Systemic Anti Cancer Treatment Protocol

Olaparib
Gynaecological Cancer

PROTOCOL REF: MPHAGYNOLA
(Version No: 1.1)

Approved for use in:

- High grade serous epithelial ovarian, fallopian tube, or primary peritoneal cancer
- Patients with BRCA1 or BRCA2 mutations
- Following third line platinum based chemotherapy where there has been either complete or partial response

Dosage:

Drug	Dosage	Route	Frequency
Olaparib capsules	400mg	PO	Twice daily, continuously until disease progression

Treatment will be supplied every 28 days

Supportive treatments:

Domperidone 10mg oral tablets, up to 3 times a day or as required

Extravasation risk:

Not applicable - Oral agent

Administration:

Patients should take olaparib at least one hour after food, and refrain from eating preferably for up to 2 hours afterwards

For patients of child-bearing potential, ensure appropriate contraception is discussed

Interactions:

Olaparib under goes extensive metabolism by CYP3A4/5 and P-gp therefore inducers or inhibitors of this isoenzymes should be avoided. Please check with pharmacist for further information

Olaparib may also induce several hepatic CYP metabolic pathways potentially reducing efficacy of hormonal contraceptives.

CYP3A Inhibitors (not exhaustive list)

Itraconazole, telithromycin, clarithromycin, boosted protease inhibitors, indinavir, saquinavir, nelfinavir, boceprevir, telaprevir

Concomitant administration of olaparib with fluconazole is NOT recommended. If it cannot be avoided the dose of olaparib should be limited to 200mg twice daily.

CYP3A Inducers (not exhaustive list)

Phenobarbital, phenytoin, rifampicin, rifabutin, rifapentine, carbamazepine, nevirapine and St John's Wort.

Increased exposure to the following medicines may also occur: digoxin, dabigatran, colchicine, methotrexate, rosuvastatin and sulfasalazine, glibenclamide, repaglinide, statins, and valsartan, metformin, cyclosporin, ergot alkaloids, fentanyl, pimozide, tacrolimus and quetiapine

Main Toxicities:

Olaparib	
Haematological toxicity	Very common - Anaemia, neutropenia, thrombocytopenia and lymphopenia
Gastrointestinal disorders	Very common- Nausea, Vomiting, Diarrhoea, Dyspepsia Common - Upper abdominal pain, Stomatitis
General disorders	Very common Fatigue (including asthenia), Decreased appetite, Headache, Dizziness, taste disturbance

Pneumonitis	Reported in a small number of patients, monitor patients for new or worsening respiratory symptoms such as dyspnoea, cough and fever
Embryofoetal toxicity	Olaparib should not be used during pregnancy and in women of childbearing potential not using reliable contraception during therapy and for 1 month after receiving the last dose of olaparib.

Investigations:

	Pre	Cycle 1	Cycle 2	Cycle 3	Cycle 4	Cycle 5	Cycle 6	Ongoing
Medical Assessment	X				X			Every 3 cycles or as per patients' management plan
SACT Assessment	X	X	X	X	X	X	X	Every cycle
FBC	X	X	X	X	X	X	X	Every cycle
U&E & LFT	X	X	X	X	X	X	X	Every cycle
CA125	X	X	X	X	X	X	X	Every cycle
CT scan	X							If clinically indicated
Informed Consent	X							
PS recorded	X	X	X	X	X	X	X	Every cycle
Toxicities documented	X	X	X	X	X	X	X	Every cycle
Weight recorded	X	X	X	X	X	X	X	Every cycle

Dose Modifications and Toxicity Management:

Haematological toxicity

Proceed on day 1 if:-

ANC ≥ 1.0 x 10^9/L	Platelets ≥ 100 x 10^9/L

Delay 1 week on day 1 if:-

ANC ≤ 0.9 x 10^9/L	Platelets ≤ 99 x 10^9/L

If platelets or ANC still below required levels for treatment at week 2, delay treatment again and patient will need assessed and chemotherapy dose reduction by Oncologist

Non-haematological toxicities

Treat must be interrupted for any patient who experiences an intolerable grade 2 or any grade 3 or 4 adverse event using the CTCAE V3/4, treatment can be restarted at a reduced dose when the toxicity returns to grade 1 or less.

Dose adjustments	
Initial dose	400mg twice daily
First dose reduction	200mg twice daily
Second dose reduction	100mg twice daily

Renal and hepatic impairment

Renal impairment
Treatment can be administered in patients with mild renal impairment (creatinine clearance > 50 mL/min). There is limited data in patients with moderate impairment (creatinine clearance < 50 mL/min) or severe impairment (creatinine clearance < 30 mL/min) therefore; olaparib is not recommended for use in these renally impaired patients.

Hepatic impairment
Olaparib undergoes extensive hepatic metabolism before excretion via the urine and faeces. Treatment is not recommended for use in patients with hepatic impairment (serum bilirubin > 1.5 time upper limit of normal).

References:

Lynparza 50mg hard capsules, Summary of Product Characteristics, AstraZeneca UK, United Kingdom, 16/12/14. Available from www.medicines.org.uk/emc/medicine. Last Updated 18/05/2015

NICE TA 381
Olaparib for maintenance treatment of relapsed, platinum sensitive, BRCA mutation positive ovarian, fallopian tube and peritoneal cancer after response to second line or subsequent platinum based chemotherapy