Regimen Monograph

A - Regimen Name

CETU Regimen

Cetuximab

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.

Rationale and Uses

For the treatment of locally advanced, unresectable or metastatic squamous cell carcinoma of the skin.

Note: Recommendation based on a single arm phase II study in 36 patients with a response rate of 28%; two prolonged complete responses were reported. Nine of 10 responding patients had local or regional disease only.

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B - Drug Regimen

Loading Dose:

cetuximab	400 mg /m²	IV	Week 1

(This drug is not currently publicly funded for this regimen and intent)

THEN Maintenance Doses (Week 2 and onwards):

cetuximab	250 mg /m²	IV	Week 2 and onwards

(This drug is not currently publicly funded for this regimen and intent)

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C - Cycle Frequency

For maintenance dose:

REPEAT WEEKLY

Until disease progression or unacceptable toxicity.

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D - Premedication and Supportive Measures

Antiemetic Regimen: Minimal

- 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.

Premedications (prophylaxis for infusion reaction):

- H1-receptor antagonist (e.g. diphenhydramine 50 mg IV) 30-60 minutes prior to the dose.
- Corticosteroid IV 30-60 minutes prior to the dose.
- Consider discontinuing pre-medications after the 2nd infusion based on clinical judgment and the presence/severity of IR.

Other Supportive Care:

- Patients should use sun protection while receiving cetuximab and for 2 months after treatment completion.
- Consider pre-emptive therapy for EGFR inhibitor-related skin toxicity; the following was shown to be of benefit with panitumumab treatment, starting the day before treatment and continued until week 6. (Lacouture et al, 2010):
  - Skin moisturizer applied to the face, hands, feet, neck, back and chest in the morning
  - Sunscreen to exposed areas (SPF ≥ 15, UVA and UVB) before going outdoors
  - Hydrocortisone 1% cream to the face, hands, feet, neck, back and chest at bedtime
  - Doxycycline (or minocycline) PO
- Refer to the Canadian recommendations for the management of skin rash during EGFR-targeted monoclonal antibody treatment for GI malignancies. (Melosky et al, 2009)

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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

Dose Level	Cetuximab Dose (mg/m² weekly)
0	250
-1	200
-2	150
-3	Discontinue

Toxicity	Action	Next cycle
Pneumonitis	Hold and investigate	Discontinue if confirmed.
Keratitis	Hold and refer to ophthalmologist	Consider discontinuation.

Dosage modification for skin toxicity:

Grade 3 or 4 Rash	Action	Outcome	Cetuximab Dose
1st occurrence	Delay infusion 1 to 2 weeks	Improvement	Resume at same dose
		No improvement	Discontinue
2nd occurrence	Delay infusion 1 to 2 weeks	Improvement	Resume at 1 dose level ↓
		No improvement	Discontinue
3rd occurrence	Delay infusion 1 to 2 weeks	Improvement	Resume at 1 dose level ↓
		No improvement	Discontinue
4th occurrence OR any occurrence of SJS/TENS	Discontinue		

Management of Infusion-related reactions:

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. **Restart:** • The infusion may be restarted at a slower rate (50% of the rate at which the IR occurred) once symptoms have resolved.	• Re-challenge with a reduced infusion rate of 50% at which the infusion reaction occurred.
3 or 4	• Stop treatment. • Aggressively manage symptoms. **Restart:** • Once symptoms resolve, the infusion can be restarted at a slower rate, unless a serious reaction occurred (i.e., vital signs compromised; anaphylaxis).	• Permanently discontinue (do not re-challenge).

Hepatic Impairment

Population pharmacokinetics suggest no significant impact.

Renal Impairment

Population pharmacokinetics suggest no significant impact.

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F - Adverse Effects

Refer to cetuximab 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
• Rash (may be severe) • Fatigue • Anorexia • Nausea, vomiting • Abdominal pain • Constipation	• Neuropathy • Cough, dyspnea • Hypomagnesemia • Infection (may be severe) • Diarrhea • Headache • Mucositis • Insomnia • Nail disorder	• Flu-like symptoms • Infusion-related reaction (may be severe) • Mood changes, Confusion • Musculoskeletal pain • Dry mouth • Increased LFTs • Dizziness • Dysgeusia	• Hemorrhage • Arterial/venous thromboembolism • Arrhythmia • GI obstruction/perforation • Pancreatitis • Pneumonitis • Keratitis • Nephrotoxicity • Stevens-Johnson syndrome • Toxic epidermal necrolysis

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G - Interactions

Refer to cetuximab drug monograph(s) for additional details.

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H - Drug Administration and Special Precautions

Refer to cetuximab drug monograph(s) for additional details.

Administration:

- Do not shake or further dilute the solution.
- DO NOT administer as an IV push or bolus.
- Transfer undiluted solution into a compatible empty infusion container.
- Cetuximab is compatible with:
  - glass,
  - polyolefin, polyethylene, ethylene vinyl acetate (EVA), DEHP plasticized PVC, or PVC bags,
  - polyethylene, EVA, PVC, polybutadiene or polymethane infusion sets, and
  - polyethersulfone, polyamide or polysulfone in-line filters.
- Administer the undiluted solution via a low protein binding 0.22-micrometer in-line filter, piggybacking to the patient's infusion line.
- Infuse initial loading dose over 2 hours, and maintenance dose over 1 hour (maximum rate 10 mg/min). (May require infusion at slower rate in those who experienced infusion reactions).
- Prime administration line with drug solution before infusion. May use NS to flush line at the end of infusion.
- A 1-hour observation period is recommended following each cetuximab infusion. Longer observation periods may be required in those who experienced infusion reactions.
- Should not be mixed or diluted with other drugs.
- Store unopened vials at 2-8°C.

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

Contraindications:

- Patients with known hypersensitivity to this drug or any of its components

Other Warnings/Precautions:

- Patients with a history of, or pre-existing keratitis, dry eyes or contact lens use
- Patients with poor performance status, or cardiopulmonary disease are at increased risk of severe hypersensitivity

Pregnancy/Lactation:

- This regimen is not recommended 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 not recommended during 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

- Electrolytes, including serum magnesium, potassium and calcium; Baseline, weekly, and monthly for 2 months following completion of therapy
- CBC; Baseline and as clinically indicated
- Renal function; Baseline and as clinically indicated
- Clinical toxicity assessment for infusion reactions, skin, nail, cardiac, thromboembolism, GI, hypersensitivity, respiratory symptoms, fatigue and keratitis; 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	First cycle; 2.5 hours; Subsequent cycles: 1.5 hours
Pharmacy Workload (average time per visit)	24.85 minutes
Nursing Workload (average time per visit)	55.595 minutes

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K - References

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

Lacouture, ME, Mitchell EP, Piperdi B et al. Skin toxicity evaluation protocol with panitumumab (STEPP), a phase II, open-label, randomized trial evaluating the impact of a pre-emptive skin treatment regimen on skin toxicities and quality of life in patients with metastatic colorectal cancer. J Clin Oncol 2010; 28: 1351-7.

Maubec E, Petrow P, Scheer-Senyarich I, et al. Phase II study of cetuximab as first-line single-drug therapy in patients with unresectable squamous cell carcinoma of the skin. J Clin Oncol 2011;29(25):3419-26.

Melosky B, Burkes R, Rayson D, et al. Management of skin rash during EGFR-targeted monoclonal antibody treatment for gastrointestinal malignancies: Canadian recommendations. Current Oncology 2009; 16(10): 14-24.

July 2023 Updated other supportive care, adverse effects, administration, special precautions, and monitoring 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

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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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