Regimen Monograph

A - Regimen Name

CISPDOCEFU Regimen

CISplatin-DOCEtaxel-Fluorouracil

Disease Site	Head and Neck
Intent	Neoadjuvant
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	Induction Chemotherapy (prior to radiotherapy / chemoradiotherapy) in locally advanced, unresectable head and neck cancer, for patients with ECOG status 0 to 1 and no prior chemotherapy or radiotherapy.

back to top

B - Drug Regimen

DOCEtaxel (Round to nearest 1 mg)	75 mg /m²	IV	Day 1
CISplatin (Round to nearest 1 mg)	100 mg /m²	IV	Day 1

fluorouracil (Round to nearest 50 mg)	1000 mg /m²/day	IV over 24 hours as continuous infusion	Days 1 to 4

Alternative schedule:

DOCEtaxel (Round to nearest 1 mg)	75 mg /m²	IV	Day 1
CISplatin (Round to nearest 1 mg)	75 mg /m²	IV	Day 1
fluorouracil (Round to nearest 50 mg)	750 mg /m²	IV over 24 hours as continuous infusion	Days 1 to 5

back to top

C - Cycle Frequency

REPEAT EVERY 21 DAYS

For a usual total of 4 cycles unless disease progression or unacceptable toxicity occurs

back to top

D - Premedication and Supportive Measures

Antiemetic Regimen: High (with cisplatin day 1)
Minimal (fluorouracil ONLY days)

Febrile Neutropenia Risk: High

Consider G-CSF prophylaxis for patients at high risk of febrile neutropenia. See G-CSF recommendations.

Other Supportive Care:

- Dexamethasone 8 mg bid po for 3 days starting 1 day prior to docetaxel (prevent anaphylaxis/

fluid retention.)
- In clinical trials, all patients received prophylactic antibiotics from days 5 to 15.
- Use standard regimens for cisplatin pre-medication and hydration. See Cisplatin monograph.

Also refer to CCO Antiemetic Summary

back to top

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

Toxicity Type/ Counts x 10^9/L		Toxicity Type/ Counts x 10^9/L	Docetaxel* (% previous dose)	Cisplatin* (% previous dose)	Fluorouracil* (% previous dose)
Febrile neutropenia	Or	Grade 4 neutropenia / thrombocytopenia	Hold, then 75% *	Hold, then 75% *	Hold, then 75%*
Grade 2 neurotoxicity or ototoxicity			No change; monitor	Consider dose reduction	No change
Grade 3 neurotoxicity or ototoxicity			Discontinue	Discontinue	Discontinue
Grade 3 mucositis or diarrhea			No change	No change	66%*
Grade 2 or 3 hand-foot syndrome			No change	No change	66%*
Grade 3 skin reactions			75%*; discontinue if recurs	No change	66%*
Any occurrence of cystoid macular edema			Hold and investigate; refer patient promptly to an ophthalmic examination. Discontinue if confirmed.	No change	No change

Other Grade 3 non-hematologic / organ#			Hold*, then 75%	Hold*, then 75%	Hold*, then 75%
Grade 4 non-hematologic / organ			Discontinue	Discontinue	Discontinue

*Major organ toxicity should have recovered to ≤ grade 1, ANC ≥ 1.5 x 10^9/L and platelets ≥ 100 x 10^9/L prior to retreatment. Modify the agent to which the toxicity is considered related.
Except for alopecia, fatigue, nail changes

Hepatic Impairment

	AST and/ or ALT		**Alk Phosp**		**Bilirubin**	**Cisplatin**	**Docetaxel (% previous dose)**	**Fluorouracil (% previous dose)**
Mild-moderate	> 1.5 X ULN	AND	> 2.5 x ULN			No change	Do not treat	
Severe	> 3.5 x ULN	OR	> 6 x ULN	OR	> ULN		Do not treat. Discontinue if treatment already started.	
					> 4 ULN			Discontinue

Renal Impairment

Creatinine clearance	**Cisplatin (% previous dose)**	**Fluorouracil (% previous dose)**	**Docetaxel**
46-60	75%	No change	No change
30-45	50%	No change	No change
<30	Discontinue	Consider ↓	No change

Dosage in the Elderly

No adjustment required, but caution should be exercised in elderly patients with poor performance status who are receiving docetaxel.

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

back to top

F - Adverse Effects

Refer to DOCEtaxel, CISplatin, fluorouracil drug monograph(s) for additional details of adverse effects

Prolonged 5FU regimens have more Hand-Foot Syndrome but less myelosuppression and GI effects compared to bolus infusions.

Most Common Side Effects	Less Common Side Effects, but may be Severe or Life-Threatening
• Myelosuppression ± infections, bleeding (may be severe) • Hypersensitivity reactions (may be severe) • Fluid retention (may be severe) • Neuropathy, ototoxicity (may be severe) • Cutaneous effects • Alopecia • GI (nausea, stomatitis, diarrhea) • Rash (may be severe) • Musculoskeletal pain (may be severe) • Nephrotoxicity • Fatigue • Hand-foot syndrome • Lacrimation/ lacrimal duct obstruction	• Secondary malignancies • Pneumonitis • Arterial thromboembolism • Venous thromboembolism • GI obstruction / perforation • DIC • Arrhythmia, heart failure • Thrombotic microangiopathy, hemolytic uremic syndrome • Raynaud's syndrome • Cystoid macular edema

back to top

G - Interactions

Refer to DOCEtaxel, CISplatin, fluorouracil drug monograph(s) for additional details

back to top

H - Drug Administration and Special Precautions

Refer to DOCEtaxel, CISplatin, fluorouracil drug monograph(s) for additional details

back to top

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 cycle
- Baseline and regular renal function tests (including electrolytes and magnesium) and urinalysis
- Baseline and regular liver functions tests
- Clinical toxicity assessment (including neurologic, GI, ototoxicity, hypersensitivity, lethargy, fluid retention, cutaneous effects, infection, bleeding, musculoskeletal pain, thromboembolism, ophthalmic, respiratory); at each visit

- Grade toxicity using the current NCI-CTCAE (Common Terminology Criteria for Adverse Events) version

back to top

J - Administrative Information

Approximate Patient Visit	Day 1: 5-6 hours; 5FU only days: 0.5 hour
Pharmacy Workload (average time per visit)	37.412 minutes
Nursing Workload (average time per visit)	92.083 minutes

back to top

K - References

Cisplatin, docetaxel, fluorouracil drug monographs, Cancer Care Ontario.

Posner MR, Hershock DM, Blajman CR, et al. Cisplatin and Fluorouracil Alone or with Docetaxel in Head and Neck Cancer. N Engl J Med 2007; 357: 1705-15.

Vermorken JB, Remenar E, Van Herpen C et al. Cisplatin, Fluorouracil, and Docetaxel in Unresectable Head and Neck Cancer. N Engl J Med 2007; 357: 1695-704.

PEBC Advice Documents or Guidelines

- The Management of Head and Neck Cancer in Ontario
- Systemic Therapy in the Curative Treatment of Head and Neck Squamous Cell Cancer

February 2017 Added PEBC guideline link

back to top

M - Disclaimer

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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back to top