# OLAPARIB (Lynparza)

**INDICATION (ICD10) C50, C56, C61**

*Check the most recent Blueteq eligibility criteria before prescribing. Blueteq registration required. (www.england.nhs.uk/publication/national-cancer-drugs-fund-list/)* (OLAP1a) (OLAP1b) (OLAP") (OLAP3) (OLAP5) (OLAP6) (OLAP7) (OLAP8) (OLAP10)

1. For maintenance treatment in patients with high grade epithelial **ovarian, fallopian tube or primary peritoneal carcinoma** who have a deleterious or suspected deleterious germline and/or somatic BRCA mutation and who have a recent SECOND OR SUBSEQUENT relapse of platinum-sensitive disease and who are now in partial or complete response without evidence of progressive disease following a THIRD OR SUBSEQUENT platinum-based chemotherapy, having received a minimum of 4 cycles of platinum based treatment. ECOG PS 0 or 1. (OLAP3) (TA620)
2. For the maintenance treatment in patients with high grade epithelial stage III or IV **ovarian, fallopian tube or primary peritoneal carcinoma** who are in response following a minimum of 4 cycles of platinum-based FIRST line chemotherapy with no evidence of progressive disease AND who have a deleterious or suspected deleterious germline and/or somatic BRCA mutation. ECOG PS 0 or 1. (OLAP1a) (TA962)
3. For the maintenance treatment in patients with high grade epithelial BRCA mutation positive stage III or IV **ovarian, fallopian tube or primary peritoneal** carcinoma who responded to platinum-based FIRST line chemotherapy AND who still have stable residual disease after 2 years of olaparib maintenance therapy and who are planned to continue with maintenance Olaparib as likely to benefit from continuing treatment. ECOG PS sufficient to continue Olaparib maintenance. (OLA1b) (TA962)
4. Olaparib monotherapy as adjuvant treatment of high-risk TRIPLE NEGATIVE early **breast** cancer previously treated with neoadjuvant or adjuvant chemotherapy (at least 6 cycles of anthracycline and / or taxane containing regimens) and completed definitive local therapy (at least 2 weeks after completing RT or at least 3 weeks since last chemotherapy, but no previous PARP treatment) in patients with a deleterious or suspected deleterious germline BRCA mutation ECOG PS 0 or 1. (OLAP5) (TA886)
5. Olaparib in combination with hormone therapy (an aromatase inhibitor or an anti-oestrogen or a LHRH agonist) as adjuvant treatment of high-risk HORMONE RECEPOR POSITIVE HER 2 NEGATIVE early **breast** cancer previously treated with neoadjuvant or adjuvant chemotherapy (at least 6 cycles of anthracycline and / or taxane containing regimens) and completed definitive local therapy (at least 2 weeks after completing RT or at least 3 weeks since last chemotherapy, ideally 8 weeks or less but no more than 12 weeks from the date of the last treatment (surgery, chemotherapy, radiotherapy), but no previous PARP treatment) in patients with a deleterious or suspected deleterious germline BRCA mutation. ECOG PS 0 or 1. (OLAP6) (TA886)
7. Olaparib monotherapy for metastatic hormone-relapsed castration-resistant **prostate** cancer (PSA ≥50ng/ml) bearing germline and/or somatic BRCA 1 or 2 mutations in patients who have progressed following previous treatment with an androgen receptor targeted agent (enzalutamide or apalutamide or darolutamide or abiraterone) AND HAVE ALSO BEEN TREATED WITH DOCETAXEL and progressed after such treatment, but no previous PARP treatment. ECOG PS of 0 or 1 or 2. (OLAP7) (TA887)
8. Olaparib monotherapy for metastatic hormone relapsed, castration-resistant **prostate** (PSA ≥50ng/ml) cancer bearing germline and/or somatic BRCA 1 or 2 mutations in patients who have progressed following previous treatment with an androgen receptor targeted agent (enzalutamide or apalutamide or darolutamide or abiraterone) AND HAVE NOT BEEN PREVIOUSLY TREATED WITH DOCETAXEL but no previous PARP. ECOG PS of 0 or 1 or 2. (OLAP8) (TA887)

9. Olaparib monotherapy for the maintenance treatment in patients with high grade serous or **endometrial** or epithelial or clear cell **ovarian, fallopian tube or primary peritoneal** carcinoma who HAVE a deleterious or suspected deleterious germline and/or somatic BRCA mutation and who have a recent FIRST RELAPSE of platinum sensitive disease and who are now in response following a minimum of 4 cycles of SECOND platinum based chemotherapy (the last infusion of this last cycle was less than 8 weeks ago). ECOG PS 0 or 1. (OLAP2) (TA908)
10. Olaparib monotherapy for treatment of adults with deleterious or suspected deleterious germline BRCA1 or 2 mutations who have HER-2 negative locally advanced or metastatic **breast** cancer with a germline deleterious or suspected deleterious BRCA 1 or BRCA 2 mutations, previously treated with an anthracycline and a taxane in the adjuvant/neoadjuvant/advanced disease settings and also treated with prior endocrine-based therapy if the patient has hormone-receptor positive disease. Any brain metastases or leptomeningeal metastases in this patient are symptomatically stable. ECOG PS 0 or 1. (OLAP10) (TA1040)

**REGIMEN**

Breast adjuvant triple negative – first cycle to start at least 2 weeks after completing RT or at least 3 weeks since last chemotherapy.
Breast adjuvant hormone receptor HER2-ve – first cycle to start ideally 8 weeks or less but no more than 12 weeks from the date of the last treatment (surgery, chemotherapy, radiotherapy).
Gynae - first cycle to start no more than 8 weeks after completion of last cycle of the 3rd or subsequent line of platinum-based chemotherapy.

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|---|---|---|---|---|
| Days 1 to 28 | **OLAPARIB** | 300mg | oral | twice daily |

**CYCLE FREQUENCY AND NUMBER OF CYCLES**

**Calendar years - maximum duration of treatment from initiation of the treatment, the treatment must stop at that maximum time duration irrespective of any breaks in treatment.**
Daily for 28 days. A formal medical review as to whether olaparib should continue or not will be scheduled to occur at least by the start of the third 4-weekly cycle of treatment.
Breast adjuvant - for a total treatment duration of 1 **calendar** year from the date of commencing adjuvant olaparib.
Breast advanced / metastatic - continuously until progression.
Gynae after 1st line treatment - for a total treatment duration of 2 years if the patient is in complete remission at the end of the 2 year treatment period.
For those patients with stable residual disease after completing 2 years of treatment, treatment with maintenance olaparib can continue if the treating clinician considers that the patient will derive further benefit. If treatment beyond 2 years is to occur, CDF form OLAP1b must be completed prior to continuation otherwise olaparib will not be funded by the CDF.
Gynae second or subsequent relapse - continuously until progression.
Prostate - continuously until progression.

**ADMINISTRATION**

Available as 100mg and 150mg tablets
Swallow whole with or without food.

**ANTI-EMETICS**

Low emetic risk all days

## CONCURRENT MEDICATION REQUIRED

| | |
|---|---|
| Olaparib | Breast - high-risk hormone receptor positive HER2 negative in combination with hormone therapy. |
| Olaparib | Prostate - 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<br>Neutrophils x $10^9$/L ≥1.5<br>Neutrophils x $10^9$/L ≥1.0 provided patient is well (gynae patients)<br>Platelets ≥100x$10^9$/L | baseline then minimum monthly for first 4 months then alternate months if no issues (check SPC) |
| Serum creatinine | baseline then minimum monthly for first 4 months then alternate months if no issues (check SPC) |
| CA125 (gynae patients) | baseline and every 3rd cycle |
| Virology | before cycle 1 if not previously checked |
| Weight | baseline and every cycle |

## MAIN TOXICITES AND ADVERSE REACTIONS

| | |
|---|---|
| Olaparib | Diarrhoea<br>Myelosuppression<br>Nausea, vomiting<br>Raised creatinine |

## INTERACTIONS WHICH MAY REQUIRE DOSE MODIFICATIONS

**(not exhaustive list check SPC/BNF/Stockleys)**

| | |
|---|---|
| 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

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

### Hepatic impairment

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**

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. Moore, K et al; NEJM 2018; 379: 2495-2505

Assessments

| | Pre | Cycle 1 | Cycle 2 | Cycle 3 | Cycle 4 | Ongoing |
|---|---|---|---|---|---|---|
| Clinical assessment | X | | Pre cycle | | Pre cycle | Every cycle |
| SACT assessment (PS and toxicities) | X | X | X | X | X | Every cycle |
| FBC | X | X | X | X | X | then alternate months if no issues |
| U&E, calcium & LFT | X | X | X | X | X | then alternate months if no issues |
| CrCl | X | X | X | X | X | Every cycle |
| CA125 (gynae) | X | | | X | | then every 3rd cycle |
| CT scan | X | | | | | At cycle 6, Inform consultant team if not booked |
| Informed consent | X | | | | | Verbal each cycle |
| Height | X | | | | | |
| Weight recorded | X | X | X | X | X | Every cycle |