PRESCRIBING INFORMATION

LYNPARZA™ (olaparib) 150mg & 100mg FILM-COATED TABLETS

Consult Summary of Product Characteristics before prescribing.

Indication: Ovarian Cancer: As monotherapy for the maintenance treatment of adult patients with advanced (FIGO stages III and IV) BRCA1/2-mutated (germline and/or somatic) high-grade epithelial ovarian, fallopian tube or primary peritoneal cancer who are in response (complete or partial) following completion of first-line platinum-based chemotherapy. As monotherapy for the maintenance treatment of adult patients with platinum-sensitive relapsed high-grade epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in response (complete or partial) to platinum-based chemotherapy.

Breast Cancer: As monotherapy for the treatment of adult patients with germline BRCA1/2-mutations, who have HER2 negative locally advanced or metastatic breast cancer. Patients should have previously been treated with an anthracycline and a taxane in the (neo)adjuvant or metastatic setting unless patients were not suitable for these treatments. Patients with hormone receptor (HR)-positive breast cancer should also have progressed on or after prior endocrine therapy, or be considered unsuitable for endocrine therapy.

Presentation: 150mg and 100mg olaparib film-coated tablets.

Dosage and Administration: Treatment should be initiated and supervised by a physician experienced in the use of anticancer therapies. Before Lynparza treatment is initiated, patients must have confirmation of deleterious or suspected deleterious germline and/or somatic mutations in the breast cancer susceptibility genes (BRCA) 1 or 2 using a validated test. There is no requirement for BRCA1/2 testing prior to using Lynparza for the maintenance treatment of relapsed EOC, FTC or PPC who are in a complete or partial response to platinum-based therapy. For germline breast cancer susceptibility genes (gBRCA1/2) mutated human epidermal growth factor receptor 2 (HER2)-negative metastatic breast cancer, patients must have confirmation of deleterious or suspected deleterious gBRCA1/2 mutation before Lynparza treatment is initiated. gBRCA1/2 mutation status should be determined by an experienced laboratory using a validated test method in breast cancer and ovarian cancer patients. Genetic counselling for patients tested for mutations in BRCA1/2 genes should be performed. Recommended dose is 300mg (two 150mg tablets) twice daily, equivalent to a total daily dose of 600mg. The 100mg tablet is available for dose reduction.

Tablets should be swallowed whole and not chewed, crushed, dissolved or divided and may be taken without regard to meals. Recommended that treatment be continued until progression of the underlying disease or unacceptable toxicity. Patients with platinum-sensitive relapsed high-grade epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in response (complete or partial) to platinum-based chemotherapy should start Lynparza treatment no later than 8 weeks after completion of their final dose of platinum-containing regime. First-line maintenance treatment of BRCA-mutated advanced ovarian cancer: Patients can continue treatment until radiological disease progression, unacceptable toxicity or for up to 2 years if there is no radiological evidence of disease after 2 years of treatment. Patients with evidence of disease at 2 years, who in the opinion of the treating physician can derive further benefit from continuous treatment, can be treated beyond 2 years. Maintenance treatment of platinum sensitive relapsed ovarian cancer: For patients with platinum sensitive relapsed high-grade epithelial ovarian, fallopian tube or primary peritoneal cancer, it is recommended
that treatment be continued until progression of the underlying disease or unacceptable toxicity. **gBRCA1/2-mutated HER2-negative metastatic breast cancer:** It is recommended that treatment be continued until progression of the underlying disease or unacceptable toxicity. There are no data on retreatment with Lynparza following first or subsequent relapse in ovarian cancer patients or on retreatment of breast cancer patients. **The tablets and capsules should not be substituted for each other on a milligram-to-milligram basis due to differences in the dosing and bioavailability of each formulation. Specific dose recommendations for each formulation should be followed.** If a dose is missed, take next normal dose at its scheduled time. **Dose adjustments:** Treatment interruption to manage adverse reactions such as nausea, vomiting, diarrhoea, anaemia and dose reduction can be considered. Recommended dose reduction is to 250mg (one 150mg tablet and one 100mg tablet) twice daily, equivalent to a total daily dose of 500mg. If further dose reduction is required, then reduction to 200mg (two 100mg tablets) twice daily, equivalent to a total daily dose of 400mg is recommended. 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, recommended dose reduction is to 100mg (one 100mg tablet) twice daily, equivalent to a total daily dose of 200mg. If a moderate CYP3A inhibitor must be co-administered, recommended dose reduction is to 150mg (one 150mg tablet) twice daily, equivalent to a total daily dose of 300mg. **Elderly:** No adjustment in starting dose is required. There are limited clinical data in patients aged 75 years and over. **Renal impairment:** Patients with moderate renal impairment (creatinine clearance 31 to 50 ml/min) the recommended dose is 200mg (two 100mg tablets) twice daily, equivalent to a total daily dose of 400mg. Lynparza can be administered in patients with mild renal impairment (creatinine clearance 51 to 80 ml/min) with no dose adjustment. No studies have been conducted in patients with severe renal impairment or end-stage renal disease (creatinine clearance ≤ 30 ml/min) and Lynparza is not recommended for use. It may only be used in patients with severe renal impairment if the benefit outweighs the potential risk with careful monitoring of renal function and adverse events. **Hepatic impairment:** Can be administered in patients with mild or moderate hepatic impairment (Child-Pugh A or B) with no dose adjustment. Not recommended in patients with severe hepatic impairment (Child-Pugh C).

**Contraindications:** Hypersensitivity to the active substance or to any of the excipients. Breast-feeding during treatment and for 1 month after the last dose.

**Warnings and Precautions:** **Haematological toxicity:** Treatment should not be started in patients until they have recovered from haematological toxicity caused by previous anticancer therapy (haemoglobin, platelet and neutrophil levels should be ≤CTCAE grade 1). Baseline testing followed by monthly monitoring of complete blood counts is recommended for first 12 months of treatment and periodically thereafter. Treatment should be interrupted and appropriate haematological testing should be initiated if patient develops severe haematological toxicity or blood transfusion dependence. **Myelodysplastic syndrome/Acute Myeloid Leukaemia (MDS/AML):** If confirmed while on treatment, it is recommended that Lynparza should be discontinued and the patient treated appropriately. **Pneumonitis:** Interrupt Lynparza treatment and promptly investigate as appropriate. Discontinue Lynparza if pneumonitis is confirmed and treat patient appropriately. **Embryofetal toxicity:** Lynparza could cause foetal harm when administered to a pregnant woman. **Pregnancy/contraception:** Lynparza should not be used during pregnancy. Women of childbearing potential must use two forms of reliable contraception, before starting Lynparza, during therapy and 1 month after receiving the last dose. Two highly effective and complementary forms of contraception are recommended. Male patients
and their female partners of childbearing potential should use reliable contraception during therapy and for 3 months after receiving the last dose.

**Drug Interactions:** The recommended Lynparza monotherapy dose is not suitable for combination with myelosuppressive anticancer medicinal products. Caution and close monitoring if vaccines or immunosuppressant agents are co-administered. **Effect of other drugs on Lynparza:** Strong CYP3A inhibitors (e.g. itraconazole, telithromycin, clarithromycin, protease inhibitors boosted with ritonavir or cobicistat, boceprevir, telaprevir) or moderate CYP3A inhibitors (e.g. erythromycin, diltiazem, fluconazole, verapamil) are not recommended. If co-administered, the dose of Lynparza should be reduced. It is also not recommended to consume grapefruit juice. Strong CYP3A inducers (e.g. phenytoin, rifampicin, rifapentine, carbamazepine, nevirapine, phenobarbital, and St John’s Wort) are not recommended with Lynparza as the efficacy of Lynparza could be substantially reduced. The magnitude of the effect of moderate to strong inducers (e.g. efavirenz, rifabutin) on olaparib exposure is not established, therefore the co-administration of Lynparza with these medicinal products is also not recommended. **Effect of Lynparza on other drugs:** Caution and appropriate clinical monitoring is recommended when sensitive CYP3A substrates or substrates with a narrow therapeutic margin (e.g. simvastatin, cisapride, cyclosporine, ergot alkaloids, fentanyl, pimozide, sirolimus, tacrolimus and quetiapine) or P-gp substrates (e.g. simvastatin, pravastatin, dabigatran, digoxin and colchicine) are combined with Lynparza. Lynparza may reduce efficacy of hormonal contraceptives. Lynparza may increase the exposure to substrates of BCRP (e.g. methotrexate, rosuvastatin), OATP1B1 (e.g. bosentan, glibenclamide, repaglinide, statins and valsartan), OCT1, MATE1, MATE2K (e.g. metformin), OCT2 (e.g. serum creatinine), OAT3 (e.g. furosemide and methotrexate). Caution if co-administered with any statin.

**Pregnancy and Lactation:** Women of childbearing potential should not become pregnant while on Lynparza and not be pregnant at the beginning of treatment. A pregnancy test should be performed prior to treatment and considered regularly throughout treatment. The efficacy of some hormonal contraceptives may be reduced if co-administered with Lynparza. Therefore, an additional non-hormonal contraceptive method should be considered during treatment. For women with hormone dependent cancer, two non-hormonal contraceptives should be considered. Lynparza could cause foetal harm to a pregnant woman. Lynparza is contraindicated during breast-feeding and for 1 month after receiving last dose. Male patients must use a condom during therapy and for 3 months after receiving last dose when having sexual intercourse with a pregnant woman or with a woman of childbearing potential. Female partners of male patients must also use highly effective contraception. Male patients should not donate sperm during therapy and for 3 months after treatment.

**Ability to Drive and Use Machines:** Asthenia, fatigue and dizziness have been reported and patients who experience these symptoms should observe caution when driving or using machines.

**Undesirable Events:** Consult SmPC for full list of side effects. **Very common:** Anaemia, neutropenia, thrombocytopenia, leukopenia, nausea, vomiting, diarrhoea, dyspepsia, upper abdominal pain, dysgeusia, decreased appetite, fatigue (including asthenia), headache, dizziness, cough, dyspnoea. **Common:** Lymphopenia, stomatitis, rash, increase in blood creatinine. **Uncommon:** Hypersensitivity, dermatitis, mean corpuscular volume elevation.

**Legal Category:** POM.
**Marketing Authorisation Number:** EU/1/14/959/002 (100mg tablets); EU/1/14/959/004 (150 mg tablets).

**Presentation & Basic NHS Cost:** 56 Film-Coated Tablets 150mg (7 blisters of 8 tablets each): £2,317.50 (14-days), 56 Film-Coated Tablets 100mg (7 blisters of 8 tablets each): £2,317.50 (14-days).

**Marketing Authorisation Holder:** AstraZeneca AB, SE-151 85 Södertälje, Sweden.

**Further information is Available From:** AstraZeneca UK Ltd., 600 Capability Green, Luton, LU1 3LU, UK.

LYNPARZA is a trade mark of the AstraZeneca group of companies.

Date of preparation: 07/2019

ONC 19 0035

Adverse events should be reported. Reporting forms and information can be found at [www.mhra.gov.uk/yellowcard](http://www.mhra.gov.uk/yellowcard). Adverse events should also be reported to AstraZeneca by visiting [https://aereporting.astrazeneca.com](https://aereporting.astrazeneca.com) or by calling 0800 783 0033.
LYNPARZA™ (olaparib) 50mg HARD CAPSULES

Consult Summary of Product Characteristics before prescribing.

**Indication:** As monotherapy for the maintenance treatment of adult patients with platinum-sensitive relapsed BRCA-mutated (germline and/or somatic) high grade serous epithelial ovarian, fallopian tube or primary peritoneal cancer who are in response (complete response or partial response) to platinum-based chemotherapy.

**Presentation:** 50mg olaparib hard capsules.

**Dosage and Administration:** Treatment should be initiated and supervised by a physician experienced in the use of anticancer therapies. Patients must have confirmation of a deleterious or suspected deleterious breast cancer susceptibility gene (BRCA) mutation (either germline or tumour) before treatment is initiated. BRCA mutation status should be determined by an experienced laboratory using a validated test method. Genetic counselling for patients with BRCA1/2 mutations should be performed. Recommended dose is 400mg (8 capsules) twice daily, equivalent to a total daily dose of 800mg. Take at least 1 hour after food; refrain from food preferably for up to 2 hours afterwards. Patients should start treatment with Lynparza no later than 8 weeks after completion of their final dose of the platinum-containing regimen. It is recommended that treatment be continued until progression of the underlying disease or unacceptable toxicity. There are no data on retreatment following subsequent relapse. The tablets and capsules should not be substituted for each other on a milligram-to-milligram basis due to differences in the dosing and bioavailability of each formulation. Specific dose recommendations for each formulation should be followed. If a dose is missed, take next normal dose at its scheduled time.

**Dose adjustments:** Treatment interruption to manage adverse reactions such as nausea, vomiting, diarrhoea, anaemia and dose reduction can be considered. Recommended dose reduction is to 200mg twice daily (equivalent to a total daily dose of 400mg). If a further dose reduction is required, then reduction to 100mg twice daily (equivalent to a total daily dose of 200mg) is recommended. 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 dose reduction is 150mg twice daily equivalent to a total daily dose of 300mg. If a moderate CYP3A inhibitor must be co-administered, recommended dose reduction is 200mg taken twice daily, equivalent to a total daily dose of 400mg. Elderly: No adjustment in starting dose is required. There are limited clinical data in patients aged 75 years and over. Renal impairment: Recommended dose is 300mg twice daily, equivalent to a total daily dose of 600mg for patients with moderate renal impairment (creatinine clearance 31 to 50 ml/min). Lynparza be administered in patients with mild renal impairment (creatinine clearance 51 to 80 ml/min) with no dose adjustment. No studies have been conducted in patients with severe renal impairment or end-stage renal disease (creatinine clearance ≤ 30 ml/min) and is not recommended for use. It may only be used in patients with severe renal impairment if the benefit outweighs the potential risk with careful monitoring of renal function and adverse events. Hepatic impairment: Can be administered in patients with mild or moderate hepatic impairment (Child-Pugh A or B) with no dose adjustment. Not recommended in patients with severe hepatic impairment (Child-Pugh C).

**Contraindications:** Hypersensitivity to the active substance or to any of the excipients. Breast-feeding during treatment and for 1 month after the last dose.
**Warnings and Precautions:**

**Haematological toxicity:** Treatment should not be started in patients until they have recovered from haematological toxicity caused by previous anticancer therapy (haemoglobin, platelet and neutrophil levels should be ≤CTCAE grade 1). Baseline testing followed by monthly monitoring of complete blood counts is recommended for first 12 months of treatment and periodically thereafter. Treatment should be interrupted and appropriate haematological testing should be initiated if patient develops severe haematological toxicity or blood transfusion dependence.

**Myelodysplastic syndrome/Acute Myeloid Leukaemia (MDS/AML):** If confirmed while on treatment, it is recommended that Lynparza should be discontinued and the patient treated appropriately.

**Pneumonitis:** Interrupt Lynparza treatment and promptly investigate as appropriate. Discontinue Lynparza if pneumonitis is confirmed and treat patient appropriately.

**Embryofetal toxicity:** Lynparza could cause foetal harm when administered to a pregnant woman.

**Pregnancy/contraception:** Lynparza should not be used during pregnancy. Women of childbearing potential must use two forms of reliable contraception, before starting Lynparza, during therapy and 1 month after receiving the last dose. Two highly effective and complementary forms of contraception are recommended.

**Drug Interactions:** The recommended Lynparza monotherapy dose is not suitable for combination with myelosuppressive anticancer medicinal products. Caution and close monitoring if vaccines or immunosuppressant agents are co-administered. **Effect of other drugs on Lynparza:** Strong CYP3A inhibitors (e.g. itraconazole, telithromycin, clarithromycin, protease inhibitors boosted with ritonavir or cobicistat, boceprevir, telaprevir) or moderate CYP3A inhibitors (e.g. erythromycin, diltiazem, fluconazole, verapamil) are not recommended. If co-administered, the dose of Lynparza should be reduced. It is also not recommended to consume grapefruit juice. Strong CYP3A inducers (e.g. phenytoin, rifampicin, rifapentine, carbamazepine, nevirapine, phenobarbital, and St John’s Wort) are not recommended with Lynparza as the efficacy of Lynparza could be substantially reduced. The magnitude of the effect of moderate to strong inducers (e.g. efavirenz, rifabutin) on olaparib exposure is not established, therefore the co-administration of Lynparza with these medicinal products is also not recommended. **Effect of Lynparza on other drugs:** Caution and appropriate clinical monitoring is recommended when sensitive CYP3A substrates or substrates with a narrow therapeutic margin (e.g. simvastatin, cisapride, cyclosporine, ergot alkaloids, fentanyl, pimozide, sirolimus, tacrolimus and quetiapine) or P-gp substrates (e.g. simvastatin, pravastatin, dabigatran, digoxin and colchicine) are combined with Lynparza. Lynparza may reduce efficacy of hormonal contraceptives. Lynparza may increase the exposure to substrates of BCRP (e.g. methotrexate, rosuvastatin), OATP1B1 (e.g. bosentan, glibenclamide, repaglinide, statins and valsartan), OCT1, MATE1, MATE2K (e.g. metformin), OCT2 (e.g. serum creatinine), OAT3 (e.g. furosemide and methotrexate). Caution if co-administered with any statin.

**Pregnancy and Lactation:** Women of childbearing potential should not become pregnant while on Lynparza and not be pregnant at the beginning of treatment. A pregnancy test should be performed prior to treatment and considered regularly throughout treatment. The efficacy of some hormonal contraceptives may be reduced if co-administered with Lynparza. Therefore, an additional non-hormonal contraceptive method should be considered during treatment. For women with hormone dependent cancer, two non-hormonal contraceptives should be considered.

**Ability to Drive and Use Machines:** Asthenia, fatigue and dizziness have been reported and patients who experience these symptoms should observe caution when driving or using machines.
Undesirable Events: Consult SmPC for full list of side effects. Very common: Anaemia, neutropenia, thrombocytopenia, leukopenia, nausea, vomiting, diarrhoea, dyspepsia, dysgeusia, decreased appetite, fatigue (including asthenia), headache, dizziness, cough, dyspnoea, upper abdominal pain. Common: Lymphopenia, stomatitis, rash, increase in blood creatinine. Uncommon: hypersensitivity, dermatitis, mean corpuscular volume elevation.

Legal Category: POM.

Marketing Authorisation Number: EU/1/14/959/001.

Presentation & Basic NHS Cost: 448 Hard Capsules (4 bottles of 112 capsules); £3550.


Further Information is Available From: AstraZeneca UK Ltd., 600 Capability Green, Luton, LU1 3LU, UK.

LYNPARZA is a trade mark of the AstraZeneca group of companies.

Date of preparation: 07/2019

ONC 19 0034

Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard. Adverse events should also be reported to AstraZeneca by visiting https://aereporting.astrazeneca.com or by calling 0800 783 0033.