Regimen Monograph

Regimen Name | Drug Regimen | Cycle Frequency | Premedication and Supportive Measures | Dose Modifications | Adverse Effects | Interactions | Drug Administration and Special Precautions | Recommended Clinical Monitoring | Administrative Information | References | Other Notes | Disclaimer

A - Regimen Name

CISP(RT-W) Regimen

CISplatin (weekly)

Disease Site	Gynecologic - Cervix
Intent	Curative 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	• Primary treatment of cervical cancer with concurrent radiotherapy, including patients:
	  ◦ With locally advanced cervical cancer
	  ◦ With bulky clinical stage 1B (>4cm) cervical cancer, who are treated with radiotherapy
	  ◦ With high-risk early-stage cervical cancer (node positive or margin positive), who will be treated with radiotherapy following hysterectomy

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B - Drug Regimen

CISplatin[1]	40 mg /m²	IV	Day 1

[1] Some clinical trials used a maximum cisplatin dose of 70 mg.

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C - Cycle Frequency

REPEAT WEEKLY

Concurrently with Radiotherapy. Maximum of 6 weekly doses are usually given.

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D - Premedication and Supportive Measures

Antiemetic Regimen: Moderate

Febrile Neutropenia Risk: Low

Other Supportive Care:
Follow standard regimens for cisplatin premedication and hydration. Refer to Cisplatin monograph

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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 in Previous Cycle	Dose for next cycle*
Grade 4 platelets, grade 4 ANC ≥ 5 days, thrombocytopenic bleeding or febrile neutropenia	↓ 25%
Grade 2 Neurotoxicity /ototoxicity	↓ 25%
Grade 3 or 4 Neurotoxicity/ototoxicity	Discontinue
Other grade 3 non-hematologic/organ toxicity	↓ 25%
Other grade 4 non-hematologic/organ toxicity	Discontinue
Hemolysis, optic neuritis, arterial thromboembolism, severe hypersensitivity reactions, grade 3 or 4 ↑ LFTs	Discontinue
* do not retreat until platelets ≥ 100 $x10^9$/L, ANC ≥ 1.5 $x10^9$/L, toxicity has recovered to ≤ grade 2 (grade 1 for neurotoxicity) and creatinine ≤ ULN	

Hepatic Impairment

No adjustment required

Renal Impairment

In general, renal function should have normalized before patients are retreated. If continued treatment is considered to be mandatory, the following dose modifications could be considered at the physician's discretion:

Creatinine clearance	% previous dose
46-60	75%
30-45	50%
<30	Discontinue

Dosage in the Elderly

Geriatric patients may be at higher risk of developing nephrotoxicity, ototoxicity/neurotoxicity or hematologic adverse effects with cisplatin.

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F - Adverse Effects

Refer to CISplatin 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 • Nausea and vomiting • Nephrotoxicity (may be severe) • Electrolyte abnormalities • Neurotoxicity and ototoxicity (may be severe) • Hyperuricemia • Reproductive risk	• Arterial thromboembolism • Arrhythmia • Hemolytic uremic syndrome • Secondary malignancies • Seizures • Hypersensitivity • Hemolysis • Optic neuritis • Vasculitis

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G - Interactions

Refer to CISplatin drug monograph(s) for additional details

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H - Drug Administration and Special Precautions

Refer to CISplatin drug monograph(s) for additional details

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I - Recommended Clinical Monitoring

Recommended Clinical Monitoring

- CBC; baseline and regular
- Renal function tests; baseline and regular
- Electrolytes, including magnesium, sodium, potassium, phosphate and calcium; baseline and regular
- Audiogram; baseline and as clinically indicated
- Clinical toxicity assessment of infection, bleeding, nausea/vomiting, neurotoxicity, ototoxicity, thromboembolism; regular
- Grade toxicity using the current NCI-CTCAE (Common Terminology Criteria for Adverse Events) version

Suggested Clinical Monitoring

- Audiogram; periodic
- Liver function tests; baseline and regular

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J - Administrative Information

Approximate Patient Visit	2 to 3 hours
Pharmacy Workload (average time per visit)	21.749 minutes
Nursing Workload (average time per visit)	41.667 minutes

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K - References

DiSilvestro PA, Ali S, Craighead PS, et al. Phase III randomized trial of weekly cisplatin and irradiation versus cisplatin and tirapazamine and irradiation in stages IB2, IIA, IIB, IIIB, and IVA cervical carcinoma limited to the pelvis: a Gynecologic Oncology Group study. J Clin Oncol 2014;32(5):458-64.

Dueñas-González A, Zarbá JJ, Patel F, et al. Phase III, open-label, randomized study comparing concurrent gemcitabine plus cisplatin and radiation followed by adjuvant gemcitabine and cisplatin versus concurrent cisplatin and radiation in patients with stage IIB to IVA carcinoma of the cervix. J

Clin Oncol 2011 May 1;29(13):1678-85.

Keys HM, Bundy BN, Stehman FB, et al. Cisplatin, radiation and adjuvant hysterectomy compared with radiation and adjuvant hysterectomy for bulky stage IB cervical carcinoma. N Engl J Med 1999;340:1154-61.

Lanciano R, Calkins A, Bundy BN, et al. Randomized comparison of weekly cisplatin or protracted venous infusion of fluorouracil in combination with pelvic radiation in advanced cervix cancer: a gynecologic oncology group study. J Clin Oncol 2005 Nov 20;23(33):8289-95.

Pearcey R, Brundage M, Drouin P, et al. Phase III trial comparing radical radiotherapy with and without cisplatin chemotherapy in patients with advanced squamous cell cancer of the cervix. J Clin Oncol 2002;4:966-72.

Pu J, Qin S-s, Ding J-x, et al. A randomized controlled study of single-agent cisplatin and radiotherapy versus docetaxel/cisplatin and radiotherapy in high-risk early-stage cervical cancer after radical surgery. J Cancer Res Clin Oncol. 2013;139(4):703-8.

Rose PG, Bundy BN, Watkins EB, et al. Concurrent cisplatin-based radiotherapy and chemotherapy for locally advanced cervical cancer. N Engl J Med 1999;340:1144-53.

Ryu SY, Lee WM, Kim K, et al. Randomized clinical trial of weekly vs. triweekly cisplatin-based chemotherapy concurrent with radiotherapy in the treatment of locally advanced cervical cancer. Int J Radiat Oncol Biol Phys 2011 Nov 15;81(4):e577-81.

Sehouli J, Runnebaum IB, Fotopoulou C, et al. A randomized phase III adjuvant study in high-risk cervical cancer: simultaneous radiochemotherapy with cisplatin (S-RC) versus systemic paclitaxel and carboplatin followed by percutaneous radiation (PC-R): a NOGGO-AGO Intergroup Study. Ann Oncol 2012;23(9):2259-64.

Wang S, Zhang D-S, Pan T, et al. Efficacy of concurrent chemoradiotherapy plus adjuvant chemotherapy on advanced cervical cancer. Chin J Cancer. 2010;29(11):959-63.

Zuliani AC, Esteves SCB, Teixeira LC, et al. Concomitant cisplatin plus radiotherapy and high-dose-rate brachytherapy versus radiotherapy alone for stage IIIB epidermoid cervical cancer: a randomized controlled trial. J Clin Oncol 2014;32(6):542-7.

PEBC Advice Documents or Guidelines

- Primary Treatment for Locally Advanced Cervical Cancer: Concurrent Platinum-based Chemotherapy and Radiation

February 2021 Added additional references; modified Drug Regimen footnote

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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.

The format and content of the drug monographs, regimen monographs, appendices and symptom management information contained in the Formulary will change as they are reviewed and revised on a periodic basis. The date of last revision will be visible on each page of the monograph and regimen. Since standards of usage are constantly evolving, it is advised that the Formulary not be used as the sole source of information. It is strongly recommended that original references or product monograph be consulted prior to using a chemotherapy regimen for the first time.

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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