Regimen Monograph

A - Regimen Name

PGLDX Regimen

Pegylated Liposomal DOXOrubicin

Disease Site	Sarcoma Kaposi's Sarcoma
Intent	Palliative
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	Standard therapy for the treatment of HIV-positive Kaposi’s sarcoma
Supplementary Public Funding	**pegylated liposomal DOXOrubicin** New Drug Funding Program (Liposomal Doxorubicin - HIV-positive Kaposi's Sarcoma) (NDFP Website)

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B - Drug Regimen

Pegylated liposomal doxorubicin is **not interchangeable** with other doxorubicin formulations.

pegylated liposomal DOXOrubicin	20 mg /m²	IV	Day 1

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C - Cycle Frequency

REPEAT EVERY 14 DAYS

Until disease progression or unacceptable toxicity.

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D - Premedication and Supportive Measures

Antiemetic Regimen: Low

- 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

Worst Toxicity & Toxicity on day of planned dosing	Action*: Week 3	Action*: Week 4
Grade 1 skin	If was ≥grade 3, delay for 1 week; otherwise treat on time	If still grade 1, ↓ dose by 25%
Grade 1 stomatitis	Treat on time with no dose modification	Not applicable
Grade 2 skin	Delay for 1 week	If still grade 2, ↓ dose by 50% If grade 1, ↓ dose by 25%
Grade 2 stomatitis	Delay for 1 week	If still grade 2, ↓ dose by 25%
Grade 3 skin	Delay for 1 week	If still grade 3, discontinue If grade 2, then ↓ dose by 50% If grade 1, ↓ dose by 25%
Grade 3 stomatitis	Delay for 1 week	If improved, ↓ dose by 25%
Grade 4 skin	Delay for 1 week	If still ≥ grade 3, discontinue If ≤ grade 2, ↓ dose by 50%
Grade 4 stomatitis	Delay for 1 week	If still grade 4, discontinue If improved, ↓ dose by 50%
Grade 3 myelosuppression	↓ dose by 25%	
Grade 4 ANC, platelets, febrile neutropenia or thrombocytopenic bleeding	↓ dose by 50%	
Significant cardiotoxicity	Discontinue	
Grade 3 other	↓ dose by 25%	
Grade 4 other	Discontinue or ↓ dose by 50%	
*Do not retreat until ANC > 1 x 10^9/L, platelets > 50-100 x 10^9/L and other toxicity ≤ grade 2 / or as indicated above		

Management of Infusion-related reactions with Anthracyclines:

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

Grade	Management	Re-challenge
1 or 2	• Stop or slow the infusion rate. • Manage the symptoms.	• Consider pre-medications and administering at a slower infusion rate.
3 or 4	• Stop treatment. • Aggressively manage symptoms.	• Re-challenge is discouraged, especially if vital signs have been affected. • Consider desensitization if therapy is necessary.

Hepatic Impairment

Bilirubin (µmol/L)	% Standard Dose (any cycle)
21-51	50%
>51	25%

Renal Impairment

No modifications are necessary for mild to moderate renal impairment (creatinine clearance > 30 mL/min). No studies have been done in patients with severe renal impairment.

Dosage in the Elderly

Limited information in patients ≥ 60 years. Use with caution.

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F - Adverse Effects

Refer to pegylated liposomal DOXOrubicin drug monograph(s) for additional details of adverse effects.

Most Common Side Effects	Less Common Side Effects, but may be Severe or Life-Threatening
• Myelosuppression ± infection/bleeding (may be severe) • Palmar-plantar erythrodysesthesia (Hand-foot syndrome) • Stomatitis • Fatigue • Acute Hypersensitivity reactions (first infusion) • Nausea and vomiting • Rash (may be severe) • Alopecia • Anorexia	• Arterial, venous thromboembolism • Secondary malignancy • Cardiotoxicity • Phlebitis

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G - Interactions

Refer to pegylated liposomal DOXOrubicin drug monograph(s) for additional details.

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H - Drug Administration and Special Precautions

Refer to pegylated liposomal DOXOrubicin drug monograph(s) for additional details.

Administration:

Pegylated liposomal doxorubicin is **not interchangeable** with other doxorubicin formulations.

- Pegylated liposomal doxorubicin is administered as an IV infusion.
- For dose < 90mg, dilute drug in 250mL D5W.
- For dose ≥ 90mg, dilute drug in 500mL D5W.
- Only use 5% Dextrose solution for further dilution. Use of other diluents or ones containing bacteriostatic agents (i.e. benzyl alcohol) may cause drug precipitation.
- Do not administer as a bolus injection or undiluted solution. The pegylated liposomal doxorubicin infusion line can be connected through the side port of a 5% Dextrose infusion for further diluent, or to minimize risk of thrombosis or extravasation.
- Do not use in-line filters. Do not admix with other drugs.
- To minimize the risk of infusion reactions, the initial dose is administered at a rate no greater than 1 mg/minute. If no infusion reaction is observed, subsequent infusions may be administered over 30 minutes (for Kaposi's sarcoma patients).
- The following graduated rate was used for patients who experienced an infusion reaction in the breast clinical trial: 5% of the total dose infused IV over 15 minutes. If tolerated, double the infusion rate for the next 15 minutes. If tolerated, complete the infusion over the next hour for a total infusion time of 90 minutes.
- Avoid extravasation. It may occur with or without an accompanying stinging or burning sensation, and even if blood returns well on aspiration of the infusion needle. 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.

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

Contraindications:

- patients who have a history of hypersensitivity reactions to a conventional formulation of doxorubicin, other anthracyclines, anthracenediones, or components of the pegylated liposome
- patients with Kaposi's Sarcoma and HIV who have had splenectomy (no experience)

Other Warnings/ Precautions:

- use with caution in patients with a history of cardiovascular disease and/or prior anthracycline use
- care should be exercised in patients with diabetes as the infusate is dextrose water
- pegylated liposomal doxorubicin is a unique formulation of doxorubicin and should never be used interchangeably with other formulations of doxorubicin

Pregnancy and Lactation:

- This regimen is **contraindicated** for use 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 **contraindicated** 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: Unknown

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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

- Cardiac function tests (Echo, RNA and/or MUGA scans) for all patients with cardiac risk factors; baseline and as clinically indicated. Regular cardiac function tests before each additional dose over the cumulative dose threshold of 450 mg/m^2. (Cumulative dose lower for high risk patients.)
- CBC; baseline and before each cycle
- Liver function tests; baseline and at each visit
- Clinical toxicity assessment for stomatitis, rash, hand-foot syndrome, hypersensitivity, infection, bleeding and cardiac symptoms; at each visit

- 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 hour
Pharmacy Workload (average time per visit)	19.371 minutes
Nursing Workload (average time per visit)	39.167 minutes

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K - References

Gill PS, Wernz J, Scadden DT, et al. Randomized phase III trial of liposomal daunorubicin versus doxorubicin, bleomycin, and vincristine in AIDS-related Kaposi's sarcoma. J Clin Oncol 1996;14:2353-64.

Northfelt DW, Dezube B, Miller B, et al. Randomized comparative trial of Doxil vs. Adriamycin, bleomycin, and vincristine (ABV) in the treatment of severe AIDS-related Kaposi's sarcoma (AIDS-KS) [abstract no. 1515]. Blood 1995; 86(10) suppl. 1: 382a

Osoba D, Northfelt DW, Budd DW et al. Effect of treatment on health-related quality of life in acquired immunodeficiency syndrome (AIDS)-related Kaposi's sarcoma: a randomized trial of pegylated –liposomal doxorubicin versus doxorubicin, bleomycin, and vincristine. Cancer Investigation 2001;19(6):573-80.

Pegylated liposomal doxorubicin drug monograph, Ontario Health (Cancer Care Ontario).

Stewart JSW, Jablonowski H, Goebel FD, et al. Randomized comparative trial of pegylated liposomal doxorubicin versus bleomycin and vincristine in the treatment of AIDS-related Kaposi's sarcoma. International Pegylated Liposomal Doxorubicin Study Group. J Clin Oncol 1998;16(2):683-91.

March 2025 Updated pregnancy/lactation section; added non-interchangeability statement

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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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