Regimen Monograph

A - Regimen Name

CISP(RT-W) Regimen

CISplatin (weekly)

Disease Site	Genitourinary - Bladder
Intent	Adjuvant 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	As a radiosensitizer concurrent with pelvic radiotherapy in patients with localized muscle invasive transitional cell bladder cancer, who decline cystectomy or who are not medically operable

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B - Drug Regimen

CISplatin	40 mg /m²	IV over 1 hour	Day 1

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C - Cycle Frequency

REPEAT WEEKLY

Concurrent with radiotherapy

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D - Premedication and Supportive Measures

Antiemetic Regimen: Moderate

Febrile Neutropenia Risk: Low

Other Supportive Care:

Standard regimens for Cisplatin premedication and hydration should be followed. 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. The following recommendations have been adapted from clinical trials or product monographs and could be considered.

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

Worst Toxicity in Previous Cycle	Dose for next cycle*
Hemolysis, optic neuritis, arterial thromboembolism, severe hypersensitivity reactions, grade 3 or 4 ↑ LFTs	Discontinue
* Do not retreat until platelets ≥100 x 10^9/L, ANC ≥ 1.5 x 10^9/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. (Continued on next page)

Creatinine clearance	% previous dose
46-60	75%
30-45	Hold or 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

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

Recommended Clinical Monitoring

- CBC; baseline and before each dose
- Renal function tests; baseline and before each dose
- 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; at each visit

- 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

Chung PW, Bristow RG, Milosevic MF, et al. Long-term outcome of radiation-based conservation therapy for invasive bladder cancer. Urol Oncol 2007 Jul-Aug;25(4):303-9.

Coppin CM, Gospodarowicz MK, James K, et. al. Improved local control of invasive bladder cancer by concurrent cisplatin and preoperative or definitive radiation. The National Cancer Institute of Canada Clinical Trials Group. J Clin Oncol 1996;14(11):2901-7.

Gogna NK, Matthews JH, Turner SL, et al. Efficacy and tolerability of concurrent weekly low dose cisplatin during radiation treatment of localised muscle invasive bladder transitional cell carcinoma: a report of two sequential Phase II studies from the Trans Tasman Radiation Oncology Group. Radiother Oncol 2006;81(1):9-17.

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.

Rödel C, Grabenbauer GG, Kühn R, et al. Combined-modality treatment and selective organ preservation in invasive bladder cancer: long-term results. J Clin Oncol 2002 Jul 15;20(14):3061-

71.

September 2017 added palliative intent as per ST-QBP

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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.

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