

**Regimen Monograph**

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**A - Regimen Name**

# CISP Regimen

CISplatin

**Disease Site**      Skin  
                            Squamous cell

**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.

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**B - Drug Regimen****CISplatin**50-75 mg /m<sup>2</sup>

IV

Day 1

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For a usual total of 6 cycles unless disease progression or unacceptable toxicity occurs

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**Antiemetic Regimen:** High ( $\geq 70$  mg/m<sup>2</sup>)  
Moderate ( $< 70$  mg/m<sup>2</sup>)

- 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.

**Other Supportive Care:**

- All patients should receive adequate hydration and premedication for emesis, according to local guidelines.

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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 $\geq$ 5 days, thrombocytopenic bleeding or febrile neutropenia	↓ 25%
Grade 2 neurotoxicity/ototoxicity	↓ 25% or discontinue depending on risk-benefit
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 or venous thromboembolism, grade 3 or 4 ↑ LFTs, PRES, leukoencephalopathy	Discontinue
* Do not retreat until platelets $\geq$ 100 x 10 <sup>9</sup> /L, ANC $\geq$ 1.5 x 10 <sup>9</sup> /L, toxicity has recovered to $\leq$ grade 2 (grade 1 for neurotoxicity) and creatinine $\leq$ ULN.	

### Management of Infusion-related reactions:

Also refer to the CCO guideline for detailed description of [Management of Cancer Medication-Related Infusion Reactions](#).

There is insufficient evidence that routine prophylaxis with extended infusion reduces IR rates.

Grade	Management	Re-challenge
1 or 2	<ul style="list-style-type: none"> <li>Stop or slow the infusion rate.</li> <li>Manage the symptoms.</li> </ul> <p><b>Restart:</b></p> <ul style="list-style-type: none"> <li>After symptom resolution, restart with pre-medications <math>\pm</math> reduced infusion rate.</li> </ul>	<ul style="list-style-type: none"> <li>Consider pre-medications* and infusing at a reduced infusion rate prior to re-challenge.</li> <li>May consider adding oral montelukast <math>\pm</math> oral acetylsalicylic acid.</li> </ul>

3 or 4	<ul style="list-style-type: none"> <li>• Stop treatment.</li> <li>• Aggressively manage symptoms.</li> </ul>	<ul style="list-style-type: none"> <li>• Re-challenge is discouraged, especially if vital signs have been affected.</li> <li>• Consider desensitization if therapy is necessary.</li> </ul>
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\* Up to 50% of patients can experience recurrent reactions during re-challenge **despite** using pre-medications (e.g. corticosteroid and H1/H2-receptor antagonist).

### **Hepatic Impairment**

No adjustment required.

### **Renal Impairment**

Refer to specific protocol.

A repeat course of Cisplatin should not be given until creatinine is  $\leq$  ULN. If continued treatment is considered to be mandatory, the following dose modifications could be considered at the physician's discretion (Kintzel 1995):

Creatinine Clearance	% Previous Dose
46-60	75%
30-45	50%*
<30	Discontinue

\*if clinically appropriate, consider discontinuing or using alternative (i.e. carboplatin).

### **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.

Very common (≥ 50%)	Common (25-49%)	Less common (10-24%)	Uncommon (< 10%), but may be severe or life-threatening
<ul style="list-style-type: none"> <li>• Nausea, vomiting (may be severe)</li> </ul>	<ul style="list-style-type: none"> <li>• Ototoxicity (may be severe)</li> <li>• Nephrotoxicity (may be severe)</li> <li>• Myelosuppression +/- bleeding, infection</li> <li>• Neurotoxicity (may be severe)</li> <li>• Electrolyte abnormalities</li> </ul>	<ul style="list-style-type: none"> <li>• ↑ LFTs</li> </ul>	<ul style="list-style-type: none"> <li>• Arterial / venous thromboembolism</li> <li>• Conduction disorder</li> <li>• Hemolytic uremic syndrome</li> <li>• Hypersensitivity</li> <li>• Injection site reaction</li> <li>• Secondary malignancy</li> <li>• PRES</li> <li>• Leukoencephalopathy</li> <li>• Seizures</li> <li>• Optic neuritis / other eye disorders</li> <li>• Hyperuricemia</li> <li>• Raynaud's</li> <li>• Vasculitis</li> <li>• SIADH</li> </ul>

**The following adverse reactions (incidence unknown) have been identified from clinical trials or post-marketing surveillance:**

Dermatological: Alopecia, rash

Gastrointestinal: Diarrhea, mucositis

General: Fatigue

Hematological: Hemolysis (Coombs positive)

Hepatobiliary: ↑ Amylase, ↑ LFTs (transient)

Musculoskeletal: Muscle cramps, Musculoskeletal pain

Nervous System: Dysgeusia

Respiratory: Hiccups

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## G - Interactions

Refer to [Cisplatin](#) drug monograph(s) for additional details.

- Ascertain renal function prior to giving renally excreted drugs; monitor for toxicity.
- Avoid nephrotoxic drugs; use with extreme caution during or shortly after cisplatin treatment (1 to 2 weeks).
- Avoid concomitant use of ototoxic drugs; use with extreme caution if essential.
- Monitor INR (with warfarin) and serum levels for lithium and anticonvulsant agents (valproic acid, carbamazepine, phenytoin); adjust dose if necessary.

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## H - Drug Administration and Special Precautions

Refer to [Cisplatin](#) drug monograph(s) for additional details.

### Administration:

- Cisplatin is physically incompatible with any IV set, needle or syringe containing aluminum.
- Drug dilution and infusion durations vary according to the regimen. Some centres dilute cisplatin in 500 to 1000 mL of NS, depending on the dose.
- All patients should receive adequate hydration and premedication for emesis, according to local guidelines.
- Additional hydration may be ordered for hypovolemic patients.
- Hydration and diuresis for patients with pre-existing renal, cardiac, or diabetic history at discretion of physician.
- Adequate hydration and urinary output must be maintained for 24 hours following cisplatin treatment.
- Oral hydration with 8 glasses of fluid per day is strongly encouraged on treatment day and for 1-2 days after cisplatin; if nausea and vomiting prevent oral hydration, the patient may need to return for more IV hydration.

- Store unopened vials between 15°C to 25°C and protect from light. Do not refrigerate or freeze since precipitation will occur.

Also refer to the CCO guideline for detailed description of [Management of Cancer Medication-Related Infusion Reactions](#).

### Contraindications:

- Patients with known severe hypersensitivity to platinum containing compounds
- Patients who are myelosuppressed
- Patients with pre-existing renal impairment and hearing impairment, unless the possible benefits of treatment outweigh the risks

### Pregnancy/Lactation:

- Cisplatin is not recommended for use in pregnancy.
  - Adequate contraception should be used by both sexes during treatment, and for at least **26 weeks** (in females) and **14 weeks** (in males) after the last dose.
  - For patients with end-stage renal disease, adequate contraception should be used during treatment, and for **31 weeks** (in females) and **19 weeks** (in males) after the last dose, due to a longer cisplatin washout period.
  - Male patients should not donate semen while using cisplatin and up to **2 years** after the last dose.
- Breastfeeding is not recommended as cisplatin is secreted into breast milk.
- 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.

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### Recommended Clinical Monitoring

- CBC; Baseline and at each cycle
- Renal function tests; Baseline and at each cycle
- Electrolytes, including magnesium, sodium, potassium, phosphate and calcium; Baseline and at each cycle
- Audiogram; Baseline and as clinically indicated
- Liver function tests; Baseline and as clinically indicated
- Clinical toxicity assessment of injection site reactions, infection, bleeding, nausea/vomiting, neurotoxicity, ototoxicity, ocular toxicity, arterial and venous thromboembolism; At each cycle
- Grade toxicity using the current [NCI-CTCAE \(Common Terminology Criteria for Adverse Events\) version](#)

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### **J - Administrative Information**

Approximate Patient Visit	2 to 3 hours
Pharmacy Workload (average time per visit)	36.087 minutes
Nursing Workload (average time per visit)	41.667 minutes

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### **K - References**

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

Guthrie TH Jr, Porubsky ES, Luxenberg MN, et al. Cisplatin-based chemotherapy in advanced basal and squamous cell carcinomas of the skin: results in 28 patients including 13 patients receiving multimodality therapy. J Clin Oncol 1990;8(2):342-6.

**April 2023** Modified Dosage in renal impairment, Interactions and Pregnancy/lactation sections

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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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