OLAPARIB (Lynparza) ABIRATERONE Prednisolone

INDICATION (ICD10) C61

Check the most recent Blueteq eligibility criteria before prescribing. Blueteq registration required. (www.england.nhs.uk/publication/national-cancer-drugs-fund-list/) (OLAP9)

1. Olaparib plus abiraterone for the treatment of widespread metastatic progressive hormone-relapsed (castrate-resistant) prostate adenocarcinoma cancer (serum PSA of at least 50ng/ml) in patients who are treatment naïve to androgen receptor inhibitors and in whom chemotherapy is not yet clinically indicated or appropriate and has not been treated with chemotherapy for the hormone-relapsed (castrate-resistant). PS 0 or 1.

REGIMEN

Days 1 to 28	OLAPARIB	300mg orally twice daily
	ABIRATERONE	1000mg orally once daily
	Prednisolone	5mg orally twice daily

CYCLE FREQUENCY AND NUMBER OF CYCLES

Until disease progression.

A formal medical review as to how olaparib and abiraterone are being tolerated and whether treatment with olaparib plus abiraterone should continue or not will be scheduled to occur at least by the start of the third 4-weekly cycle of treatment.

ADMINISTRATION

Abiraterone available as 500mg tablets

Swallowed whole with water, taken at least one hour before or at least two hours after eating.

Olaparib available as 100mg and 150mg tablets.

Swallow whole with or without food.

ANTI-EMETICS

Low emetic risk all days

CONCURRENT MEDICATION REQUIRED

Abiraterone	Prednisolone 5mg orally twice daily (must be used in combination with prednisolone, not approved for use in combination with dexamethasone)
Olaparib	It is expected that treatment with LHRH agonists/antagonists will continue unless the patient has undergone surgical castration.

EXTRAVASATION AND TYPE OF LINE / FILTERS

Not applicable

INVESTIGATIONS

Blood results required before SACT administration

FBC, U&E and LFTs every 2 weeks for 3 cycles then every cycle

Neutrophils x 10^9/L ≥1.5

Platelets x 10^9/L ≥100

Creatinine every cycle

Blood pressure weekly initially, once monthly when stable

PSA every cycle initially then every 3 cycles

Baseline weight and every cycle

MAIN TOXICITES AND ADVERSE REACTIONS

Abiraterone	Hypertension, hypokalaemia and fluid retention use with caution Adrenocortical insufficiency Hepatotoxicity
Olaparib	Diarrhoea Hepatotoxicity Myelosuppression Nausea, vomiting Pneumonitis Raised creatinine VTE

INTERACTIONS WHICH MAY REQUIRE DOSE MODIFICATIONS
(not exhaustive list check SPC/BNF/Stockleys)

Abiraterone	Strong inducers of CYP3A4 (eg phenytoin, carbamazepine, rifampicin, rifabutin, rifapentine, phenobarbital, St John's wort) during treatment are to be avoided. Strong inhibitors of CYP3A4 (eg itraconazole, clarithromycin, voriconazole) may be used with caution
Olaparib	Concomitant use of strong or moderate CYP3A inhibitors is not recommended and alternative agents should be considered. If a strong CYP3A inhibitor must be co-administered, the recommended olaparib dose reduction is to 100mg twice daily. If a moderate CYP3A inhibitor must be co-administered, the recommended olaparib dose reduction is to 150mg twice daily.

DOSE MODIFICATIONS

Olaparib

When dose reduction is necessary, the olaparib dose may be reduced to 250mg twice daily and further to 200mg twice daily.

Non-haematological

Abiraterone

In patients with pre-existing hypokalaemia or those that develop hypokalaemia whilst being treated with abiraterone, consider maintaining the patient's potassium level at ≥4.0mM.

For patients who develop grade ≥3 toxicities including hypertension, hypokalaemia, oedema and other non-mineralocorticoid toxicities, treatment should be withheld and appropriate medical management should be instituted. Treatment with abiraterone should not be reinitiated until symptoms of the toxicity have resolved to grade 1 or baseline.

Hepatic impairment
Abiraterone
No dose adjustment is required in pre-existing mild hepatic impairment.
Abiraterone should be avoided in severe hepatic impairment.

ALT or AST >5-19xULN	Withhold abiraterone treatment until ALT or AST recovered to the patient's baseline. Re-treatment may then be considered at a reduced dose of 500mg once daily. For patients being re-treated, serum transaminases should be monitored at a minimum of every two weeks for three months and monthly thereafter. If hepatotoxicity recurs at the reduced dose of 500mg daily, treatment should be discontinued.
ALT or AST ≥20xULN	Discontinue permanently

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

Renal impairment
Abiraterone
Caution advised in patients with severe renal impairment.

Olaparib
No dose adjustment is necessary for patient with CrCl >50ml/minute.
The recommended starting dose is 200mg twice daily for patients with CrCl 31–50ml/minute.
Olaparib is not recommended for patients with CrCl ≤30ml/min.

REFERENCES
1. CDF