Regimen Monograph

A - Regimen Name

NIRP Regimen

Niraparib

Disease Site

Gynecologic
Ovary

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

For the treatment of newly diagnosed or recurrent high grade epithelial, ovarian, fallopian tube or primary peritoneal cancer as maintenance in patients with good performance status, who have achieved complete or partial radiological response
(Refer to EAP for full funding criteria)

Supplementary Public Funding

niraparib
Exceptional Access Program (niraparib - For the maintenance treatment of newly diagnosed or recurrent high grade epithelial ovarian, fallopian tube, or primary peritoneal cancer, according to clinical criteria) (EAP Website)

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B - Drug Regimen

To start within 12 weeks of completing chemotherapy.†

Patients <77 kg **or** with a platelet count <150 x 10^9/L:*

niraparib	200 mg	PO	Daily

Patients ≥77 kg **and** with a platelet count ≥150 x 10^9/L:*

niraparib	300 mg	PO	Daily

*based on pCODR, Berek et al

† Disease progression should be excluded before starting niraparib, if > 8 weeks have elapsed from last chemotherapy treatment.

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C - Cycle Frequency

CONTINUOUS TREATMENT

Maintenance for recurrent disease: Until disease progression or unacceptable toxicity

First-line maintenance: Funding will be considered until disease progression or toxicity, OR up to a maximum of 3 years if there is no evidence of disease recurrence

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D - Premedication and Supportive Measures

Antiemetic Regimen: Moderate – Consider prophylaxis daily

Other Supportive Care:

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.

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E - Dose Modifications

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

Patients should have recovered from hematologic toxicities (≤ grade 1) from previous chemotherapy prior to initiating niraparib treatment.

Existing hypertension should be adequately controlled before initiating niraparib treatment.

Dosage with toxicity

Dose Level	Niraparib Dose (mg/day)	
0	200	300
-1	100	200
-2	Discontinue	100
-3		Discontinue

Toxicity	Criteria	Action
Platelet count <100 x 10^9/L	First occurrence	Hold. Monitor blood counts weekly* Resume at same dose or at 1 dose level ↓. If platelet count was <75 x 10^9/L, resume at 1 dose level ↓.
	Second occurrence	Hold. Monitor blood counts weekly.* Resume at 1 dose level ↓.
Neutrophil <1 x 10^9/L		Hold. Monitor blood counts weekly.* Resume at 1 dose level ↓.

Hemoglobin <80 g/L		Hold. Monitor blood counts weekly.* Resume at 1 dose level ↓.
Hematologic adverse reaction requiring transfusion or hematopoietic growth factor support		Hold. Consider platelet transfusion for platelets ≤10 x 10^9/L. If other risk factors are present (e.g., coadministration of anticoagulation or antiplatelet drugs), consider interruption of concurrent therapy and/or transfuse at a higher platelet count. Resume at 1 dose level ↓.
Signs and symptoms of myelodysplastic syndrome or acute myeloid leukemia (MDS/AML)	Any	If MDS/AML is confirmed, discontinue
Hypertension	Not adequately controlled with antihypertensive therapy Or Hypertensive crisis	Discontinue
Signs and symptoms of Posterior Reversible Encephalopathy Syndrome (PRES)	Any	Treat specific symptoms and discontinue
All other non-hematologic toxicities that persists despite treatment/prophylaxis	≥ Grade 3	Hold.* Resume at same dose or at 1 dose level ↓.

*Do not restart until platelets ≥100 x 10^9/L, ANC ≥1.5 x 10^9/L, Hb ≥90 g/L and other toxicities have resolved. Discontinue if toxicities have not recovered within 28 days of dose interruption. If blood parameters remain abnormal after 28 days, bone marrow analysis and/or blood cytogenetic analysis are recommended.

Hepatic Impairment

Hepatic Impairment	Bilirubin		AST	Niraparib Dose
Mild	≤1.5xULN	and	any	No dose adjustment required
	≤ULN	and	>ULN	
Moderate	>1.5 to 3 xULN	and	any	↓ 1 dose level
Moderate or Severe	>3xULN	and	any	Has not been studied

Renal Impairment

Creatinine Clearance (mL/min)	Niraparib Dose
≥ 30	No dose adjustment required
< 30 or ESRD	Has not been studied

Dosage in the Elderly

No dose adjustment required. No overall differences in safety and effectiveness of niraparib were observed between patients ≥ 65 years old and younger but greater sensitivity of some older patients cannot be ruled out.

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F - Adverse Effects

Refer to niraparib 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
• Myelosuppression ± infection (including anemia) • Nausea, vomiting	• Fatigue • Musculoskeletal pain • Constipation • Abdominal pain	• Headache • Insomnia • Mucositis • Anorexia • Cough, dyspnea • Dyspepsia • Hypertension • Diarrhea • Acute kidney injury (↑ creatinine/urea, renal failure) • Dizziness • Hot flashes • Dysgeusia • Palpitations	• Hypersensitivity • GI obstruction • RPLS / PRES • Secondary Leukemia (MDS/AML) • Pneumonitis • Cognitive disturbance, hallucinations

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G - Interactions

Refer to niraparib drug monograph(s) for additional details

No formal drug interaction studies have been performed with niraparib.

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H - Drug Administration and Special Precautions

Refer to niraparib drug monograph(s) for additional details

Administration

- Niraparib should be taken with or without food at approximately the same time each day. (Bedtime administration may help manage nausea).
- The dose should be swallowed whole, not chewed, crushed, or split.
- If a dose of niraparib is missed, patients should take the next dose at the regularly scheduled time. Patients should not take an additional dose if vomiting or missed doses occur.
- Store at a temperature up to 25°C.

Contraindications

- Patients who have a hypersensitivity to the drug or to any of its components or components of the container.

Other Warnings/Precautions

- Niraparib has moderate influence on the ability to drive or use machines. Caution should be exercised when driving or operating a vehicle or potentially dangerous machinery due to fatigue and dizziness.
- Patients should be counselled to avoid sun exposure when possible while on treatment.
- Niraparib capsules contain tartrazine (FD&C Yellow #5), which may cause allergic-type reactions.
- Niraparib capsules and tablets contain lactose; carefully consider use in patients with hereditary galactose intolerance, severe lactase deficiency or glucose-galactose malabsorption.

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 **contraindicated** during this treatment and after the last treatment dose. Refer to the drug monograph(s) for recommendations after the last treatment dose (if available).
- Fertility Effects: Documented in male animals

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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

- CBC; Baseline and weekly for the first month of treatment then monthly for the next 11 months and as clinically indicated
- Blood pressure and heart rate; Baseline and at minimum weekly for the first 2 months of treatment, then monthly for the first year and as clinically indicated (More frequent monitoring may be required in patients with cardiovascular disorders, especially coronary insufficiency, cardiac arrhythmias, and hypertension)
- Clinical toxicity assessment for infection, hypersensitivity, fatigue, musculoskeletal pain, hot flashes, secondary malignancy, GI, cardiovascular, neurologic and respiratory effects; At each visit

Suggested Clinical Monitoring

- Liver function tests; Baseline and as clinically indicated
- Renal function tests; Baseline and as clinically indicated

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J - Administrative Information

Outpatient prescription for home administration

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K - References

Berek JS, Matulonis UA, Peen U, et al. Safety and dose modification for patients receiving niraparib. Ann Oncol 2018 Aug 1;29(8):1784-92.

Mirza MR, Monk BJ, Herrstedt J, et al. Niraparib maintenance therapy in platinum-sensitive, recurrent ovarian cancer. N Engl J Med 2016;375:2154-64.DOI: 10.1056/NEJMoa1611310

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

pCODR expert review committee: final recommendation. Niraparib (recurrent ovarian cancer), September 2020.

PEBC Advice Documents or Guidelines

- Consolidation or Maintenance Systemic Therapy for Newly Diagnosed Stage II, III, or IV Epithelial Ovary, Fallopian Tube, or Primary Peritoneal Carcinoma

October 2023 Modified Drug administration and Other warnings/precautions 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

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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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