Olaparib

Indication
Maintenance treatment of relapsed, platinum sensitive ovarian, fallopian tube or peritoneal cancer in patients who have BRCA1 or BRCA2 mutations whose disease has partially or completely responded to a third or subsequent course of platinum based chemotherapy.

(NICE TA 381)

ICD-10 codes
Codes with a pre fix C48, 56, 57

Regimen details

Day	Drug	Dose	Route
Continuous	Olaparib **capsules**	400mg 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 who remain on treatment after 15 months the company will supply the drug free of charge.

Administration
Olaparib is available as 50mg capsules. The dose should be taken two hours before food or one hour after food.

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 50mg capsules should not be substituted for olaparib tablets (100 mg and 150 mg) due to differences in the dosing and bioavailability of each formulation. This protocol and NICE TA381 only refers to olaparib capsules.

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

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	400mg BD
31-50	300mg 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

- **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

References

- Summary of Product Characteristics Olaparib (Astra Zeneca) accessed 20 September 2018 via www.medicines.org.uk
- National Institute for Clinical Excellence (TA 381) accessed 20 September 2018 via www.nice.org.uk
- Ledermann, J et al; Olaparib Maintenance Therapy in Platinum-Sensitive Relapsed Ovarian Cancer. NEJM 2012; 366: 1382 - 1392

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Date: September 2018