Olaparib tablets (Gynae)

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 in patients with a BRCA mutation.
(NICE TA598)

Maintenance treatment of relapsed, platinum-sensitive, high-grade epithelial ovarian, fallopian tube, or primary peritoneal cancer that has responded to platinum-based chemotherapy only if they have a BRCA1 or BRCA2 mutation and have had 2 or more courses of platinum-based chemotherapy.
(NICE TA903)

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. An additional Blueteq continuation form must be completed.

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

Dose level	Dose
Full dose	300mg BD
1st dose reduction	250mg BD
2nd dose reduction	200mg BD

- **Haematological toxicity**

If neutrophils < 1.5 x 10^9/L or platelets < 75 x 10^9/L or symptomatic anaemia, withhold Olaparib until recovery and consider dose reduction.

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	Consider 50% of the original dose, consultant decision

NB. Creatinine may increase during treatment with Olaparib due to OCT2 transporter inhibition. This is not thought to represent a true decline in renal function and would be expected to resolve on stopping treatment.

- **Hepatic impairment**

No dose adjustment is required in mild or moderate hepatic impairment (Child Pugh A-B). Consider using 50% dose in severe hepatic impairment (Child Pugh C), consultant decision.

- **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 permanently.

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
Hyperglycaemia

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 CYP3A inhibitor must be co-administered, reduce the Olaparib dose to 100mg BD. If a moderate CYP3A inhibitor must be co-administered reduce the Olaparib dose to 150mg BD.

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** so may increase the exposure to substrates of these transporters.

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.
For patients undergoing surgery (except minor procedures) Olaparib should be withheld a few days before the procedure and until wound healing has occurred after surgery.

References

- Summary of Product Characteristics Olaparib (Astra Zeneca) accessed 07 June 2023 via www.medicines.org.uk
- National Institute for Clinical Excellence (TA598) accessed 07 June 2023 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 07 June 2023 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.
- Krens S D, Lassche, Jansman G F G A, et al. Dose recommendations for anticancer drugs in patients with renal or hepatic impairment. *Lancet Oncol* 2019; 20: e201–08.

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