Regimen Monograph

A - Regimen Name

OLAP Regimen

Olaparib

Disease Site	Breast
Intent	Adjuvant
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	Adjuvant treatment for patients with deleterious or suspected deleterious germline BRCA-mutated, HER2-negative high risk early breast cancer, who completed definitive local treatment, and neoadjuvant or adjuvant chemotherapy (Refer to EAP for full details.)
Supplementary Public Funding	**olaparib** Exceptional Access Program (olaparib - For the treatment of adult patients with deleterious or suspected deleterious germline BRCA-mutated, human epidermal growth factor receptor 2-negative high risk early breast cancer, according to specific criteria) (EAP Website)

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B - Drug Regimen

Start at least 2 weeks (no more than 12 weeks) after completion of the last treatment, including surgery, chemotherapy, or radiation therapy:

olaparib	300 mg	PO	BID

Continue endocrine therapy in patients with hormone receptor positive breast cancer as per clinical guidelines.

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C - Cycle Frequency

CONTINUOUS TREATMENT

For a usual total of 52 weeks, unless disease progression or unacceptable toxicity occurs

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D - Premedication and Supportive Measures

Antiemetic Regimen: Low – No routine prophylaxis; PRN recommended

- 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 prior hematologic toxicities before starting olaparib (Hgb, ANC and platelets ≤ grade 1).

Dosage with toxicity

Dose Level	Olaparib Dose
0	300 mg BID
-1	250 mg BID
-2	200 mg BID
-3	Discontinue

Toxicity	Severity	Action
Platelets or ANC	≥ Grade 3 or blood transfusion dependence	Hold up to 4 weeks* and monitor CBC. Then, may consider dose reduction.
Hemoglobin		Hold up to 4 weeks* and monitor CBC. Then, consider dose reduction after severe anemia, to avoid multiple transfusions.
Signs and symptoms of pneumonitis	Any	Hold and investigate. If confirmed, discontinue and treat appropriately.
MDS, AML or other clonal disorders		Hold and investigate. If confirmed, discontinue and treat appropriately.
Other non-hematologic	Grade 3 or 4	Hold up to 4 weeks** Upon recovery, consider dose reduction.

*Hold until ≤ grade 1. If blood parameters remain abnormal after 4 weeks, bone marrow analysis and/or blood cytogenetic analysis are recommended.

**Hold until ≤ grade 1. If toxicity recurs, reduce an additional dose level. Discontinue if more than 2 dose reductions are required.

Hepatic Impairment

Hepatic Impairment	Olaparib Dose
Child-Pugh A or B	No dose adjustment required
Child-Pugh C	Not recommended (not studied)

Renal Impairment

Creatinine Clearance (mL/min)	Olaparib Dose
> 50	No dose adjustment required
31-50	200 mg BID
≤ 30 or end stage renal disease	Not recommended (limited data)

Dosage in the Elderly

Dose adjustment is not required. There is limited data in patients aged 75 and older.

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F - Adverse Effects

Refer to olaparib 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
• Nausea, vomiting • Fatigue	• Myelosuppression, anemia ± infection, bleeding (May be severe) • Diarrhea • Constipation • Dysgeusia	• Headache • Anorexia • Dizziness • Abdominal pain • Cough, dyspnea • Dyspepsia • Mucositis • Rash	• Hypersensitivity • Secondary malignancy (MDS, AML) • Pneumonitis • Venous thromboembolism

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G - Interactions

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

- Co-administration with strong and moderate CYP3A inducers is not recommended due to the potential for decreased olaparib efficacy.
- Co-administration with strong and moderate CYP3A inhibitors is not recommended due to the increased risk of toxicity. If unavoidable, olaparib dose should be reduced to 100 mg bid (with strong inhibitors) or 150 mg bid (with moderate inhibitors).
- Co-administration with myelosuppressive agents should be avoided due to potentiation and prolongation of myelosuppression.

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H - Drug Administration and Special Precautions

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

Administration:

- Olaparib can be taken with or without food.
- Tablets should be swallowed whole and not chewed, crushed, dissolved or divided.
- Avoid grapefruit, starfruit, pomegranate, Seville oranges, their juices or products during treatment.
- If a dose is missed, the next dose should be taken at the regular scheduled time. A double dose should not be taken to make up for forgotten tablets.
- Store between 2 to 30^{o}C in original packaging to protect from moisture.

Contraindications:

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

Other Warnings/Precautions:

- Do not co-administer with other myelosuppressive agents.
- Use with caution in patients who have received prior DNA damaging agents. MDS and AML have been reported.
- Use with caution in patients with lung cancer or metastases to the lungs, underlying pulmonary disease, smoking history and/or previous chemotherapy and radiotherapy as these patients are at increased risk of pneumonitis.
- Patients experiencing fatigue and dizziness should use caution when driving or operating machines.

Pregnancy and 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: Documented in 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 monthly for the first 12 months, then periodically thereafter, and as clinically indicated
- Liver function tests; baseline and as clinically indicated
- Renal function tests; baseline and as clinically indicated
- Clinical toxicity assessment for nausea and other GI and respiratory effects, fatigue, anemia, MDS, infection and bleeding, venous thromboembolism; At each visit
- Grade toxicity using the current NCI-CTCAE (Common Terminology Criteria for Adverse Events) version

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J - Administrative Information

Outpatient prescription for home administration

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K - References

CADTH reimbursement recommendation: Olaparib (adjuvant treatment of adult patients with deleterious or suspected deleterious germline BRCA-mutated, human epidermal growth factor receptor 2-negative high risk early breast cancer). March 2023.

Olaparib drug monograph. Ontario Health (Cancer Care Ontario).

Tutt ANJ, Garber JE, Kaufman B, et al. Adjuvant olaparib for patients with *BRCA1*- or *BRCA2*-mutated breast cancer. N Engl J Med. 2021;384(25):2394-405. doi: 10.1056/NEJMoa2105215

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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.

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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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