride 0.9%

- consider administering dose in 1000 mL sodium chloride 0.9% for subsequent doses or insertion of a CVAD if severe pain persists.

Bleomycin

Prior to administration:

- test dose is recommended in lymphoma patients for the first two treatments. However, the usefulness of a test dose for predicting hypersensitivity reactions remains controversial. Refer to local policy for administration details
- premedication: if prescribed.

Administer bleomycin (irritant):

- over 10 minutes
  - via a minibag **OR**
  - by IV bolus via a side port of a freely flowing IV infusion
- flush with ~ 100 mL of sodium chloride 0.9%
- hypersensitivity reaction can occur with any dose of bleomycin regardless of whether a test dose has been administered.

Remove IV cannula and/or deaccess TIVAD or CVAD.

Continue safe handling precautions until 7 days after completion of drug(s)

Discharge information

Antiemetics

- Antiemetics as prescribed.

Laxatives

- Ensure patient has prophylactic laxatives.

Growth factor support

- Arrangements for administration if prescribed.

Prophylaxis medications

- Prophylaxis medications (if prescribed) i.e. tumour lysis prophylaxis, PJP prophylaxis, antivirals.

Patient information

- Ensure patient receives patient information sheet.

Side effects

The side effects listed below are not a complete list of all possible side effects for this treatment. Side effects are categorised into the approximate onset of presentation and should only be used as a guide.

Immediate (onset hours to days)	
Extravasation, tissue or vein injury	The unintentional instillation or leakage of a drug or substance out of a blood vessel into surrounding tissue. This has the potential to cause damage to affected tissue. Read more about extravasation management
Flare reaction	Anthracycline flare reaction is caused by a localised allergic reaction. It is characterised by erythematous vein streaking, urticaria and pruritus which may occur during drug administration and is often associated with too rapid an infusion. Extravasation must be ruled out if flare occurs.
Flu-like symptoms	
Headache	
Hypersensitivity reaction	Anaphylaxis and infusion related reactions can occur with this treatment. Read more about hypersensitivity reaction
Nausea and vomiting	Read more about prevention of treatment induced nausea and vomiting
Red-orange discolouration of urine	Pink/red/orange discolouration of the urine. This can last for up to 48 hours after some anthracycline drugs.
Taste and smell alteration	Read more about taste and smell changes

Early (onset days to weeks)	
Neutropenia	Abnormally low levels of neutrophils in the blood. This increases the risk of infection. Any fever or suspicion of infection should be investigated immediately and managed aggressively. Read more about immediate management of neutropenic fever
Thrombocytopenia	A reduction in the normal levels of functional platelets, increasing the risk of abnormal bleeding. Read more about thrombocytopenia
Anorexia	Loss of appetite accompanied by decreased food intake. Read more about anorexia
Constipation	
Fatigue	Read more about fatigue
Oral mucositis	Erythematous and ulcerative lesions of the gastrointestinal tract (GIT). It commonly develops following chemotherapy, radiation therapy to the head, neck or oesophagus, and high dose chemotherapy followed by a blood and marrow transplant (BMT). Read more about oral mucositis
Peripheral neuropathy	Typically symmetrical sensory neuropathy, affecting the fingers and toes, sometimes progressing to the hands and feet. It is associated with several classes of anti-cancer drugs. These include taxanes, platinum-based compounds, vinca alkaloids and some drugs used to treat multiple myeloma. Read more about peripheral neuropathy
Photosensitivity	Increased sensitivity to ultraviolet (UV) light resulting in an exaggerated sunburn-like reaction accompanied by stinging sensations and urticaria.
Skin rash	Anti-cancer drugs can cause a number of changes in the skin with maculo-papular rash the most common type of drug-induced skin reaction. Read more about skin rash

Late (onset weeks to months)	
Anaemia	Abnormally low levels of red blood cells (RBCs) or haemoglobin in the blood. Read more about anaemia
Alopecia	Hair loss may occur from all parts of the body. Patients can also experience mild to moderate discomfort of the hair follicles, and rarely pain as the hair is falling out. Read more about alopecia and scalp cooling
Cognitive changes (chemo fog)	Changes in cognition characterised by memory loss, forgetfulness and feeling vague. This is also referred to as 'chemo brain' or 'chemo fog'. Read more about cognitive changes (chemo fog)
Nail changes	Hyperpigmentation, paronychia, onycholysis, splinter haemorrhage, pyogenic granuloma formation, subungal haematoma and subungal hyperkeratosis are some of the nail changes associated with anti-cancer drugs. Read more about nail toxicities
Pulmonary toxicity	Pulmonary toxicity may include damage to the lungs, airways, pleura and pulmonary circulation.

Delayed (onset months to years)	
Cardiotoxicity	Anthracyclines are the most frequently implicated anti-cancer drugs associated with cardiotoxicity, which typically manifests as a reduction in left ventricular ejection fraction (LVEF), cardiomyopathy, or symptomatic CHF. Anthracycline induced cardiotoxicity has been categorised into acute, early-onset chronic progressive and late-onset chronic progressive and is usually not reversible. The risk of clinical cardiotoxicity increases with a number of risk factors including higher total cumulative doses. Read more about cardiac toxicity associated with anthracyclines

Evidence

The combination of doxorubicin, bleomycin, vinblastine and dacarbazine (ABVD) for treatment of advanced Hodgkin lymphoma was first reported by Bonadonna et al.[6] ABVD was shown to be superior to the previous standard regimen, mechlorethamine, vincristine, procarbazine and prednisone (MOPP), alone[7, 8, 9]and less toxic than the MOPP/ABVD combination, with minimal infertility and reduced rates of secondary malignancy compared with radiation therapy (RT) or MOPP.[10]

A Cochrane meta-analysis in 2017[11] concluded that based on “moderate-to high-quality evidence that adult patients between 16 and 60 years of age with early unfavourable and advanced stage HL benefit regarding overal survival (OS) and progression-free survival (PFS) from first-line chemotherapy including escalated bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, and prednisone (BEACOPP). The proven benefit in OS for patients with advanced HL is a new finding of this updated review due to the inclusion of the results from the EORTC 20012 trial. Furthermore, there is only low-quality evidence of a difference in the total number of secondary malignancies, as the follow-up period might be too short to detect meaningful differences. Low-quality evidence also suggests that people treated with escalated BEACOPP may have a higher risk to develop secondary AML or MDS. Due to the availability of only very low-quality evidence available, we are unable to come to a conclusion in terms of infertility. This review does, for the first time suggest a survival benefit. However, it is clear from this review that escalated BEACOPP may be more toxic than ABVD, and very important long-term side effects of second malignancies and infertility have not been sufficiently analysed yet.

Of note that studies using PET directed therapy were not included in the Cochrane review. Two important studies were published recently. In the RATHL study, 1129 patients have underwent interim PET-CT after 2 cycles of ABVD chemotherapy[1]. PET negative patients were randomised to ABVD or AVD, while PET positive patients were treated with 4 cycles of either BEACOPP-14 or escalated BEACOPP. Updated results presented at ICL-14[12] conference in 2017 showed that following a negative PET2, 952 pts were randomised to continue ABVD or AVD. With a median follow-up of 52 months, PFS at 3 years for ABVD was 85.4% and for AVD 84.0%. Among 172 pts with a positive PET2, 5 year PFS was 65.7% and 5 year OS 85.1%. The primary outcome measure was the PFS rate among patients who were randomly assigned to continue or stop bleomycin after negative findings on an interim PET-CT scan; the aim was to exclude a difference of 5 percentage points at 3 years. The observed upper boundary of the 95% confidence interval (5.3 percentage points) was just over this margin, and this is probably due to the lower-than-expected 3-year PFS rate of 85.7% in the ABVD group, which would require more events to exclude a 5-percentage-point difference. The inclusion of bleomycin in the first two cycles may still make a positive contribution to the control of disease, but its omission after negative findings on an interim PET-CT scan carries a minimal risk of treatment failure, estimated in our trial to be 1.6%, and there was no

significant difference in survival between the randomised groups.

Efficacy

Evidence of the efficacy of ABVD in advanced stage Hodgkin lymphoma comes from several RCTs comparing ABVD with other regimens (see table). In these studies, complete remission (CR) rates range from 76-89% with 5 year overall survival (OS) 73-90%.

Study	Trial Design	Results for ABVD arm				
		n =	CR	FFS @ 5yrs	PFS @ 5yrs	OS @ 5yrs
Canellos (1992)[9]	6-8 x ABVD vs MOPP vs MOPP/ABVD; no RT	115	82%	61%	-	73%
Chisesi (2002)[13]	6 x ABVD vs MEC vs Stanford V; ± RT	98	89.7%	81.4%*	91.5%*	94.7%*
Duggan (2003)[14]	8-10 x ABVD vs MOPP/ABV; no RT	433	76%	63%	-	82%
Johnson (2005)[15]	6-8 x ABVD vs multidrug regimens; ± RT	262	68%	-	75%*	90%*
Gobbi (2005)[16]	6 x ABVD vs mod Stanford V vs MOPPEBVCAD; ± RT	122	89%	78%	85%	90%
Federico (2009)[17]	6 x ABVD vs BEACOPP vs CEC; ± RT	99	84%	65%	68%	84%
Hoskin (2009)[18]	6-8 x ABVD vs Stanford V; ± RT	261	92%**	-	76%	90%

** outcome percentages are at 3 years, not 5 years as the other studies summarised here*
*** overall response rate (CR + PR)*

NB:

MOPP= mechlorethamine + vincristine + procarbazine + prednisone

Stanford V= doxorubicin + vinblastine + mechlorethamine + vincristine + bleomycin + etoposide + prednisone

MOPPEBVCAD= mechlorethamine + vincristine + procarbazine + prednisone + epidoxirubicin + bleomycin + vinblastine + lomustine + doxorubicin + vindesine

CEC (COPPEBVCAD)= cyclophosphamide + lomustine + vindesine + melphalan + prednisone + epidoxirubicin + vincristine + procarbazine + vinblastine + bleomycin

BEACOPP= bleomycin + etoposide + doxorubicin + cyclophosphamide + vincristine + procarbazine + prednisone

ABVD is one of the two main international standard treatments for advanced stage Hodgkin lymphoma, the other being escalated BEACOPP (see link).

Toxicity

ABVD causes grade 3-4 neutropenia in 30-34% of patients[16, 17] Despite this rates of significant infections are low (1-2% Grade 3-4).[9, 16] Evens et al demonstrated that G-CSF support is not required to maintain near 100% dose intensity during ABVD treatment.[4] In their study 58% of 658 ABVD treatments were administered with an ANC <1.0 x 10^9/L without an increase in infection (incidence rate, 0.44%) when compared with those given G-CSF (incidence rate, 0.78%). Other Grade 3-4 early toxicities include alopecia (24-30%),[9, 17] nausea and vomiting (6-13%)[16, 17] and pulmonary (6-10%).[9, 18]

Fertility is relatively preserved after ABVD. 30-54% of people assigned male at birth experience transient oligo/azospermia however most fully recover.[19, 20] Transient amenorrhoea occurs in around one third of people assigned female at birth of reproductive age (< 45 years) but permanent amenorrhoea secondary to ABVD alone is uncommon.[20] Furthermore, people assigned female at birth attempting pregnancy after ABVD had fertility comparable with case controls with a 12 month pregnancy rate of 70%.[21]

Although second malignancies occur in patients post-ABVD (6% at 6-10 years follow up) rates of secondary MDS/AML are very low and do not appear to be significantly increased.[14, 22, 11] Other long term toxicities include bleomycin-induced lung injury (link to Pulmonary toxicity associated with anti-cancer drugs) and doxorubicin-related cardiac toxicity (link to Cardiac toxicity associated with anthracyclines).

In the most recent Cochrane review[23], authors concluded that: “The risk of secondary acute myeloid leukaemia and myelodysplastic syndrome (AML/MDS) is increased but efficacy is improved among patients treated with intensified chemotherapy protocols. Treatment decisions must be tailored for individual patients. Consolidating radiotherapy is associated with an increased rate of secondary malignancies; therefore it appears important to define which patients can safely be treated without radiotherapy after chemotherapy, both for early and advanced stages. For early stages, treatment optimisation methods such as use of fewer chemotherapy cycles and reduced field or reduced-dose radiotherapy did not appear to markedly affect

efficacy or secondary malignancy risk. Due to the limited amount of long-term follow-up in this meta-analysis, further long-term investigations of late events are needed, particularly with respect to secondary solid tumours. Since many older studies have been included, possible improvement of radiotherapy techniques must be considered when interpreting these results.

References

1 Johnson, P., M. Federico, A. Kirkwood, et al. 2016. "Adapted Treatment Guided by Interim PET-CT Scan in Advanced Hodgkin's Lymphoma." N Engl J Med 374(25):2419-2429.

2 Australian Medicines Handbook Pty Ltd. January 2015 Edition

3 Stefanou, A. and J. Siderov. 2001. "Medical errors. Dosage nomenclature of bleomycin needs to be standardised to avoid errors." BMJ 322(7299):1423-1424.

4 Evens, A. M., J. Cilley, T. Ortiz, et al. 2007. "G-CSF is not necessary to maintain over 99% dose-intensity with ABVD in the treatment of Hodgkin lymphoma: low toxicity and excellent outcomes in a 10-year analysis." Br J Haematol 137(6):545-552.

5 Anderson, R. A., R. Remedios, A. A. Kirkwood, et al. 2018. "Determinants of ovarian function after response-adapted therapy in patients with advanced Hodgkin's lymphoma (RATHL): a secondary analysis of a randomised phase 3 trial." Lancet Oncol 19(10):1328-1337.

6 Bonadonna, G., R. Zucali, S. Monfardini, et al. 1975. "Combination chemotherapy of Hodgkin's disease with adriamycin, bleomycin, vinblastine, and imidazole carboxamide versus MOPP." Cancer 36(1):252-259.

7 Santoro, A., G. Bonadonna, P. Valagussa, et al. 1987. "Long-term results of combined chemotherapy-radiotherapy approach in Hodgkin's disease: superiority of ABVD plus radiotherapy versus MOPP plus radiotherapy." J Clin Oncol 5(1):27-37.

8 Canellos, G. P. and D. Niedzwiecki. 2002. "Long-term follow-up of Hodgkin's disease trial." N.Eng.J.Med. 346(18):1417-1418.

9 Canellos, G. P., J. R. Anderson, K. J. Propert, et al. 1992. "Chemotherapy of advanced Hodgkin's disease with MOPP, ABVD, or MOPP alternating with ABVD." N.Engl.J.Med.;327(21):1478-1484.

10 Valagussa, P., A. Santoro, F. Fossati Bellani, et al. 1982. "Absence of treatment-induced second neoplasms after ABVD in Hodgkin's disease." Blood 59(3):488-494.

11 Skoetz, N., A. Will, I. Monsef, et al. 2017. "Comparison of first-line chemotherapy including escalated BEACOPP versus chemotherapy including ABVD for people with early unfavourable or advanced stage Hodgkin lymphoma." Cochrane Database Syst Rev 5:CD007941.

12 Trotman J., A. Fossa, M. Federico, et al. "Response adapted therapy for advanced Hodgkin lymphoma (RATHL) trial: longer follow-up confirms efficacy of de-escalation after a negative interim PET (CRUK/07/033)". ICL-14 meeting 2017.

13 Chisesi, T., M. Federico, A. Levis, et al. 2002. "ABVD versus stanford V versus MEC in unfavourable Hodgkin's lymphoma: results of a randomised trial." Ann Oncol 13 Suppl 1:102-106.

14 Duggan, D. B., G. R. Petroni, J. L. Johnson, et al. 2003. "Randomized comparison of ABVD and MOPP/ABV hybrid for the treatment of advanced Hodgkin's disease: report of an intergroup trial." J Clin Oncol 21(4):607-614.

15 Johnson, P. W., J. A. Radford, M. H. Cullen, et al. 2005. "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 (ISRCTN97144519)." J Clin Oncol 23(36):9208-9218.

16 Gobbi, P. G., A. Levis, T. Chisesi, et al. 2005. "ABVD versus modified stanford V versus MOPPEBVCAD with optional and limited radiotherapy in intermediate- and advanced-stage Hodgkin's lymphoma: final results of a multicenter randomized trial by the Intergruppo Italiano Linfomi." J Clin Oncol 23(36):9198-9207.

17 Federico, M., S. Luminari, E. Iannitto, et al. 2009. "ABVD compared with BEACOPP compared with CEC for the initial

treatment of patients with advanced Hodgkin's lymphoma: results from the HD2000 Gruppo Italiano per lo Studio dei Linfomi Trial." J Clin Oncol 27(5):805-811.

18 Hoskin, P. J., L. Lowry, A. Horwich, et al. 2009. "Randomized comparison of the stanford V regimen and ABVD in the treatment of advanced Hodgkin's Lymphoma: United Kingdom National Cancer Research Institute Lymphoma Group Study ISRCTN 64141244." J Clin Oncol 27(32):5390-5396.

19 Viviani, S., A. Santoro, G. Ragni, et al. 1985. "Gonadal toxicity after combination chemotherapy for Hodgkin's disease. Comparative results of MOPP vs ABVD." Eur J Cancer Clin Oncol 21(5):601-605.

20 van der Kaaij, M. A., J. van Echten-Arends, A. H. Simons, et al. 2010. "Fertility preservation after chemotherapy for Hodgkin lymphoma." Hematol Oncol 28(4):168-179.

21 Hodgson, D., M. Pintilie, L. Gitterman, et al. 2007. "Fertility among female hodgkin lymphoma survivors attempting pregnancy following ABVD chemotherapy." Hematological oncology 25(1):11-5.

22 Engert, A., V. Diehl, J. Franklin, et al. 2009. "Escalated-dose BEACOPP in the treatment of patients with advanced-stage Hodgkin's lymphoma: 10 years of follow-up of the GHSG HD9 study." J Clin Oncol 27(27):4548-4554.

23 Franklin, J., D. A. Eichenauer, I. Becker, et al. 2017. "Optimisation of chemotherapy and radiotherapy for untreated Hodgkin lymphoma patients with respect to second malignant neoplasms, overall and progression-free survival: individual participant data analysis." Cochrane Database Syst Rev 9:CD008814.

History

Version 6

Date	Summary of changes
27/03/2020	Protocol presented and reviewed at the March 2020 Haematology Reference Committee meeting. • Updated to 6 cycles, as standard practice • Notes added regarding bleomycin • Evidence section updated
31/08/2022	Bleomycin extravasation category updated to align with extravasation clinical resources update.
28/04/2023	Reviewed electronically by Haematology reference committee. • Updated links in side effects and patient information For review in 4 years.
09/01/2024	Drug cost updated to exclude dacarbazine as it is not available on the PBS.

Version 5

Date	Summary of changes
19/10/2006	Clarification of bleomycin equivalence doses
07/12/2007	Further clarification of bleomycin equivalence
20/05/2008	Clarification of belomycin administration; Review and addition of information to increase the comprehensiveness of the protocol
26/06/2008	Re-wording of administration of vesicants to the standardised format
25/01/2010	Removed recommendation to apply heat along vein to relieve pain caused by dacarbazine infusion as literature supports the use of both heat and cold.
25/01/2010	Review of dose modifications and transferred to eviQ
26/11/2010	Reviewed at Reference Committee meeting (RCM)
15/11/2011	New format to allow for export of protocol information

Date	Summary of changes
	Protocol version number changed to *V.2* Antiemetics and premedications added to the treatment schedule Additional Clinical Information, Key Prescribing table and Key Administration table combined into new section titled Clinical Considerations Drug specific information placed behind the drug name link
14/11/2011	PHC view added
18/12/2012	Old evidence removed, note added in the evidence section. Changes made as per RCM November 2010.
18/12/2012	Republished on eviQ
11/10/2013	Reviewed at Haematology Reference Committee meeting (HRCM). Evidence updated. Emend changed from 125mg on day 1 and 80mg on day 2 & 3 to 165mg on day 1. Protocol version number changed to *V.3* PHC view removed
11/09/2015	Reviewed at HRCM: no major changes - links to HL Radiotherapy protocols and IPS document made.
09/03/2016	PJP prophylaxis preclin added to clinical considerations.
24/05/2016	Changed the order of Bleomycin and Dacarbazine in the treatment schedule and nursing admin sections to be in line with the correct order of administration.
29/08/2016	Changed the order of drugs in the treatment schedule summary and patient information sheet as per the ABVD acronym.
15/09/2016	Updated the volume of vinblastine to 50 mL in the treatment schedule.
31/05/2017	Transferred to new eviQ website. Version number changed to V.4. Antiemetic change: Netupitant/palonosetron combination has replaced aprepitant and a $5HT_3$ receptor antagonist in combination with dexamethasone for all highly emetogenic regimens.
03/07/2018	Protocol reviewed and presented at the May 2018 eviQ Lymphoma and CLL Reference Committee meeting. Discussion continued over email and document approved for publication with the following changes: • Removal of urinalysis in the administration section. • Evidence section updated. • Version change to V.5.
11/07/2019	Potential drug interaction of bleomycin and G-CSF added to footnote under the treatment schedule and G-CSF clinical information block. Lung damage with bleomycin information reiterated in "Other information about your treatment" section of the patient information page.

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The currency of this information is guaranteed only up until the date of printing, for any updates please check:
https://www.eviq.org.au/p/56
01 Mar 2024

Patient information - Hodgkin lymphoma - ABVD (doxorubicin, bleomycin, vinblastine, dacarbazine) advanced stage

Patient's name:

Your treatment

The treatment schedule below explains how the drugs for this treatment are given.

ABVD (doxorubicin, bleomycin, vinblastine, dacarbazine)			
This treatment cycle is repeated every 28 days. You will usually have 6 cycles. Your doctor will advise you of the number of treatments you will have.			
Day	**Treatment**	**How it is given**	**How long it takes**
1 and 15	**Doxorubicin** (*dox-oh-roo-bi-sin*)	By a drip into a vein	About 3 hours
	Vinblastine (*vin-BLAS-teen*)		
	Dacarbazine (*da-CAR-ba-zeen*)		
	Bleomycin (*blee-oh-MYE-sin*)		

When to get help

Anticancer drugs (drugs used to treat cancer) can sometimes cause serious problems. It is important to get medical help immediately if you become unwell.

IMMEDIATELY go to your nearest hospital Emergency Department, or contact your doctor or nurse if you have any of the following at any time:	**Emergency contact details** Ask your doctor or nurse from your treating team who to contact if you have a problem
• a temperature of 38°C or higher • chills, sweats, shivers or shakes • shortness of breath • uncontrolled vomiting or diarrhoea • pain, tingling or discomfort in your chest or arms • you become unwell.	Daytime: Night/weekend: Other instructions:

During your treatment immediately tell the doctor or nurse looking after you if you get any of the following problems:

- leaking from the area where the drugs are being given
- pain, stinging, swelling or redness in the area where the drugs are being given or at any injection sites
- a skin rash, itching, feeling short of breath, wheezing, fever, shivers, or feeling dizzy or unwell in any way (allergic reaction).

Other information about your treatment

Changes to your dose or treatment delays

Sometimes a treatment may be started at a lower dose or the dose needs to be changed during treatment. There may also be times when your treatment is delayed. This can happen if your doctor thinks you are likely to have severe side effects, if you get severe side effects, if your blood counts are affected and causing delays in treatment, or if you are finding it hard to cope with the treatment. This is called a dose reduction, dose change or treatment delay. Your doctor will explain if you need any changes or delays to your treatment and the reason why.

Blood tests and monitoring

You will need to have a blood test before you start treatment and regularly throughout your treatment. Your doctor or nurse will tell you when to have these blood tests.

Lung damage with bleomycin

Bleomycin can cause lung damage in some people. This can be very serious and can sometimes cause life-threatening problems. Make sure that you let people know that you have had bleomycin. This is important if you need any hospital treatment that may include having oxygen.

Ask your doctor or nurse for eviQ patient information about lung damage from bleomycin treatment.

Central venous access devices (CVADs)

This treatment may involve having chemotherapy through a central venous access device (CVAD). Your doctor or nurse will explain this to you. For more information, see the eviQ patient information sheets on CVADs.

Other medications given during this treatment

- **Anti-sickness (anti-nausea) medication:** you may be given some anti-sickness medication. Make sure you take this medication as your doctor or nurse tells you, even if you don't feel sick. This can help to prevent the sickness starting.
- **Laxatives:** you may be given some medication to prevent or treat constipation. Your doctor or nurse will tell you how and when to take the laxatives.
- **Prophylaxis medication:** you may need to take some medications to prevent infection and to help prevent or reduce some of the side effects of the chemotherapy. Your doctor or nurse will tell you how and when to take these medications.
- **G-CSF:** you may be given injection(s) of a drug called G-CSF (also called filgrastim, lipegfilgrastim or pegfilgrastim) under your skin. This helps to boost your white blood cell count. Your white blood cells help to fight infection. Lipegfilgrastim and pegfilgrastim are given once. Filgrastim is given for several days until your white blood cells recover. Your doctor will decide if you need this medication. Follow this link to read more information on how to give this injection.

Side effects

Cancer treatments can cause damage to normal cells in your body, which can cause side effects. Everyone gets different side effects, and some people will have more problems than others.

The table below shows some of the side effects you may get with this treatment. You are unlikely to get all of those listed and you may also get some side effects that have not been listed.

Tell your doctor or nurse about any side effects that worry you. Follow the instructions below and those given to you by your doctor or nurse.

Immediate (onset hours to days)	
Pain or swelling at injection site (extravasation)	• This treatment can cause serious injury if it leaks from the area where it is going into the vein. • This can cause pain, stinging, swelling or redness at or near the site where the drug enters the vein. • If not treated correctly, you may get blistering and ulceration. • **Tell your doctor or nurse immediately if you get any of the symptoms listed above during or after treatment.**

Redness and itching along vein	• You may get redness and itching along the vein where your chemotherapy is being infused. • This will usually go away within 30 minutes of stopping the injection. • **Tell your doctor or nurse as soon as possible if you get any of the symptoms listed above. Your nurse will check to make sure the drug has not leaked out of the vein.**
Flu-like symptoms	• You may get: ◦ a fever ◦ chills or sweats ◦ muscle and joint pain ◦ a cough ◦ headaches. • The drug bleomycin can cause a fever or flu-like illness within the first day of having the treatment. • You can take paracetamol to help settle these symptoms. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if the symptoms do not settle or you become unwell.**
Headache	• You can take paracetamol if you have a headache. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you get a very bad headache that is not helped by pain medication.**
Allergic reaction	• Allergic reactions are uncommon but can be life threatening. • **If you feel unwell during the infusion or shortly after it, or:** ◦ **get a fever, shivers or shakes** ◦ **feel dizzy, faint, confused or anxious** ◦ **start wheezing or have difficulty breathing** ◦ **have a rash, itch or redness of the face** **<u>While you are in hospital:</u> Tell your doctor or nurse immediately.** **<u>After you leave:</u> Contact your doctor or nurse immediately, or go to the nearest hospital Emergency Department.**
Nausea and vomiting	• You may feel sick (nausea) or be sick (vomit). • Take your anti-sickness medication as directed even if you don't feel sick. • Drink plenty of fluids (unless you are fluid restricted). • Eat small meals more frequently. • Try food that does not require much preparation. • Try bland foods like dry biscuits or toast. • Gentle exercise may help with nausea. • Ask your doctor or nurse for eviQ patient information - Nausea and vomiting during cancer treatment. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you have uncontrolled vomiting or feel dizzy or light-headed.**
Urine turning orange or red	• Your urine will turn an orange or red colour. • This is not harmful and should only last for up to 48 hours after treatment.
Taste and smell changes	• You may find that food loses its taste or tastes different. • These changes are likely to go away with time. • Do your mouth care regularly. • Chew on sugar-free gum or eat sugar-free mints. • Add flavour to your food with sauces and herbs. • Ask your doctor or nurse for eviQ patient information - Taste and smell changes during cancer treatment.

Early (onset days to weeks)

Infection risk (neutropenia)	• This treatment lowers the amount of white blood cells in your body. The type of white blood cells that help to fight infection are called neutrophils. Having low level of neutrophils is called neutropenia. If you have neutropenia, you are at greater risk of getting an infection. It also means that your body can't fight infections as well as usual. This is a serious side effect, and can be life threatening. • Wash your hands often. • Keep a thermometer at home and take your temperature regularly, and if you feel unwell. • Do your mouth care regularly. • Inspect your central line site (if you have one) daily for any redness, pus or swelling. • Limit contact with people who are sick. • Learn how to recognise the signs of infection. • Ask your doctor or nurse for eviQ patient information - Infection during cancer treatment. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you get any of the following signs or symptoms:** ◦ **a temperature of 38°C or higher** ◦ **chills, shivers, sweats or shakes** ◦ **a sore throat or cough** ◦ **uncontrolled diarrhoea** ◦ **shortness of breath** ◦ **a fast heartbeat** ◦ **become unwell even without a temperature.**
Low platelets (thrombocytopenia)	• This treatment lowers the amount of platelets in your blood. Platelets help your blood to clot. When they are low, you are at an increased risk of bleeding and bruising. • Try not to bruise or cut yourself. • Avoid contact sport or vigorous exercise. • Clear your nose by blowing gently. • Avoid constipation. • Brush your teeth with a soft toothbrush. • Don't take aspirin, ibuprofen or other similar anti-inflammatory medications unless your doctor tells you to. • Tell your doctor or nurse if you have any bruising or bleeding. • **Tell your doctor or nurse immediately, or go to your nearest hospital Emergency Department if you have any uncontrolled bleeding.**
Appetite loss (anorexia)	• You may not feel like eating. • Try to avoid drinking fluids at meal times. • Try to eat small meals or snacks regularly throughout the day. • Try to eat food that is high in protein and calories. • If you are worried about how much food you can eat, or if you are losing weight, ask to speak to a dietitian.
Constipation	• You may have bowel motions (stools, poo) that are less frequent, harder, smaller, painful or difficult to pass. • You may also get: ◦ bloating, cramping or pain ◦ a loss of appetite ◦ nausea or vomiting. • Drink plenty of fluids (unless you are fluid restricted). • Eat plenty of fibre-containing foods such as fruit, vegetables and bran. • Take laxatives as directed by your doctor. • Try some gentle exercise daily. • **Tell your doctor or nurse if you have not opened your bowels for more than 3 days.**

Tiredness and lack of energy (fatigue)	• You may feel very tired, have no energy, sleep a lot, and not be able to do normal activities or things you enjoy. • Do not drive or operate machinery if you are feeling tired. • Nap for short periods (only 1 hour at a time) • Prioritise your tasks to ensure the best use of your energy. • Eat a well balanced diet and drink plenty of fluids (unless you are fluid restricted). • Try some gentle exercise daily. • Allow your friends and family to help. • **Tell your doctor or nurse if you get any of the symptoms listed above.**
Mouth pain and soreness (mucositis)	• You may have: ◦ bleeding gums ◦ mouth ulcers ◦ a white coating on your tongue ◦ pain in the mouth or throat ◦ difficulty eating or swallowing. • Avoid spicy, acidic or crunchy foods and very hot or cold food and drinks. • Try bland and soft foods. • Brush your teeth gently with a soft toothbrush after each meal and at bedtime. If you normally floss continue to do so. • Rinse your mouth after you eat and brush your teeth, using either: ◦ 1/4 teaspoon of salt in 1 cup of warm water, or ◦ 1/4 teaspoon of bicarbonate of soda in 1 cup of warm water • Ask your doctor or nurse for eviQ patient information - Mouth problems during cancer treatment. • **Tell your doctor or nurse if you get any of the symptoms listed above.**
Nerve damage (peripheral neuropathy)	• You may notice a change in the sensations in your hands and feet, including: ◦ tingling or pins and needles ◦ numbness or loss of feeling ◦ pain. • You may find it difficult to do everyday activities, such as doing up buttons or picking up small objects. • Test water temperature with your elbow when bathing to avoid burns. • Use rubber gloves, pot holders and oven mitts in the kitchen. • Wear rubber shoes or boots when working in the garden or garage. • Keep rooms well lit and uncluttered. • Ask your doctor or nurse for eviQ patient information – Nerve problems during cancer treatment. • Tell your doctor or nurse if you get any of the symptoms listed above.
Skin that is more sensitive to the sun (photosensitivity)	• After being out in the sun you may develop a rash like a bad sunburn. • Your skin may become red, swollen and blistered. • Avoid direct sunlight. • Protect your skin from the sun by wearing sun-protective clothing, a wide-brimmed hat, sunglasses and a sunscreen of SPF 50 or higher. • **Tell your doctor or nurse if you get any of the symptoms listed above.**
Skin rash	• You may get a red, bumpy rash and dry, itchy skin. • Moisturise your skin with a gentle non-perfumed moisturising cream like sorbolene or aqueous cream. • Do not scratch your skin. • Protect your skin from the sun by wearing sun-protective clothing, a wide-brimmed hat, sunglasses and sunscreen of SPF 50 or higher. • **Talk to your doctor or nurse about other ways to manage your skin rash.**

Late (onset weeks to months)	
Low red blood cells (anaemia)	• You may feel dizzy, light-headed, tired and appear more pale than usual. • Tell your doctor or nurse if you have any of these signs or symptoms. You might need a blood transfusion. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you have any chest pain, trouble breathing, or feel like your heart is racing.**
Hair loss (alopecia)	• Your hair may start to fall out from your head and body. • Hair loss usually starts 2 to 3 weeks after your first treatment. • You may become completely bald and your scalp might feel tender. • Use a gentle shampoo and a soft brush. • Take care with hair products like hairspray, hair dye, bleaches and perms. • Protect your scalp from the cold with a hat, scarf or wig. • Protect your scalp from the sun with a hat or sunscreen of SPF 50 or higher. • Moisturise your scalp to prevent itching. • Ask your doctor or nurse about the Look Good Feel Better program
Chemo brain (chemotherapy-related cognitive impairment)	• You may notice that you are unable to concentrate, feel unusually disorganised or tired (lethargic) and have trouble with your memory. • These symptoms usually improve once treatment is completed. • Ask your doctor or nurse for eviQ patient information – Memory changes and chemotherapy (chemo brain). • Tell your doctor or nurse if you get any of the symptoms listed above.

Nail changes	• Your nails may:
	  ◦ grow more slowly
	  ◦ become darker
	  ◦ develop ridges or white lines
	  ◦ become brittle and flaky
	• In some cases, you may lose your nails completely.
	• Keep your nails clean and short.
	• Avoid things like biting your fingernails, getting a manicure, pedicure or false nails.
	• Wear gloves when you wash the dishes, work in the garden, or clean the house.

Lung problems	• Lung problems are rare, but can be serious. They may occur throughout treatment or after the completion of treatment.
	• You may get:
	  ◦ shortness of breath
	  ◦ fever
	  ◦ dry cough
	  ◦ wheezing
	  ◦ fast heartbeat
	  ◦ chest pain.
	• Your doctor will monitor how well your lungs are working during your treatment.
	• **Tell you doctor or nurse immediately, or go to the nearest hospital Emergency Department if you have chest pain or become short of breath.**
	• Ask your doctor or nurse for eviQ patient information about lung damage from bleomycin treatment.

Delayed (onset months to years)	
Heart problems	• You may get: ◦ chest pain or tightness ◦ shortness of breath ◦ swelling of your ankles ◦ an abnormal heartbeat. • Heart problems can occur months to years after treatment. • Tell your doctor if you have a history of heart problems or high blood pressure. • Before or during treatment, you may be asked to have a test to see how well your heart is working. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you get any of the symptoms listed above.**

General advice for patients having cancer treatment

Chemotherapy safety

- Learn how to keep you and your family safe while you are having anticancer drugs.
- See our patient information sheet - Chemotherapy safety at home.

Blood clot risk

- Cancer and anticancer drugs can increase the risk of a blood clot (thrombosis).
- Tell your doctor if you have a family history of blood clots.
- A blood clot can cause pain, redness, swelling in your arms or legs, shortness of breath or chest pain.
- If you have any of these symptoms go to your nearest hospital Emergency Department.

Medications and vaccinations

- Before you start treatment, tell your doctor about any medications you are taking, including vitamins or herbal supplements.
- Don't stop or start any medications during treatment without talking to your doctor and pharmacist first.
- Paracetamol is safe to take if you have a headache or other mild aches and pains. It is recommended that you avoid taking aspirin, ibuprofen and other anti-inflammatory type medications for pain while you are having treatment. However, if these medications have been prescribed by your doctor, do not stop taking them without speaking with your doctor.
- Vaccinations such as flu and tetanus vaccines are safe to receive while having treatment. Do not have any live vaccines during your treatment or for 6 months after it finishes. If you are unsure, check with your doctor before you have any vaccinations.
- People you live with should be fully vaccinated, including having live vaccines according to the current vaccination schedule. Extra care needs to be taken with hand washing and careful disposal of soiled nappies for infants who have recently received the rotavirus vaccine.

Other medical and dental treatment

- If you go to hospital or any other medical appointment (including dental appointments), always tell the person treating you that you are receiving anticancer drugs.
- Before you have any dental treatment, talk to your doctor.

Diet and food safety

- While you are receiving this treatment, it is important that you try to maintain a healthy diet.
- Grapefruit and grapefruit juice can interact with your medication and should be avoided while you are on this treatment.
- Speak to your doctor or nurse about whether drinking alcohol is safe with your treatment.
- If you have any concerns about recent weight loss or weight gain or questions about your diet, ask to speak to a dietitian.
- There are some foods that may cause infection in high risk individuals and should be avoided. For further information on foods to avoid and food hygiene please ask for a copy of the Listeria and food brochure.

Fertility

- Some cancer treatments can reduce your fertility. This can make it difficult or impossible to get pregnant or father a child.
- Talk to your doctor or nurse before you start any treatment. Depending on your situation there may be fertility sparing options available to you and/or your partner, discuss these with your doctor or nurse.

Pregnancy and breastfeeding

- Some cancer treatments can be dangerous to unborn babies. Talk to your doctor or nurse if you think there is any chance that you could be pregnant.
- Do not try to get pregnant or father a child during this treatment. Contraception should be used during treatment and after stopping treatment. Ask your doctor or nurse about what type of contraception you should use.
- If you are planning pregnancy/fatherhood after completing this treatment, talk to your doctor. Some doctors advise waiting between 6 months and 2 years after treatment.
- Do not breastfeed if you are on this treatment, as anti-cancer medications can also pass into breast milk.

Sex life and sexuality

- The desire to have sex may decrease as a result of this treatment or its side effects.
- Your emotions and the way you feel about yourself may also be affected by this treatment.
- It may help to discuss your concerns with your partner and doctor or nurse.

Risk of developing a second cancer

- Some anticancer treatments can increase your chance of developing a second cancer, this is rare. Your doctor will discuss with you the specific risks of your treatment.

Quitting smoking

- It is never too late to quit smoking. Quitting smoking is one of the best things you can do to help your treatment work better.
- There are many effective tools to improve your chances of quitting.
- Talk to your treating team for more information and referral to a smoking cessation support service.

Staying active

- Research shows that exercise, no matter how small, has many benefits for people during and after cancer treatment.
- Talk to your doctor before starting an exercise program. Your doctor can advise whether you need a modified exercise program.

For more information about cancer treatment, side effects and side effect management see our Patient and carers section.

Where to get more information

Telephone support

- Call Cancer Council on 13 11 20 for cancer information and support
- Call the Leukaemia Foundation on 1800 620 420 (Mon to Fri 9am – 5pm)
- Call the Lymphoma Nurse Support Line on 1800 953 081 (Mon to Fri 9am - 5pm)
- Call the Myeloma Australia Support Line on 1800 693 566 (Mon to Fri 9am - 5pm)

Haematology, transplant and cellular therapy information

- Arrow bone marrow transplant foundation – arrow.org.au
- Australasian Menopause Society – menopause.org.au
- Chris O'Brien Lifehouse - Total Body Irradiation - mylifehouse.org.au/departments/radiation-oncology/total-body-irradiation/
- Healthy Male Andrology Australia – healthymale.org.au/
- International Myeloma Foundation – myeloma.org
- Leukaemia Foundation – leukaemia.org.au
- Lymphoma Australia – lymphoma.org.au
- Myeloma Australia – myeloma.org.au
- NSW Agency for Clinical Innovation, Blood & Marrow Transplant Network – https://aci.health.nsw.gov.au/networks/bmtct
- NSW Agency for Clinical Innovation - aci.health.nsw.gov.au/projects/immune-effector-cell-service
- NCCN Guidelines for Patients Immunotherapy Side Effects: CAR T-Cell Therapy - nccn.org/patientresources/patient-resources/guidelines-for-patients
- Talk Blood Cancer – cmlsupport.org.uk/organisation-type/social-media-groups

General cancer information and support

- Australian Rare Cancer (ARC) Portal – arcportal.org.au/
- Beyond Blue – beyondblue.org.au

- Cancer Australia – canceraustralia.gov.au
- Cancer Council Australia – cancer.org.au
- Cancer Voices Australia – cancervoicesaustralia.org
- CanTeen – canteen.org.au
- Carers Australia – carersaustralia.com.au
- Carer Help - carerhelp.com.au
- eviQ Cancer Treatments Online – eviQ.org.au
- Food Standards Australia New Zealand: Listeria & Food Safety – https://www.foodstandards.gov.au/publications/listeriabrochuretext
- LGBTQI+ People and Cancer - cancercouncil.com.au/cancer-information/lgbtqi
- Look Good Feel Better – lgfb.org.au
- Patient Information - patients.cancer.nsw.gov.au
- Radiation Oncology Targeting Cancer - targetingcancer.com.au
- Redkite – redkite.org.au
- Return Unwanted Medicines – returnmed.com.au
- Staying active during cancer treatment – patients.cancer.nsw.gov.au/coping-with-cancer/physical-wellbeing/staying-active

Quit smoking information and support

Quitting smoking is helpful even after you have been diagnosed with cancer. The following resources provide useful information and support to help you quit smoking. Talk to your treating team about any other questions you may have.

- Call Quitline on 13 QUIT (13 78 48)
- iCanQuit – iCanQuit.com.au
- Patient Information - patients.cancer.nsw.gov.au/coping-with-cancer/physical-wellbeing/quitting-smoking
- Quitnow – quitnow.gov.au

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