Olaparib (Tablet) Monotherapy

INDICATIONS FOR USE:

INDICATION	ICD10	Regimen Code	HSE approved reimbursement status*
Maintenance treatment of adult patients with advanced (FIGO stages III and IV) *BRCA 1/2*-mutated (germline and/or somatic) • High-grade epithelial ovarian • fallopian tube cancer • primary peritoneal carcinoma who are in response (complete or partial) following completion of first-line platinum based chemotherapy	C56 C48 C57	00588a 00588b 00588c	CDS 01/12/2020
Maintenance treatment of adult patients with platinum-sensitive relapsed *BRCA*-mutated (germline and/or somatic) • high grade serous epithelial ovarian cancer • fallopian tube cancer • primary peritoneal cancer who are in response (complete response or partial) to platinum-based chemotherapy	C56 C48 C57	00588d 00588e 00588f	CDS
As monotherapy for the treatment of adult patients with metastatic castration-resistant prostate cancer and BRCA1/2-mutations (germline and/or somatic) who have progressed following prior therapy that included a new hormonal agent.	C61	00588g	CDS 01/03/2023
As monotherapy or in combination with endocrine therapy for the adjuvant treatment of adult patients with germline *BRCA1/2*-mutations who have HER2-negative high risk early breast cancer previously treated with neoadjuvant or adjuvant chemotherapy.	C50	00588h	N/A
As monotherapy for the maintenance treatment of adult patients with germline *BRCA1/2*-mutations who have metastatic adenocarcinoma of the pancreas and have not progressed after a minimum of 16 weeks of platinum treatment within a first-line chemotherapy regimen.	C25	00588i	N/A

*This is for post 2012 indications only

TREATMENT:

The starting dose of the drugs detailed below may be adjusted downward by the prescribing clinician, using their independent medical judgement, to consider each patient's individual clinical circumstances.

1L Maintenance treatment of BRCA-mutated advanced ovarian cancer:

Olaparib is taken twice daily continuously until radiological disease progression, unacceptable toxicity, or for up to 2 years if there is no radiological evidence of disease after 2 years of treatment. Patients with evidence of disease at 2 years, who in the opinion of the treating physician can derive further benefit from continuous treatment, can be treated beyond 2 years.

Maintenance treatment of:

- **Platinum-sensitive relapsed BRCA-mutated ovarian cancer**
- ***BRCA1/2* mutated metastatic adenocarcinoma of the pancreas**

Olaparib is taken twice daily continuously until disease progression or unacceptable toxicity develops.

Treatment of prostate cancer:
Olaparib is taken twice daily continuously until disease progression or unacceptable toxicity develops. Medical castration with luteinising hormone releasing hormone (LHRH) analogue should be continued during treatment in patients not surgically castrated.

Adjuvant treatment of germline BRCA-mutated high risk early breast cancer:
Olaparib is taken twice daily continuously for up to 1 year, or until disease recurrence, or unacceptable toxicity, whichever occurs first.

Drug	Dose	Route	Cycle
Olaparib tablets	300mg twice daily*	PO	Continuous
*Total daily dose 600mg.			
If a patient misses a dose of olaparib, they should take their next normal dose at its scheduled time.			
Olaparib tablets should be swallowed whole and not chewed, crushed, dissolved or divided. Olaparib tablets may be taken without regard to meals.			
Olaparib tablets are commonly available as 100 mg and 150 mg tablets.			

ELIGIBILITY:

- Indications as above
- Adequate organ function

1L Maintenance treatment of BRCA-mutated advanced ovarian cancer:

- Platinum-responsive histologically confirmed high risk advanced (FIGO stage III-IV) BRCA mutated high grade serous or high-grade endometrioid ovarian cancer, primary peritoneal cancer or fallopian-tube cancer:
    - Platinum-responsive defined as partial or complete clinical response to platinum treatment,
    - Completed at least 4 cycles of first-line platinum chemotherapy and in radiologic (complete or partial) response, and
    - Last dose of platinum chemotherapy within 8 weeks of starting olaparib maintenance*
- BRCA 1/2 mutation (germline and/or somatic) as demonstrated by an accurate and validated test method**
- Stage III or IV disease (patients may have upfront or interval debulking surgery)
    - *Where debulking surgery is required last dose of platinum chemotherapy should be within 12 weeks of starting olaparib maintenance
- ECOG 0-1
- Where patients who have commenced treatment with bevacizumab concomitant with chemotherapy are found to have BRCA 1/2mutation (germline or somatic) bevacizumab may be discontinued and treatment with olaparib maintenance commenced 4-8 weeks after the last dose of chemotherapy

Maintenance treatment of platinum-sensitive relapsed BRCA-mutated ovarian cancer:

- BRCA 1/2 mutation (germline and/or somatic) as demonstrated by an accurate and validated test method**
- ECOG status 0-2
- Completed their previous platinum containing chemotherapy regimen in the previous 8 weeks
- Completed at least two courses of platinum-based chemotherapy
- The cancer is required to be platinum-sensitive (an objective response to the penultimate platinum-based regimen of more than six months) and the most recent regimen must have induced an objective response (either partial (PR) or complete response (CR))
- Patients' pre-treatment CA-125 value is within the upper limit of normal, or if greater, then a repeated level after seven days increased by less than 15% of the first measurement
- Life expectancy at least 16 weeks

Treatment of prostate cancer:

- BRCA 1/2 mutation (germline and/or somatic) as demonstrated by an accurate and validated test method**
- ECOG 0-2

Adjuvant treatment of germline BRCA-mutated high risk early breast cancer:

- Germline BRCA 1/2 mutation as demonstrated by an accurate and validated test method**
- HER2 negative breast cancer
    - Please see *Recommendations on Reporting on HER2 Status in Breast Cancer Patients* Available on the NCCP website .
    - Ideally, adjuvant treatment with olaparib should be initiated within 12 weeks of completion of last treatment (surgery, chemotherapy, or radiation)
- High risk early breast cancer defined as follows:
    - **Triple Negative Breast Cancer (TNBC**)
        - Treated with neoadjuvant chemotherapy who have residual invasive breast cancer in the breast or resected lymph nodes (i.e. no pathological complete response from neoadjuvant therapy)
        - Treated with adjuvant chemotherapy and have axillary node–positive disease or node negative with a primary tumour ≥ 2cm on pathological analysis
    - **Hormone Receptor Positive/HER2 negative Breast Cancer**
        - Treated with neoadjuvant chemotherapy who have not had a pathological complete response and have a CPS+EG score of 3 or higher based on pre-treatment clinical and post-treatment pathological stage, receptor status and histological grade
        - Treated with adjuvant chemotherapy and have at least four pathologically confirmed positive lymph nodes
- ECOG 0-2

- **1L Maintenance treatment of *BRCA1/2* mutated metastatic adenocarcinoma of the pancreas**
    - Germline BRCA 1/2 mutation as demonstrated by an accurate and validated test method**
    - ECOG 0-2

** Information on BRCA testing for olaparib is Available on the NCCP website

EXCLUSIONS:

- Hypersensitivity to olaparib, or any of the excipients.
- Previous treatment with PARP inhibitor

Ovarian, breast and pancreatic cancer indications:

- Breastfeeding during treatment and for 1 month after the last dose
- Pregnancy

PRESCRIPTIVE AUTHORITY:

- The treatment plan must be initiated by a Consultant Medical Oncologist

TESTS:

Baseline tests:

- Confirmation of germline and/or somatic BRCA1/2 mutations
  - Information on BRCA testing for olaparib is Available on the NCCP website
- FBC, renal and liver profile

Ovarian, breast and pancreatic cancer indications:

- A pregnancy test should be performed on all premenopausal women prior to treatment

Regular tests:

- FBC, renal and liver profile every 4 weeks for the first 12 months and then as clinically indicated

Ovarian, breast and pancreatic cancer indications:

- Consider regular pregnancy testing as indicated

Disease monitoring:

Disease monitoring should be in line with the patient's treatment plan and any other test/s as directed by the supervising Consultant.

DOSE MODIFICATIONS:

- Any dose modification should be discussed with a Consultant
- Treatment may be interrupted to manage adverse reactions such as nausea, vomiting, diarrhoea, and anaemia and dose reduction can be considered (Table 1)

Table 1: Dose reduction levels of olaparib

Dose Level	Dose Recommendation	Total Daily Dose
Starting dose	300mg Twice Daily	600mg
Dose -1	250mg Twice Daily	500mg
Dose -2	200mg Twice Daily	400mg

Haematological:

Table 2: Recommended dose modification of olaparib in haematological toxicity

ANC ($x10^9$/L)		Platelets ($x10^9$/L)	Dose
≥1	And	≥100	100% of previous cycle's dose
<1	Or	<100	Delay until recovery then restart at a reduced dose level as per Table 1 above 4th occurrence: Cease olaparib
Febrile Neutropenia			Delay until recovery then restart at a reduced dose level as per Table 1 above 4th occurrence: Cease olaparib For grade 4 febrile neutropenia consider restarting olaparib at dose reduction of two dose levels

Renal and Hepatic Impairment:

Table 3: Recommended dose modification of olaparib in renal and hepatic impairment

Renal Impairment		Hepatic Impairment	
Cr Cl (ml/min)	**Dose**	**Impairment Level**	**Dose**
>50	No dose adjustment	Mild/Child-Pugh A	No dose adjustment is needed
30-50	200mg PO twice daily	Moderate/Child-Pugh B	No dose adjustment is needed
<30	Consider 50% of the original dose	Severe/Child-Pugh C	Consider 50% of the original dose
Haemodialysis	Consider 50% of the original dose		
Renal and hepatic recommendations: Giraud et al, 2023			

Dose adjustments for co-administration with CYP3A inhibitors

- Concomitant use of strong and moderate CYP3A inhibitors is not recommended and alternative agents should be considered
    - Examples of strong inhibitors: clarithromycin, itraconazole, ketoconazole, grapefruit juice.

- Examples of moderate inhibitors: aprepitant, erythromycin, diltiazem, fluconazole, ciclosporin, ciprofloxacin.

- If a strong or moderate CYP3A inhibitor must be co-administered the recommended dose of olaparib is shown in Table 4 below.

Table 4: Recommended olaparib dose reduction when co-administered with strong or moderate CYP3A inhibitors

Class of CYP3A inhibitor	Dose	Total daily dose
Strong CYP3A inhibitor	100mg twice daily	200mg
Moderate CYP3A inhibitor	150mg twice daily	300mg

SUPPORTIVE CARE:

EMETOGENIC POTENTIAL:

- As outlined in NCCP Classification Document for Systemic AntiCancer Therapy (SACT) Induced Nausea and Vomiting Available on the NCCP website

Moderate to high (**Refer to local policy).**

For information:
Within NCIS regimens, antiemetics have been standardised by the Medical Oncologists and Haemato-oncologists and information is available in the following documents:

- NCCP Supportive Care Antiemetic Medicines for **Inclusion in NCIS** (Medical Oncology) - Available on the NCCP website
- NCCP Supportive Care Antiemetic Medicines for **Inclusion in NCIS** (Haemato-oncology) - Available on the NCCP website

PREMEDICATIONS:

Consider the use of:

- Anti-emetics (**Refer to local policy).**
- Proton Pump Inhibitor (**Refer to local policy).**

OTHER SUPPORTIVE CARE:

- Women of childbearing potential must use effective contraception before, during therapy and for 6 months after receiving the last dose of olaparib. Due to the potential interaction of olaparib with hormonal contraception, an additional non-hormonal contraceptive method and regular pregnancy tests should be considered during treatment. Male patients must use reliable contraception during therapy and for 3 months after receiving the last dose. Female partners of males patients must also use highly effective contraception if they are of childbearing potential.

ADVERSE EFFECTS:

- Please refer to the relevant Summary of Product Characteristics (SmPC) for details.

DRUG INTERACTIONS:

- Current SmPC and drug interaction databases should be consulted for information

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8. Giraud E L, Lijster B D, et al. Dose recommendations for anticancer drugs in patients with renal or hepatic impairment: an update. Available at: https://pubmed.ncbi.nlm.nih.gov/37269847/
9. NCCP Classification Document for Systemic AntiCancer Therapy (SACT) Induced Nausea and Vomiting. V6 2025. Available at: https://www.hse.ie/eng/services/list/5/cancer/profinfo/chemoprotocols/nccp-classification-document-for-systemic-anti-cancer-therapy-sact-induced-nausea-and-vomiting.pdf
10. Olaparib (Lynparza®) 100mg Film coated tablets. Summary of product characteristics. Last update: 20/08/2024. Accessed January 2025. Available at: https://www.ema.europa.eu/en/documents/product-information/lynparza-epar-product-information_en.pdf

Version	Date	Amendment	Approved By
1	26/11/2020		Prof Maccon Keane
2	21/12/2021	Addition of new indication	Prof Maccon Keane
3	01/03/2023	Addition of new indication	Dr Richard Bambury
4	12/11/2024	Addition of new indication	Prof Michaela Higgins
5	20/01/2025	Addition of new indication	Prof Maccon Keane
5a	09/04/2025	Update eligibility criteria for adjuvant breast indication. Update webpage link for PARPi testing	Prof Michaela Higgins

Comments and feedback welcome at oncologydrugs@cancercontrol.ie.