# Olaparib tablets

## Indication

Maintenance treatment of BRCA mutation positive, advanced (FIGO stages 3 and 4), high grade epithelial ovarian, fallopian tube or primary peritoneal cancer that has responded to first line platinum based chemotherapy.
(NICE TA598)

Maintenance treatment of relapsed, platinum-sensitive, high-grade epithelial ovarian, fallopian tube or primary peritoneal cancer in adults whose disease has responded to platinum-based chemotherapy only if they have a BRCA1 or BRCA2 mutation and have had 3 or more courses of platinum-based chemotherapy.
(Also those who have had 2 courses of platinum therapy - funding available via the CDF).
(NICE TA620)

## ICD-10 codes

Codes with a pre fix C48, 56, 57

## Regimen details

| Day | Drug | Dose | Route |
|---|---|---|---|
| 1-28 (continuous) | Olaparib tablets | 300mg BD | PO |

Treatment should be started no later than 8 weeks after completion of the final dose of platinum-containing chemotherapy.

## Cycle frequency

Continuous

## Number of cycles

Continuous until disease progression or unacceptable toxicity. For patients having as first line treatment, Olaparib should be continued for up to 2 years if there is no radiological evidence of disease. Patients with evidence of disease at 2 years who (in the opinion of the treating consultant) can derive further benefit from continuous treatment can have treatment beyond 2 years.

## Administration

Olaparib is available as 100mg and 150mg tablets. Tablets should be swallowed whole and not chewed, crushed, dissolved or divided.

If a dose is missed it should be omitted and the next dose taken as planned.

Grapefruit and grapefruit juice should be **avoided** whilst taking olaparib.

**Olaparib capsules should not be substituted for olaparib tablets due to differences in the dosing and bioavailability of each formulation.**

## Pre-medication

Nil

## Emetogenicity
This regimen has mild emetic potential.

## Additional supportive medication
Antiemetics if required.

## Extravasation
N/A

## Investigations – pre first cycle

| Investigation | Validity period |
|---|---|
| FBC | 14 days |
| U + Es (including creatinine) | 14 days |
| LFTs | 14 days |
| CA 125 | 14 days |

## Investigations – pre subsequent cycles

| Investigation | Validity period |
|---|---|
| FBC | Monthly |
| U + Es (including creatinine) | Monthly |
| LFTs | Monthly |
| CA 125 | 3 monthly |

## Standard limits for administration to go ahead
If blood results not within range, authorisation to administer **must** be given by prescriber/ consultant

| Investigation | Limit |
|---|---|
| Neutrophils | > 1.5 x $10^9$/L |
| Platelets | > 75 x $10^9$/L |
| CrCl | > 50 mL/min |
| Bilirubin | < 3 x ULN |
| ALT/AST | < 5 x ULN |

## Dose modifications
The recommended dose reduction for adverse reactions is 200 mg BD. If a further dose reduction is required, then the dose should be reduced to 100mg BD.

- **Haematological toxicity**

If a patient develops severe haematological toxicity or blood transfusion dependence, treatment should be interrupted and appropriate haematological testing should be initiated. If the blood parameters remain clinically abnormal after a 4 weeks delay, bone marrow analysis and/or blood cytogenetic analysis are recommended.

- **Renal impairment**

| **CrCl** (mL/min) | **Olaparib dose** |
|---|---|
| > 50 | 300mg BD |
| 31-50 | 200mg BD |
| ≤ 30 | Not recommended |

- **Hepatic impairment**

No dose adjustment is required in mild or moderate hepatic impairment (Child Pugh A-B). Olaparib is not recommended for use in patients with severe hepatic impairment (Child Pugh C).

- **Other toxicities**

**Pneumonitis**

Fatal pneumonitis has been reported in patients taking olaparib. If patients present with new or worsening respiratory symptoms such as dyspnoea, cough and fever, or an abnormal chest radiologic finding is observed, olaparib treatment should be interrupted and prompt investigation initiated. If pneumonitis is confirmed, olaparib should be discontinued.

## Adverse effects - for full details consult product literature/ reference texts

- **Serious side effects**

Pneumonitis
Myelodysplastic syndrome and AML
Myelosuppression
Anaemia

- **Frequently occurring side effects**

Nausea and vomiting
Dyspepsia
Fatigue
Headache
Dizziness
Cough
Stomatitis

- **Other side effects**

Taste disturbance
Decreased appetite
Increased creatinine
Rash

## Significant drug interactions – for full details consult product literature/ reference texts

**Strong or moderate CYP3A inhibitors:** (e.g. itraconazole, telithromycin, clarithromycin, erythromycin, diltiazem, fluconazole, verapamil) co-administration is not recommended. If a strong or moderate CYP3A inhibitor must be co-administered, the dose of olaparib should be reduced. See SPC for further information.

**Strong or moderate CYP3A inducers:** (e.g. phenytoin, rifampicin, carbamazepine, nevirapine, phenobarbital, St John's Wort, efavirenz, rifabutin) co-administration is not recommended. If a patient already receiving olaparib requires treatment with a strong or moderate CYP3A inducer, the prescriber should be aware that the efficacy of olaparib may be substantially reduced. See SPC for further information.

**Sensitive CYP3A substrates or substrates with a narrow therapeutic margin:** (e.g. simvastatin, cisapride, cyclosporin, ergot alkaloids, fentanyl, pimozide, sirolimus, tacrolimus and quetiapine) use with caution and close clinical monitoring.

**Hormonal contraceptives**: efficacy may be reduced, use alternative forms of contraception.

**Substrates of P-gp:** (e.g. simvastatin, pravastatin, dabigatran, digoxin and colchicine) use with caution and close clinical monitoring.

*In vitro,* olaparib has been shown to be an inhibitor of BCRP, OATP1B1, OCT1, OCT2, OAT3, MATE1 and MATE2K.

## Additional comments

Olaparib should not be used during pregnancy. Women of childbearing potential must use two forms of reliable contraception before starting treatment, during therapy and for 1 month after receiving the last dose. Two highly effective and complementary forms of contraception are recommended. Male patients and their female partners of childbearing potential should use reliable contraception during therapy and for 3 months after receiving the last dose of olaparib.

## References


- Summary of Product Characteristics Olaparib (Astra Zeneca) accessed 15 January 2020 via www.medicines.org.uk
- National Institute for Clinical Excellence (TA598) accessed 15 January 2020 via www.nice.org.uk
- Moore, K et al; Maintenance Olaparib in patients with newly diagnosed advanced ovarian cancer. NEJM 2018; 379: 2495 - 2505
- National Institute for Clinical Excellence (TA620) accessed 15 January 2020 via www.nice.org.uk
- Pujade-Lauraine, E. et al. Olaparib tablets as maintenance therapy in patients with platinum sensitive relapsed ovarian cancer and BRCA 1/2 mutation (SOLO2/ENGOT-Ov21). Lancet Oncology.2017; 18:9, 1274-1284.



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