Regimen Monograph

A - Regimen Name

ABVD Regimen

ADRIAMYCIN ® (DOXOrubicin)-Bleomycin-VinBLAStine-Dacarbazine

Disease Site
Hematologic
Lymphoma - Hodgkin

Intent
Curative

Regimen Category
Evidence-Informed :

Regimen is considered appropriate as part of the standard care of patients; meaningfully improves outcomes (survival, quality of life), tolerability or costs compared to alternatives (recommended by the Disease Site Team and national consensus body e.g. pan-Canadian Oncology Drug Review, pCODR). Recommendation is based on an appropriately conducted phase III clinical trial relevant to the Canadian context OR (where phase III trials are not feasible) an appropriately sized phase II trial. Regimens where one or more drugs are not approved by Health Canada for any indication will be identified under Rationale and Use.

Rationale and Uses
First-line therapy for Hodgkin’s lymphoma

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B - Drug Regimen

DOXOrubicin	25 mg /m²	IV	Days 1 & 15
bleomycin	10 units /m²	IV	Days 1 & 15
vinBLAStine	6 mg /m²	IV	Days 1 & 15
dacarbazine	375 mg /m²	IV	Days 1 & 15

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C - Cycle Frequency

REPEAT EVERY 28 DAYS

For a usual total of 6-8 cycles

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D - Premedication and Supportive Measures

Antiemetic Regimen: Moderate

Febrile Neutropenia Risk: Moderate

Other Supportive Care:

- Sperm banking should be offered for males due to effects on fertility.
- Women of child-bearing potential should be placed on oral contraceptives or gonadotropin-releasing hormone agonist in an effort to preserve fertility during chemotherapy.

Also refer to CCO Antiemetic Recommendations.

Screen for hepatitis B virus in all cancer patients starting systemic treatment. Refer to the hepatitis B virus screening and management guideline.

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E - Dose Modifications

Doses should be modified according to the protocol by which the patient is being treated.

Dosage with toxicity

Toxicity	Action / Dose (% Previous)*			
	Doxorubicin	**Bleomycin**	**Vinblastine**	**Dacarbazine**
Febrile neutropenia** or grade 4 ANC for ≥ 5-7 days	Consider adding G-CSF support and continuing current dose, if clinically appropriate.			
Thrombocytopenic bleeding	Hold, then 75%	Hold, then 100%	Hold, then 75%	Hold, then 75%
Grade 3 related organ / non-hematologic	Hold, then 75%	Hold, then 75%	Hold, then 75%	Hold, then 75%; discontinue if recurs after 2 dose reductions.
Grade 4 related organ / non-hematologic	Discontinue.			
Pulmonary: Pneumonitis	100% if clinically appropriate	Hold and investigate. Discontinue if confirmed; treat with corticosteroids.	100% if clinically appropriate	100% if clinically appropriate
Cardiac: ECG changes; pleuropericarditis, cardiotoxicity***	Hold and investigate. If cardiotoxicity, discontinue.	Hold and investigate. If ECG changes or pleuropericarditis, consider ↓ infusion rate or discontinue.	100% if clinically appropriate	100% if clinically appropriate

*Do not retreat until ANC ≥ 1-1.5 x 10^9L, platelets ≥ 100 x 10^9L and toxicity ≤ grade 2.

**G-CSF support should be considered after first episode of febrile neutropenia or delay of dose ≥1 week.

***including any signs and symptoms of heart failure, a greater than 10% decline in LVEF to below the lower limit of normal, a greater than 20% decline in LVEF from any level, or LVEF ≤ 45%

Hepatic Impairment

No dose adjustments required for bleomycin. No data available for dacarbazine.

DOXOrubicin

Bilirubin (µmol/L)		AST / ALT	% Usual Dose
1-2 x ULN			50%
2-4 x ULN	and/or	5-10 x ULN	25%
>4 x ULN	and/or	>10 x ULN	Consider omit

vinBLAStine

Bilirubin	% Usual Dose
>1 - 2.5 x ULN	50%
>2.5 - 4 x ULN	25%
>4 x ULN	Consider omit

Renal Impairment

Creatinine Clearance (mL/min)	DOXOrubicin (% Usual Dose)	Bleomycin (% Usual Dose)	VinBLAStine (% Usual Dose)	Dacarbazine* (% Usual Dose)
>50	No adjustment required	100%	No adjustment required	100%
>30-50		75%		75%
10-30				50% or discontinue
<10		50%		Discontinue

*modified from Kintzel et al 1995

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F - Adverse Effects

Refer to DOXOrubicin, bleomycin, vinBLAStine, dacarbazine drug monograph(s) for additional details of adverse effects.

Very common (≥ 50%)	Common (25-49%)	Less common (10-24%)	Uncommon (< 10%), but may be severe or life-threatening
• Myelosuppression ± infection, bleeding (may be severe) • Alopecia • Nausea, vomiting (may be severe) • Anorexia, weight loss • Fever, chills	• Fatigue • Hyperkeratosis • Skin hyperpigmentation • Mucositis (may be severe) • Urine discolouration	• Diarrhea • Constipation • Injection site reaction/phlebitis • Nail disorder • ECG changes • Paresthesia (may be severe) • Pneumonitis	• Cardiotoxicity • Arterial/venous thromboembolism • Arrhythmia • Secondary malignancy • Myocarditis/pericarditis • Pleuropericarditis • Blurred vision • Hearing impairment • Hemolytic uremic syndrome • ↑ LFTs • Hepatic necrosis • Veno-occlusive disease • Hypersensitivity • Rash • Photosensitivity • Radiation recall reaction • SIADH • Seizure • Autonomic/ cranial neuropathy, loss of deep tendon reflex • Tumour lysis syndrome

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G - Interactions

Refer to DOXOrubicin, bleomycin, vinBLAStine, dacarbazine drug monograph(s) for additional details.

- Avoid use of calcium channel blockers (e.g. verapamil) or bevacizumab with doxorubicin due to additive cardiotoxicity.
- Avoid anthracycline-based therapy for up to 28 weeks after stopping trastuzumab.
- Avoid use of cyclosporine with doxorubicin if possible, as it may increase doxorubicin concentrations.
- Avoid using stavudine or zidovudine with doxorubicin.
- Monitor serum digoxin levels and adjust dose as needed.
- Monitor serum phenytoin levels and adjust dose as needed.
- Monitor for pulmonary toxicity when bleomycin is used with nephrotoxic drugs (may reduce bleomycin clearance) or with other drugs that may cause pulmonary toxicity (e.g. BCNU, mitomycin, cyclophosphamide, methotrexate, gemcitabine).
- Avoid concomitant use of vinblastine with CYP3A4 inhibitors.
- Avoid concomitant use of vinblastine with CYP3A4 substrates if possible. Monitor closely or consider dose adjustment if they must be used together.
- Use vinblastine with caution in combination with neurotoxic drugs.

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H - Drug Administration and Special Precautions

Refer to DOXOrubicin, bleomycin, vinBLAStine, dacarbazine drug monograph(s) for additional details.

Administration

DOXOrubicin

- Slow push through sidearm of free flowing IV (5% Dextrose, Normal Saline). Depending on the dose volume and vein condition, administer the dose between 3 to 10 minutes to minimize thrombosis risk or extravasation.
- Do not admix with other drugs unless data are available; precipitates with fluorouracil and heparin.
- Avoid contact with alkaline solutions as this can lead to hydrolysis of doxorubicin.
- Slow down injection rate if erythematous streaking or facial flushing occurs.
- If any signs or symptoms of extravasation occur, the injection or infusion should be immediately terminated and restarted in another vein. Any known or suspected extravasation should be managed promptly as per local guidelines.
- Store vials under refrigeration (2 to 8ºC) and protect from light.

Also refer to the CCO guideline for detailed description of Management of Cancer Medication-Related Infusion Reactions.

bleomycin

- Reconstitute with 5-10mL Normal Saline.
- May be given by direct IV push over 10 minutes, followed by a Saline flush, if no IV line has been set up.
- Or may further dilute in 50-100mL Normal Saline (0.3 to 3 units/mL) and infuse over 10-15 minutes.
- Store unopened vial between 2-8ºC. Do not freeze.

Also refer to the CCO guideline for detailed description of Management of Cancer Medication-Related Infusion Reactions.

vinBLAStine

FOR INTRAVENOUS USE ONLY.
Intrathecal administration of other vinca alkaloids has resulted in death. Containers with this product should be labelled:
"**WARNING – FOR INTRAVENOUS USE ONLY. FATAL if given intrathecally.**"

- Direct IV push is not recommended to reduce the risk of inadvertently administering vinca alkaloids via intrathecal route.
- Mix in 50 mL minibag (NS or D5W).
- Dilutions in large volumes (≥ 100mL) and infusions over ≥30-60 minutes are not recommended, since these can increase the risk of vein irritation and extravasation.
- If any signs or symptoms of extravasation occur, the injection or infusion should be immediately terminated and restarted in another vein. Any known or suspected extravasation should be managed promptly according to local guidelines.
- Store unopened vials at 2 to 8ºC; protect from light.

dacarbazine

- Administration of concentrated dacarbazine solutions may cause severe perivenous pain; therefore, it is recommended to give dacarbazine as a diluted IV infusion.
- Extreme care should be taken to avoid extravasation as this may result in tissue damage and severe pain.
- May be mixed in normal saline or D5W bag (250 to 1000 mL), depending on the dose.
- Infuse over 30 to 120 minutes; refer to the institutional guidelines for infusion duration.
- Keep dacarbazine vials refrigerated (2 to 8ºC); protect the undiluted drug, infusion bags and tubing from light.

Contraindications

- Patients who have a hypersensitivity to the drugs or any of their components, other anthracyclines or anthracenediones (i.e. epirubicin, daunorubicin, mitoxantrone or mitomycin C)
- Severe or persistent myelosuppression or infection
- Severe hepatic impairment
- Severe myocardial insufficiency, arrhythmias or history of cardiac disease or recent myocardial infarction
- Previous treatment with maximum cumulative doses of doxorubicin, other anthracyclines or anthracenediones
- Intrathecal vinblastine administration is **absolutely contraindicated**.

Warnings/Precautions

- Bleomycin should be used with extreme caution in patients with pre-existing renal or pulmonary disease, and in patients over the age of 70. Patients should avoid high FIO_2 for at least a year after completion (i.e. during anesthesia).
- Use vinblastine with caution in patients with ischemic heart disease.
- Avoid the use of live vaccines during treatment and for at least 3 months after the last dose; use may result in serious infections in immunocompromised patients. Response to inactivated vaccines may be decreased.

Pregnancy/Lactation

- This regimen is **contraindicated** in pregnancy. Adequate contraception should be used by patients and their partners while on treatment and after the last treatment dose. Recommended methods and duration of contraception may differ depending on the treatment. Refer to the drug monograph(s) for more information.
- Breastfeeding is not recommended during this treatment and after the last treatment dose. Refer to the drug monograph(s) for recommendations after the last treatment dose (if available).
- Fertility effects: Yes

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I - Recommended Clinical Monitoring

Treating physicians may decide to monitor more or less frequently for individual patients but should always consider recommendations from the product monograph.

Refer to the hepatitis B virus screening and management guideline for monitoring during and after treatment.

Recommended Clinical Monitoring

- CBC; baseline and before each treatment
- Liver and renal function tests (including electrolytes); baseline and before each cycle
- Urinalysis; baseline and as clinically indicated
- Cardiac function tests (Echo, RNA and/or MUGA scans) for all patients with cardiac risk factors (including prior cardiotoxic drugs or patients at or above threshold dose levels); baseline and as clinically indicated
- Chest x-ray or CT scan; baseline and as clinically indicated
- Routine pulmonary function tests; as clinically indicated
- Clinical toxicity assessment (including infection, bleeding, hypersensitivity, injection site reactions, GI, cardiotoxicity, neurotoxicity, dermatological or pulmonary toxicity)
- Grade toxicity using the current NCI-CTCAE (Common Terminology Criteria for Adverse Events) version

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J - Administrative Information

Approximate Patient Visit	1.5 to 2 hours
Pharmacy Workload (average time per visit)	41.773 minutes
Nursing Workload (average time per visit)	62.417 minutes

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K - References

Bleomycin drug monograph, Ontario Health (Cancer Care Ontario).

Bonadonna G, Valagussa P, Santoro A. Alternating non-cross-resistant combination chemotherapy or MOPP in stage IV Hodgkin's disease: a report of 8 year results. Ann Intern Med, 1986; 104: 739-746

Canellos GP, Anderson JR, Propert KJ, et al, Chemotherapy of advanced Hodgkin's disease with MOPP, ABVD, or MOPP alternating with ABVD. N Engl J Med, 1992; 327: 1478-1484.

Dacarbazine drug monograph, Ontario Health (Cancer Care Ontario).

Doxorubicin drug monograph, Ontario Health (Cancer Care Ontario).

Vinblastine drug monograph, Ontario Health (Cancer Care Ontario).

PEBC Advice Documents or Guidelines

- First-line treatment of advanced-stage Hodgkin lymphoma

November 2024 Updated Fertility Effects section and added PEBC guideline link

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M - Disclaimer

Regimen Abstracts

A Regimen Abstract is an abbreviated version of a Regimen Monograph and contains only top level information on usage, dosing, schedule, cycle length and special notes (if available). It is intended for healthcare providers and is to be used for informational purposes only. It is not intended to constitute or be a substitute for medical advice, and all uses of the Regimen Abstract are subject to clinical judgment. Such information is provided on an "as-is" basis, without any representation, warranty, or condition, whether express, or implied, statutory or otherwise, as to the information's quality, accuracy, currency, completeness, or reliability, and Cancer Care Ontario disclaims all liability for the use of this information, and for any claims, actions, demands or suits that arise from such use.

Information in regimen abstracts is accurate to the extent of the ST-QBP regimen master listings, and has not undergone the full review process of a regimen monograph. Full regimen monographs will be published for each ST-QBP regimen as they are developed.

Regimen Monographs

Refer to the New Drug Funding Program or Ontario Public Drug Programs websites for the most up-to-date public funding information.

The information set out in the drug monographs, regimen monographs, appendices and symptom management information (for health professionals) contained in the Drug Formulary (the "Formulary") is intended for healthcare providers and is to be used for informational purposes only. The information is not intended to cover all possible uses, directions, precautions, drug interactions or adverse effects of a particular drug, nor should it be construed to indicate that use of a particular drug is safe, appropriate or effective for a given condition. The information in the Formulary is not intended to constitute or be a substitute for medical advice and should not be relied upon in any such regard. All uses of the Formulary are subject to clinical judgment and actual prescribing patterns may not follow the information provided in the Formulary.

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Some Formulary documents, such as the medication information sheets, regimen information sheets and symptom management information (for patients), are intended for patients. Patients should always consult with their healthcare provider if they have questions regarding any information set out in the Formulary documents.

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