*Test patients with HER2-negative early breast cancer at diagnosis for g*BRCA *mutations* to help inform clinical decisions and eligibility for adjuvant* LYNPARZA[1,2]

Lynparza® olaparib tablets 150 mg

WHY ?

- **Help identify patients who may be eligible for adjuvant treatment with LYNPARZA based on an FDA-approved companion diagnostic[1]**
- Inform screening for ovarian and other *BRCA*m-associated cancers[2,3]
- Provide information on genetic/familial risk[2]

WHEN

- Test HER2-negative patients at diagnosis
- Early g*BRCA*m testing may help inform surgical and post-surgical treatment decisions[2]

*Select patients for this indication based on an FDA-approved companion diagnostic for LYNPARZA.[1]

NCCN Recommended

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Genetic/Familial High-Risk Assessment: Breast, Ovarian, and Pancreatic[4]

To aid in adjuvant treatment decisions with olaparib (LYNPARZA), g*BRCA1/2* mutation testing is recommended for select adult patients of any age and gender with breast cancer that is either
- **HR-positive, HER2-negative with high risk* of recurrence**
- **TNBC†**

*High-risk disease in patients with TNBC is defined as either 1) treated with adjuvant chemotherapy and with axillary node-positive disease or an invasive breast tumor ≥2 cm on pathology analysis or 2) treated with neoadjuvant chemotherapy and with residual invasive breast cancer in the breast or resected lymph nodes. High-risk disease in patients with HR-positive, HER2-negative disease is defined as either 1) treated with adjuvant chemotherapy and with ≥4 positive pathologically confirmed lymph nodes or 2) treated with neoadjuvant chemotherapy which did not have a complete pathologic response and with a CPS&EG score of ≥3.[4]

†According to the FDA-approved indication for LYNPARZA, g*BRCA* test results may inform adjuvant treatment with LYNPARZA for patients with high risk* of TNBC recurrence.[1]

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ASBrS Recommended

The American Society of Breast Surgeons Consensus Guideline on Genetic Testing for Hereditary Breast Cancer[5]

Genetic testing, including g*BRCA1/2* mutation testing, should be made available to all patients with a personal history of breast cancer to help
- **Inform treatment decisions, including surgery, potential radiotherapy, and systemic therapy**
- **Assess hereditary risk**

INDICATION

LYNPARZA is a poly (ADP-ribose) polymerase (PARP) inhibitor indicated:

Adjuvant Treatment of g*BRCA*m, HER2-Negative, High-Risk Early Breast Cancer

For the adjuvant treatment of adult patients with deleterious or suspected deleterious 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.

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

There are no contraindications for LYNPARZA.

WARNINGS AND PRECAUTIONS

Myelodysplastic Syndrome/Acute Myeloid Leukemia (MDS/AML): Occurred in approximately 1.5% of patients exposed to LYNPARZA monotherapy, and the majority of events had a fatal outcome. The median duration of therapy in patients who developed MDS/AML was 2 years (range: <6 months to >10 years). All of these patients had 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 count 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. Discontinue LYNPARZA if MDS/AML is confirmed.

Pneumonitis: Occurred in 0.8% of patients exposed to LYNPARZA monotherapy, and some cases were fatal. If patients present with new or worsening respiratory symptoms such as dyspnea, cough, and fever, or a radiological abnormality occurs, interrupt LYNPARZA treatment and initiate prompt investigation. Discontinue LYNPARZA if pneumonitis is confirmed and treat patient appropriately.

Embryo-Fetal Toxicity: Based on its mechanism of action and findings in animals, LYNPARZA can cause fetal harm. A pregnancy test is recommended for females of reproductive potential prior to initiating treatment.

Females

Advise females of reproductive potential of the potential risk to a fetus and to use effective contraception during treatment and for 6 months following the last dose.

Males

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 and to not donate sperm during this time.

Please see additional Important Safety Information on the reverse side and [the accompanying] complete [Prescribing Information], including [Medication Guide].

*BRCA*m=*BRCA*-mutated; CPS&EG=pre-treatment clinical and post-treatment pathologic stage (CPS), estrogen receptor (ER) status, and histologic grade; g*BRCA*=germline *BRCA*; g*BRCA*m=germline *BRCA*-mutated or germline *BRCA* mutation(s); HR=hormone receptor; TNBC=triple-negative breast cancer.

WHO

- Test select female and male patients with HER2-negative early breast cancer[4,5]
- **Most patients with g*BRCA*m, HER2-negative breast cancer are HR-positive[6]**

~1 in 10 patients with HER2-negative breast cancer has a g*BRCA* mutation[6-12]

Among those patients with g*BRCA*m:

Icons are for illustrative purposes only and do not reflect the distribution of female and male patients with g*BRCA*m, HER2-negative breast cancer.

While g*BRCA* mutations are more prevalent in TNBC, the HR-positive, HER2-negative subtype is the most common subtype and accounts for the majority of patients with g*BRCA*m[6,13,14]

Lynparza® olaparib tablets 150 mg

HOW

Test your patients with the **FDA-approved**

BRACAnalysis CDx®

Call Myriad at **1-800-4-MYRIAD** or visit **[bracanalysiscdx.com]** to order test kits.

Test for gBRCA mutations* at diagnosis. Learn more at [LYNPARZAhcp.com]

*Select patients for this indication based on an FDA-approved companion diagnostic for LYNPARZA.[1]

IMPORTANT SAFETY INFORMATION (Cont'd)

ADVERSE REACTIONS—Adjuvant Treatment of g*BRCA*m, HER2-Negative, High-Risk Early Breast Cancer

Most common adverse reactions (Grades 1-4) in ≥10% of patients who received LYNPARZA in the **adjuvant setting** for **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%).

Most common laboratory abnormalities (Grades 1-4) in ≥25% of patients who received LYNPARZA in the **adjuvant setting** for **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%).

DRUG INTERACTIONS

Anticancer Agents: Clinical studies of LYNPARZA with other myelosuppressive anticancer agents, including DNA-damaging agents, indicate a potentiation and prolongation of myelosuppressive toxicity.

CYP3A Inhibitors: Avoid coadministration of strong or moderate CYP3A inhibitors when using LYNPARZA. If a strong or moderate CYP3A inhibitor must be coadministered, reduce the dose of LYNPARZA. Advise patients to avoid grapefruit, grapefruit juice, Seville oranges, and Seville orange juice during LYNPARZA treatment.

CYP3A Inducers: Avoid coadministration of strong or moderate CYP3A inducers when using LYNPARZA.

USE IN SPECIFIC POPULATIONS

Lactation: No data are available regarding the presence of olaparib in human milk, its effects on the breastfed infant or on milk production. Because of the potential for serious adverse reactions in the breastfed infant, advise a lactating woman not to breastfeed during treatment with LYNPARZA and for 1 month after receiving the final dose.

Pediatric Use: The safety and efficacy of LYNPARZA have not been established in pediatric patients.

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).

Renal Impairment: No dosage modification is recommended in patients with mild renal impairment (CLcr 51-80 mL/min estimated by Cockcroft-Gault). In patients with moderate renal impairment (CLcr 31-50 mL/min), reduce the dose of LYNPARZA to 200 mg twice daily. There are no data in patients with severe renal impairment or end-stage renal disease (CLcr ≤30 mL/min).

Please see additional Important Safety Information on the reverse side and [the accompanying] complete [Prescribing Information], including [Medication Guide].

[You are encouraged to report negative side effects of AstraZeneca prescription drugs by calling 1-800-236-9933. If you prefer to report these to the FDA, call 1-800-FDA-1088.]

[You may report side effects related to AstraZeneca products by clicking here.]

For more information, visit [LYNPARZAhcp.com]

References: 1. LYNPARZA® (olaparib) [prescribing information]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; 2022. **2.** Manahan ER, Kuerer HM, Sebastian M, et al. Consensus Guidelines on Genetic Testing for Hereditary Breast Cancer from the American Society of Breast Surgeons. *Ann Surg Oncol*. 2019;26(10):3025-3031. **3.** *BRCA* gene mutations: cancer risk and genetic testing. National Cancer Institute. Accessed February 22, 2022. https://www.cancer.gov/about-cancer/causes-prevention/genetics/brca-fact-sheet **4.** Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Genetic/Familial High-Risk Assessment: Breast, Ovarian, and Pancreatic V.2.2022. © National Comprehensive Cancer Network, Inc. 2022. All rights reserved. Accessed March 11, 2022. To view the most recent and complete version of the guideline, go online to NCCN.org. **5.** Consensus Guideline on Genetic Testing for Hereditary Breast Cancer. The American Society of Breast Surgeons. Accessed February 22, 2022. https://www.breastsurgeons.org/docs/statements/Consensus-Guideline-on-Genetic-Testing-for-Hereditary-Breast-Cancer.pdf **6.** Kurian AW, Ward KC, Howlader N, et al. Genetic testing and results in a population-based cohort of breast cancer patients and ovarian cancer patients. Supplementary material. Table S3: Genetic test results by breast cancer biomarker subtypes among breast cancer patients. *J Clin Oncol*. 2019;37(15):1305-1315. **7.** Kurian AW, Ward KC, Howlader N, et al. Genetic testing and results in a population-based cohort of breast cancer patients and ovarian cancer patients. *J Clin Oncol*. 2019;37(15):1305-1315. **8.** Winter C, Nilsson MP, Olsson E, et al. Targeted sequencing of *BRCA1* and *BRCA2* across a large unselected breast cancer cohort suggests that one-third of mutations are somatic. Supplementary material. Table S4: *BRCA* status and clinical characteristics. *Ann Oncol*. 2016;27(8):1532-1538. **9.** Copson ER, Maishman TC, Tapper WJ, et al. Germline *BRCA* mutation and outcome in young-onset breast cancer (POSH): a prospective cohort study. *Lancet Oncol*. 2018;19(2):169-180. **10.** Kim H, Choi DH, Park W. Germline *BRCA* mutation and clinical outcomes in breast cancer patients focusing on survival and failure patterns: a long-term follow-up study of Koreans. *Medicina (Kaunas)*. 2020;56(10):514. **11.** Tung N, Lin NU, Kidd J, et al. Frequency of germline mutations in 25 cancer susceptibility genes in a sequential series of patients with breast cancer. *J Clin Oncol*. 2016;34(13):1460-1468. **12.** O'Shaughnessy J, Brezden-Masley C, Cazzaniga M, et al. Prevalence of germline *BRCA* mutations in HER2-negative metastatic breast cancer: global results from the real-world, observational BREAKOUT study. *Breast Cancer Res*. 2020;22(1):114. **13.** Hu C, Polley EC, Yadav S, et al. The contribution of germline predisposition gene mutations to clinical subtypes of invasive breast cancer from a clinical genetic testing cohort. *J Natl Cancer Inst*. 2020;112(12):1231-1241. **14.** Cancer Stat Facts: female breast cancer subtypes. National Cancer Institute. Accessed February 22, 2022. https://seer.cancer.gov/statfacts/html/breast-subtypes.html

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