OLAPARIB

Monotherapy for the maintenance treatment of patients with platinum-sensitive, relapsed *BRCA*-mutated ovarian, fallopian tube, or primary peritoneal cancer who are in response (CR or PR) to platinum-based chemotherapy, only if they have had 3 or more courses of platinum-based chemotherapy.
NICE approved Jan 2016

Drug / Dosage:	Olaparib	start dose 400mg bd, to be taken continuously to disease progression
Administration:	Available as 50mg capsules, to be swallowed whole with water. The SPC advises that each dose should be taken at least one hour after food, and refrain from eating preferably for up to 2 hours afterwards. The reason given for this is that food slows the rate of absorption, while marginally increasing the extent of absorption (AUC increased by 20%). However, the clinical significance of this is unknown. As this is long-term medication, for patients who struggle to comply with this guidance, it is reasonable to counsel them to take the doses at the same time of day each day, in relation to food. Grapefruit and grapefruit juice should be avoided while on olaparib.	
Frequency:	to disease progression For patients who remain on treatment after 15 months, the drug cost of olaparib will be met by the company. Pharmacy, please ensure free of charge stock is obtained for all patients still on treatment after 15 months.	
Main Toxicities:	myelosuppression, nausea, vomiting, diarrhoea, dyspepsia, fatigue, headache, taste disturbances, decreased appetite, dizziness, raised creatinine	
Anti-emetics:	mildly emetogenic	
Regular Investigations:	FBC & U&Es	every 4 weeks for at least 4 months, then may be reduced to every 3 – 4 months in patients with stable disease
	LFTs	every 4 weeks initially, then as indicated
	CA 125	every 3 months
Interactions:	Elimination of olaparib is mainly through hepatic metabolism, with CYP3A4 being the major enzyme involved in its metabolism: Concomitant use of strong or moderate CYP3A inducers (e.g. phenytoin, rifampicin, carbamazepine, St John's Wort) with olaparib should be avoided, as this may increase the risk of therapeutic failure. Co-administration of olaparib with strong or moderate CYP3A inhibitors (e.g. itraconazole, clarithromycin) should also be avoided. If this is not possible, the recommended olaparib dose reduction is to 150 mg twice daily with a strong CYP3A inhibitor or 200 mg twice daily with a moderate CYP3A inhibitor. Caution should be exercised if olaparib is administered in combination with any statin, as it cannot be excluded that olaparib is an inhibitor of P-glycoprotein.	

Reason for Update: renal, hepatic, regular investigations, and interaction sections updated	Approved by Consultant:
Version: 3	Approved by Lead Chemotherapy Nurse:
Supersedes: Version 2	Date: 16.1.17
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Dose Modifications Patients should not start olaparib until neutrophils > 1.5 x 10^9/l and platelets > 75 x 10^9/l.

Treatment may be interrupted to manage adverse reactions such as nausea, vomiting, diarrhoea and anaemia, and dose reduction can also be considered.

The recommended dose reduction is to 200 mg twice daily.
If a further final dose reduction is required, then reduction to 100 mg twice daily could be considered.

If a patient develops severe haematological toxicity or blood transfusion dependence, treatment should be interrupted and appropriate haematological testing should be initiated.

Renal Impairment: No dose adjustment is required for patients with CrCl > 50 ml/minute.
The recommended start dose is 300mg twice daily for patients with CrCl 31 – 50 ml/minute.
Olaparib is not recommended for patients with CrCl ≤ 30 ml/min.

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

Reference: Ledermann, J et al; NEJM 2012; 366: 1382 - 1392