Regimen Monograph

A - Regimen Name

PNTM Regimen

Panitumumab

Disease Site

Gastrointestinal
- Colorectal
- Small bowel and appendix

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 patients with RAS wild-type metastatic colorectal, small bowel or appendiceal cancer, after disease progression of chemotherapy regimens containing oxaliplatin and irinotecan.

Supplementary Public Funding

PANitumumab
New Drug Funding Program (Panitumumab - Metastatic Colorectal Small Bowel or Appendiceal Cancer) (NDFP Website)

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B - Drug Regimen

PANitumumab	6 mg /kg	IV	Day 1

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C - Cycle Frequency

REPEAT EVERY 14 DAYS

Continue until evidence of 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.

Other Supportive Care:

- As sun exposure may exacerbate skin reactions, patients should be advised to use sunscreen, wear a hat and limit sun exposure.
- The following has been shown to be of benefit when used from the day before treatment to 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 product monograph and Canadian recommendations for the management of skin rash during EGFR-targeted monoclonal antibody treatment for GI malignancies. (Melosky 2009)

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E - Dose Modifications

Doses should be modified according to the protocol by which the patient is being treated.

RAS wild type status should be confirmed by validated test prior to starting treatment.

Dosage with toxicity

Toxicity	Action^	Dose Modification (% previous dose)
≥ grade 3 skin (1st occurrence)	Hold until ≤ grade 2*	Restart at 100%
≥ grade 3 skin (2nd occurrence)	Hold until ≤ grade 2*	Restart at 80%
≥ grade 3 skin (3rd occurrence)	Hold until ≤ grade 2*	Restart at 60%
≥ grade 3 skin (4th occurrence)	Discontinue	n/a
Skin or soft tissue with severe or life-threatening inflammatory or infectious complications	Hold or discontinue, depending on severity	n/a
SJS/TEN	Discontinue	n/a
≥ grade 3 diarrhea or dehydration	Hold until ≤ grade 2	Consider dose reduction, if appropriate
ILD/pneumonitis	Hold and investigate	If confirmed, discontinue.
Keratitis or ulcerative keratitis	Hold or discontinue, depending on severity or persistence	n/a
*Hold for 1 to 2 doses until recovery. Discontinue if no recovery within 4 weeks. ^For treatment of skin reactions, may refer to the Canadian recommendations for the management of skin rash during EGFR-targeted monoclonal antibody treatment for GI malignancies (Melosky 2009).		

Management of Infusion 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 the infusion. • Manage the symptoms. **Restart:** • Restart the infusion at 50% of the rate at which the IR occurred.	• Re-challenge the infusion at 50% of the rate at which the IR occurred.
3 or 4	• Stop the infusion • Aggressively manage symptoms.	• Discontinue permanently (do not re-challenge).

Hepatic Impairment

The safety and efficacy of panitumumab have not been studied in hepatic impairment.

Renal Impairment

The safety and efficacy of panitumumab have not been studied in renal impairment. Acute renal failure has been observed in patients experiencing severe diarrhea and dehydration (see dosage with toxicity table for management).

Dosage in the Elderly

No dose modifications are required. No overall differences in safety or efficacy were observed for monotherapy in patients aged 65 and older compared to younger patients.

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F - Adverse Effects

Refer to panitumumab 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 and/or soft tissue toxicity (may be severe)	• Fatigue • Paronychia • Anorexia	• Constipation • Diarrhea (may be severe) • Skin fissures • Cough, dyspnea • Nausea, vomiting • Musculoskeletal pain • Edema	• Pneumonitis • Abnormal electrolytes (↓ Mg, Ca, K) (may be delayed) • Venous thromboembolism • Hypersensitivity • Renal failure • GI obstruction • Hemorrhage • Ulcerative keratitis • Soft tissue / skin necrosis • Stevens-Johnson syndrome • Toxic epidermal necrolysis

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G - Interactions

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

Interactions with other drugs, food, herbal products, and laboratory tests have not been established.

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H - Drug Administration and Special Precautions

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

Administration:

- DO NOT administer as an IV push or bolus; MUST be administered using an IV infusion pump.
- Diluted with 0.9% sodium chloride only. Do not mix with other drugs or IV solutions.
- Dilute in a total volume of 100mL in sodium chloride 0.9% (Final concentration must be ≤ 10mg/mL). Infuse IV over 60 minutes. May give via peripheral line or in-dwelling catheter. If the first infusion is tolerated, subsequent infusions may be given over 30 to 60 minutes.
- Doses higher than 1000mg should be diluted in 150mL 0.9% sodium chloride injection, and infused IV over 90 minutes.
- Compatible with 0.9% sodium chloride in PVC bags or polyolefin bags
- Administer using a low-protein binding 0.2 micron or 0.22 micron in-line filter.
- Solution may contain a small amount of visible, amorphous, panitumumab particulates that will be removed by the low protein binding in-line filter during infusion.
- Do not shake. Mix diluted solution by gentle inversion.
- Flush line before and after administration with 0.9% sodium chloride.
- Missed Dose: Panitumumab should be given within 3 days of scheduled dose. If a dose is missed, it should be administered as soon as possible and the next dose should be given on a new schedule relative to last administered dose.
- Keep unopened vials refrigerated (2 to 8°C) in the original carton. Protect from direct sunlight and do not freeze.

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

Contraindications:

- Patients who have a hypersensitivity to this drug or any of its components
- Panitumumab is NOT indicated for patients with RAS mutant mCRC or for whom RAS mutation status is unknown.

Other Warnings/Precautions:

- Consider risks and benefits before starting treatment in patients with a history of pulmonary fibrosis or ILD. These patients were excluded from clinical trials.
- In a phase III panitumumab trial, patients with ECOG 2 had increased toxicity and shortened survival compared to those with ECOG 0-1. Assess risk vs. benefit prior to treatment in patients with ECOG 2.
- Use with caution in patients with a history of keratitis, ulcerative keratitis, or severe dry eye. Contact lens use is also a risk factor for keratitis and ulceration.

- If patients experience treatment-related effects on vision and/or ability to concentrate and react, they should not drive or operate machinery until the effect subsides.
- The panitumumab formulation contains 0.15 mmol sodium (= 3.45 mg sodium) per mL of concentrate. This sodium content should be taken into consideration in patients on sodium restriction.

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: Probable

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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 calcium, magnesium and potassium); Baseline, before each dose, and monthly for 8 weeks after completion of therapy
- CBC; Baseline and as clinically indicated
- Liver function tests; Baseline and as clinically indicated
- Renal function tests; Baseline and as clinically indicated
- Clinical pulmonary exam; Baseline and as clinically indicated
- Clinical toxicity assessment (including infusion reactions, dermatological, gastrointestinal, dehydration, pulmonary, ophthalmic).; 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	1 hour
Pharmacy Workload (average time per visit)	17.887 minutes
Nursing Workload (average time per visit)	40.75 minutes

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K - References

Amado RG, Wolf M, Peeters M, et al. Wild-type KRAS is required for panitumumab efficacy in patients with metastatic colorectal cancer. J Clin Oncol 2008; 26: 1626-34.

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.

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.

National Comprehensive Cancer Network. Colon Cancer (Version 2.2017). https://www.nccn.org/professionals/physician_gls/pdf/colon.pdf. Accessed June 30, 2017.

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

Van Custem E, Siena S, Humblet Y, et al. An open-label, single-arm study assessing safety and efficacy of panitumumab in patients with metastatic colorectal cancer refractory to standard chemotherapy. Annals of Oncology 2008; 19: 92-8.

Van Cutsem E, Peeters M, Siena S, et al. Open-label phase III trial of panitumumab plus best supportive care compared with best supportive care alone in patients with chemotherapy-refractory metastatic colorectal cancer. J Clin Oncol 2007; 25: 1658-64.

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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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