EXAMPLE OF LYNPARZA® (olaparib) TREATMENT PLAN

Instructions for using the LYNPARZA Treatment Plan for FDA-approved indications (please see full indications below). This document is a draft treatment plan for implementation in electronic medical record (EMR) or paper treatment plans. Please modify as needed to meet institutional standards. **Please see complete Prescribing Information, including Medication Guide, for additional information.**

Institution P&T Approval Date (if applicable):	
Place in Therapy/Pathway:	
Lead Physician:	**Oncology Nurse/Pharmacist:**
Approval Signature:	**Approval Signature:**

Indications	**Comments**
	LYNPARZA is indicated: – For the adjuvant treatment of adult patients with deleterious or suspected deleterious germline *BRCA*-mutated (g*BRCA*m), human epidermal growth factor receptor 2 (HER2)-negative high-risk early breast cancer who have been treated with neoadjuvant or adjuvant chemotherapy. Select patients for therapy based on an FDA-approved companion diagnostic for LYNPARZA – For the treatment of adult patients with deleterious or suspected deleterious g*BRCA*m, HER2-negative metastatic breast cancer who have been treated with chemotherapy in the neoadjuvant, adjuvant, or metastatic setting. Patients with hormone receptor (HR)-positive breast cancer should have been treated with a prior endocrine therapy or be considered inappropriate for endocrine therapy. Select patients for therapy based on an FDA-approved companion diagnostic for LYNPARZA *BRCA*m=breast cancer susceptibility gene-mutated; FDA=US Food and Drug Administration.

Contraindications	**Comments**
	None

Drug (eRx)	**Dosages**	**Comments**
Olaparib 300 mg Strengths: 150 mg tablet, 100 mg tablet	– Recommended dosage is 300 mg (two 150 mg tablets) taken orally twice daily (600 mg total daily dose) – LYNPARZA may be taken with or without food – **Adjuvant treatment of g*BRCA*m, HER2-negative high-risk early breast cancer:** Continue treatment for a total of 1 year, or until disease recurrence, or unacceptable toxicity, whichever occurs first. Patients receiving LYNPARZA for HR-positive HER2-negative breast cancer should continue concurrent treatment with endocrine therapy as per current clinical practice guidelines	If a dose of LYNPARZA is missed, do not make up for the missed dose. Instruct the patient to take the next dose as scheduled. Tablets should be swallowed whole. Instruct patients not to chew, crush, dissolve, or divide the tablet. Store in original bottle to protect from moisture and at 20°C to 25°C (68°F to 77°F), excursions permitted from 15°C to 30°C (59°F to 86°F) (see USP Controlled Room Temperature).

	– **Treatment of g*BRCA*m, HER2-negative metastatic breast cancer**: Continue treatment until disease progression or unacceptable toxicity
Recommended Dosage Modifications	**Comments**
Please see complete Prescribing Information for additional information.	**Dosage modifications for adverse reactions** – To manage adverse reactions, consider interruption of treatment or dose reduction. The recommended dose reduction is 250 mg (one 150 mg tablet and one 100 mg tablet) taken twice daily, for a total daily dose of 500 mg – If a further dose reduction is required, then reduce to 200 mg (two 100 mg tablets) taken twice daily, for a total daily dose of 400 mg **Dosage modifications for concomitant use with strong or moderate CYP3A inhibitors** – Avoid concomitant use of strong or moderate CYP3A inhibitors with LYNPARZA – If concomitant use cannot be avoided, reduce LYNPARZA dosage to 100 mg twice daily when used concomitantly with a strong CYP3A inhibitor or 150 mg twice daily when used concomitantly with a moderate CYP3A inhibitor – After the inhibitor has been discontinued for 3 to 5 elimination half-lives, resume the LYNPARZA dose taken prior to initiating the CYP3A inhibitor **Dosage modifications for patients with renal impairment** – No dosage modification is recommended in patients with mild renal impairment (CLcr 51 to 80 mL/min estimated by Cockcroft-Gault) – Reduce LYNPARZA dosage to 200 mg twice daily in patients with moderate renal impairment (CLcr 31 to 50 mL/min) – There are no data in patients with severe renal impairment or end-stage renal disease (CLcr ≤30 mL/min) **Dosage modifications for patients with hepatic impairment** – No adjustment to the starting dose is required in patients with mild or moderate hepatic impairment (Child-Pugh classification A and B) – There are no data in patients with severe hepatic impairment (Child-Pugh classification C) CYP3A=cytochrome P450, family 3, subfamily A; CLcr=creatinine clearance.
Drug Interactions	**Comments**
	Use with anticancer agents: Clinical studies of LYNPARZA with other myelosuppressive anticancer agents, including DNA-damaging agents, indicate a potentiation and prolongation of myelosuppressive toxicity. **Strong and moderate CYP3A inhibitors:** Coadministration of CYP3A inhibitors can increase olaparib concentrations, which may increase the risk for adverse reactions. Avoid coadministration of strong or moderate CYP3A inhibitors. If the strong or moderate inhibitor must be coadministered, reduce the dose of LYNPARZA. **Strong and moderate CYP3A inducers:** Concomitant use with a strong or

	moderate CYP3A inducer decreased olaparib exposure, which may reduce LYNPARZA efficacy. Avoid coadministration of strong or moderate CYP3A inducers. CYP3A=cytochrome P450, family 3, subfamily A; DNA=deoxyribonucleic acid.
Adverse Reactions	**Comments**
Please see complete Prescribing Information for additional information on adverse reactions.	**Adjuvant Treatment of Germline *BRCA*-mutated HER2-negative High Risk Early Breast Cancer** The most common adverse reactions (Grades 1-4) occurring in ≥10% of patients who received LYNPARZA in OlympiA were nausea (57%), fatigue (including asthenia) (42%), anemia (24%), vomiting (23%), headache (20%), diarrhea (18%), leukopenia (17%), neutropenia (16%), decreased appetite (13%), dysgeusia (12%), dizziness (11%), and stomatitis (10%). The most common laboratory abnormalities (Grades 1-4) reported in ≥25% of patients who received LYNPARZA in OlympiA were decrease in lymphocytes (77%), increase in mean corpuscular volume (67%), decrease in hemoglobin (65%), decrease in leukocytes (64%), and decrease in absolute neutrophil count (39%). **Germline *BRCA*-mutated HER2-negative Metastatic Breast Cancer** The most common adverse reactions (Grades 1-4) occurring in ≥20% of patients who received LYNPARZA in OlympiAD were nausea (58%), anemia (40%), fatigue (including asthenia) (37%), vomiting (30%), neutropenia (27%), respiratory tract infection (27%), leukopenia (25%), diarrhea (21%), and headache (20%). The most common laboratory abnormalities (Grades 1-4) reported in ≥25% of patients who received LYNPARZA in OlympiAD were decrease in hemoglobin (82%), decrease in lymphocytes (73%), decrease in leukocytes (71%), increase in mean corpuscular volume (71%), decrease in absolute neutrophil count (46%), and decrease in platelets (33%).
Warnings and Precautions	**Comments**
	Myelodysplastic syndrome/acute myeloid leukemia Myelodysplastic syndrome (MDS)/acute myeloid leukemia (AML) has occurred in patients treated with LYNPARZA and some cases were fatal. In clinical studies enrolling 2901 patients with various cancers who received LYNPARZA as a single agent, the cumulative incidence of MDS/AML was approximately 1.5% (43/2901). Of these, 51% (22/43) had a fatal outcome. The median duration of therapy with LYNPARZA in patients who developed MDS/AML was 2 years (range: <6 months to >10 years). All of these patients had received previous chemotherapy with platinum agents and/or other DNA-damaging agents, including radiotherapy. Do not start LYNPARZA until patients have recovered from hematological toxicity caused by previous chemotherapy (≤ Grade 1). Monitor complete blood count for cytopenia at baseline and monthly thereafter for clinically significant changes during treatment. For prolonged hematological toxicities, interrupt LYNPARZA and monitor blood counts weekly until recovery. If the levels have not recovered to Grade 1 or less after 4 weeks, refer the patient to a hematologist for further investigations, including bone marrow analysis and blood sample for cytogenetics. If MDS/AML is confirmed, discontinue LYNPARZA. **Pneumonitis** In clinical studies enrolling 2901 patients with various cancers who received

	LYNPARZA as a single agent, the incidence of pneumonitis, including fatal cases, was 0.8% (24/2901). If patients present with new or worsening respiratory symptoms such as dyspnea, cough and fever, or a radiological abnormality occurs, interrupt LYNPARZA treatment and promptly assess the source of the symptoms. If pneumonitis is confirmed, discontinue LYNPARZA treatment and treat the patient appropriately. **Embryo-fetal toxicity** LYNPARZA can cause fetal harm when administered to a pregnant woman based on its mechanism of action and findings in animals. In an animal reproduction study, administration of olaparib to pregnant rats during the period of organogenesis caused teratogenicity and embryo-fetal toxicity at exposures below those in patients receiving the recommended human dose of 300 mg twice daily. Apprise pregnant women of the potential hazard to a fetus and the potential risk for loss of the pregnancy. Advise females of reproductive potential to use effective contraception during treatment and for 6 months following the last dose of LYNPARZA. Based on findings from genetic toxicity and animal reproduction studies, advise male patients with female partners of reproductive potential or who are pregnant to use effective contraception during treatment and for 3 months following the last dose of LYNPARZA.
Use in Specific Populations	**Comments**
	Pregnancy: Based on findings in animals and its mechanism of action, LYNPARZA can cause fetal harm when administered to a pregnant woman. There are no available data on LYNPARZA use in pregnant women to inform the drug-associated risk. In an animal reproduction study, the administration of olaparib to pregnant rats during the period of organogenesis caused teratogenicity and embryo-fetal toxicity at exposures below those in patients receiving the recommended human dose of 300 mg twice daily. Apprise pregnant women of the potential hazard to the fetus and the potential risk for loss of the pregnancy. The estimated background risk of major birth defects and miscarriage for the indicated population is unknown. The estimated background risk in the U.S. general population of major birth defects is 2% to 4%; and the risk for spontaneous abortion is approximately 15% to 20% in clinically recognized pregnancies. **Lactation:** No data are available regarding the presence of olaparib in human milk, or on its effects on the breastfed infant or on milk production. Because of the potential for serious adverse reactions in the breastfed infant from LYNPARZA, advise a lactating woman not to breastfeed during treatment with LYNPARZA and for one month after receiving the last dose. **Females and males of reproductive potential:** Recommend pregnancy testing for females of reproductive potential prior to initiating treatment with LYNPARZA. **Contraception:** *Females* LYNPARZA can cause fetal harm when administered to a pregnant woman. Advise females of reproductive potential to use effective contraception during treatment with LYNPARZA and for at least 6 months following the last dose.

Males
Based on findings in genetic toxicity and animal reproduction studies, advise male patients with female partners of reproductive potential or who are pregnant to use effective contraception during treatment and for 3 months following the last dose of LYNPARZA. Advise male patients not to donate sperm during therapy and for 3 months following the last dose of LYNPARZA.

Pediatric use: Safety and efficacy of LYNPARZA have not been established in pediatric patients.

Geriatric use: Of the 2901 patients with advanced solid tumors who received LYNPARZA as a single agent, 680 (23%) patients were aged ≥65 years, and this included 206 (7%) patients who were aged ≥75 years. Thirteen (0.4%) patients were aged ≥85 years.
No overall differences in the safety or effectiveness of LYNPARZA were observed between these patients and younger patients.

Renal impairment: No dosage modification is recommended in patients with mild renal impairment (CLcr 51 to 80 mL/min estimated by Cockcroft-Gault). Reduce LYNPARZA dosage to 200 mg twice daily in patients with moderate renal impairment (CLcr 31 to 50 mL/min). In a renal impairment trial, the mean AUC increased by 24% and C_{max} by 15%, when olaparib was dosed in patients with mild renal impairment (CLcr=51-80 mL/min defined by the Cockcroft-Gault equation; n=13) and by 44% and 26%, respectively, when olaparib was dosed in patients with moderate renal impairment (CLcr=31-50 mL/min; n=13), compared to those with normal renal function (CLcr ≥81 mL/min; n=12). There was no evidence of a relationship between the extent of plasma protein binding of olaparib and creatinine clearance. There are no data in patients with severe renal impairment or end-stage renal disease (CLcr ≤30 mL/min).

Hepatic impairment: No adjustment to the starting dose is required in patients with mild or moderate hepatic impairment (Child-Pugh classification A and B). In a hepatic impairment trial, the mean AUC increased by 15% and the mean C_{max} increased by 13% when olaparib was dosed in patients with mild hepatic impairment (Child-Pugh classification A; n=10) and the mean AUC increased by 8% and the mean C_{max} decreased by 13% when olaparib was dosed in patients with moderate hepatic impairment (Child-Pugh classification B; n=8), compared to patients with normal hepatic function (n=13). Hepatic impairment has no effect on the protein binding of olaparib and, therefore, total plasma exposure was representative of free drug. There are no data in patients with severe hepatic impairment (Child-Pugh classification C).

AUC=area under the plasma drug concentration-time curve; CLcr=creatinine clearance; C_{max}=maximum drug concentration.

Verification of Appropriate Plan/Drug/Dose/Pt: **Signature:**
RN Verification:
Patient Verification:
Source: LYNPARZA® (olaparib) [prescribing information]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; 2022.