INDICATIONS AND USAGE

Lynparza is a poly (ADP-ribose) polymerase (PARP) inhibitor indicated as monotherapy in patients with deleterious or suspected deleterious germline BRCA-mutated (as detected by an FDA-approved test) advanced ovarian cancer who have been treated with three or more prior lines of chemotherapy. (1.1) The indication is approved under accelerated approval based on objective response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials. (1.1, 14)

Dosage and Administration

Recommended dose is 400 mg taken orally twice daily with or without food. (2.2)

Continue treatment until disease progression or unacceptable toxicity. (2.2)

For adverse reactions, consider dose interruption of treatment or dose reduction. (2.3)

For moderate renal impairment (CrCl 31–50 mL/min), reduce dose to 300 mg twice daily. (2.5)

Dosage Forms and Strengths

Capsules: 50 mg (3)

Contraindications

None

ADVERSE REACTIONS

Most common adverse reactions (≥20%) in clinical trials were anemia, nausea, fatigue (including asthenia), vomiting, diarrhea, dysgeusia, dyspepsia, headache, decreased appetite, nasopharyngitis/pharyngitis/UIR, cough, arthralgia/musculoskeletal pain, myalgia, back pain, dermatitis/rash and abdominal pain/discomfort. (6.1)

The most common laboratory abnormalities (≥25%) were increase in creatinine, mean corpuscular volume elevation, decrease in hemoglobin, decrease in lymphocytes, decrease in absolute neutrophil count, and decrease in platelets. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact AstraZeneca at 1-800-236-9933 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

DRUG INTERACTIONS

- CYP3A Inhibitors: Avoid concomitant use of strong and moderate CYP3A inhibitors. If the inhibitor cannot be avoided, reduce the dose. (2.3, 7.2)
- CYP3A Inducers: Avoid concomitant use of strong and moderate CYP3A inducers. If a moderate CYP3A inducer cannot be avoided, be aware of a potential for decreased efficacy. (7.3)

USE IN SPECIFIC POPULATIONS

- Lactation: Advise women not to breastfeed. (8.2)

See 17 for PATIENT COUNSELING INFORMATION and MEDICATION GUIDE

Revised: 01/2017
Lynparza™ (olaparib) capsules

2.4 Dose Modifications for Use with CYP3A Inhibitors
Avoid concomitant use of strong and moderate CYP3A inhibitors and consider alternative agents with less CYP3A inhibition. If the inhibitor cannot be avoided, reduce the Lynparza dose to 150 mg (three 50 mg capsules) taken twice daily for a strong CYP3A inhibitor or 200 mg (four 50 mg capsules) taken twice daily for a moderate CYP3A inhibitor [see Drug Interactions (7.2)].

2.5 Dose Modifications for Patients with Renal Impairment
Patients with mild renal impairment (CLcr 51-80 mL/min as estimated by Cockcroft-Gault) do not require an adjustment in Lynparza dosing. In patients with moderate renal impairment (CLcr 31-50 mL/min) the recommended dose reduction is to 300 mg (six 50 mg capsules) taken twice daily, for a total daily dose of 600 mg. The pharmacokinetics of olaparib have not been evaluated in patients with severe renal impairment or end-stage renal disease (CLcr ≤ 30 mL/min) [see Use in Specific Populations (8.7) and Clinical Pharmacology (12.3)].

3 DOSAGE FORMS AND STRENGTHS
Capsules (50 mg): white, opaque, marked in black ink with “OLAPARIB 50 mg” on the cap and the AstraZeneca logo on the body.

4 CONTRAINdications
None.

5 WARNINGS AND PRECAUTIONS
5.1 Myelodysplastic Syndrome/Acute Myeloid Leukemia
Myelodysplastic Syndrome/Acute Myeloid Leukemia (MDS/AML) have been confirmed in 6 out of 298 (2%) patients enrolled in a single arm trial of Lynparza monotherapy, in patients with deleterious or suspected deleterious germline BRCA-mutated (gBRCAm) advanced cancers. In a randomized placebo controlled trial, MDS/AML occurred in 3 out of 136 (2%) patients with advanced ovarian cancer treated with Lynparza. Overall, MDS/AML were reported in ≤1% patients treated with Lynparza in clinical studies. The majority of MDS/AML reports were fatal, and the duration of therapy with Lynparza in patients who developed secondary MDS/cancer-therapy related AML varied from ≤6 months to >2 years. All of these patients had previous chemotherapy with platinum agents and/or other DNA damaging agents including radiotherapy. Some of these patients also had a history of previous cancer or of bone marrow dysplasia.

Monitor complete blood count testing at baseline and monthly thereafter. Do not start Lynparza in these patients was 158 days.

5.2 Pneumonitis
Pneumonitis, including fatal cases, occurred in ≤1% of patients treated with Lynparza. If patients present with new or worsening respiratory symptoms such as dyspnea, fever, cough, wheezing, or a radiological abnormality occurs, interrupt treatment with Lynparza and initiate prompt investigation. If pneumonitis is confirmed, discontinue Lynparza.

5.3 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 400 mg twice daily. Apprise pregnant women of the potential hazard to a fetus. Advise females of reproductive potential to use effective contraception during treatment and for 6 months following the last dose of Lynparza [see Use in Specific Populations (8.1, 8.3), and Clinical Pharmacology (12.1)].

6 ADVERSE REACTIONS
The following adverse reactions are discussed elsewhere in the labeling:
- Myelodysplastic Syndrome/Acute Myeloid Leukemia [see Warnings and Precautions (5.1)]
- Pneumonitis [see Warnings and Precautions (5.2)]

6.1 Clinical Trial Experience
Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

Lynparza 400 mg twice daily as monotherapy, has been studied in 300 patients with gBRCA-mutated advanced ovarian cancer, and 223 of these patients had received 3 or more prior lines of chemotherapy. In the 223 patients with gBRCA-mutated ovarian cancer who received 3 or more prior lines of chemotherapy (including 137 patients in Study 1 with measurable disease) [see Clinical Studies (14)] adverse reactions led to dose interruption in 46% of patients, dose reduction in 4%, and discontinuation in 7%. There were 8 (4%) patients with adverse reactions leading to death, two were attributed to acute leukemia, and one each was attributed to COPD, cerebrovascular accident, intestinal perforation, pulmonary embolism, sepsis, and suture rupture. The median exposure to Lynparza in these patients was 158 days.

Table 1 and Table 2 summarize the common adverse reactions and abnormal laboratory findings, respectively, observed in patients treated with Lynparza.

Table 1 Adverse Reactions Reported in ≥20% of Patients with gBRCA-Mutated Advanced Ovarian Cancer Receiving Lynparza

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>Grades 1-4 N=223</th>
<th>Grades 3-4 N=223</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood and Lymphatic disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anemia</td>
<td>34</td>
<td>18</td>
</tr>
<tr>
<td>Gastrointestinal disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abdominal pain/discomfort</td>
<td>43</td>
<td>8</td>
</tr>
<tr>
<td>Decreased appetite</td>
<td>22</td>
<td>1</td>
</tr>
<tr>
<td>Nausea</td>
<td>64</td>
<td>3</td>
</tr>
<tr>
<td>Vomiting</td>
<td>43</td>
<td>4</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>31</td>
<td>1</td>
</tr>
<tr>
<td>Dyspepsia</td>
<td>25</td>
<td>0</td>
</tr>
<tr>
<td>General disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fatigue/asthenia</td>
<td>66</td>
<td>8</td>
</tr>
<tr>
<td>Infections and infestations</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nasopharyngitis/URI</td>
<td>26</td>
<td>0</td>
</tr>
<tr>
<td>Musculoskeletal and Connective Tissue disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Arthralgia/musculoskeletal pain</td>
<td>21</td>
<td>0</td>
</tr>
<tr>
<td>Myalgia</td>
<td>22</td>
<td>0</td>
</tr>
</tbody>
</table>

Table 2 Laboratory Abnormalities Reported in ≥25% Patients with gBRCA-Mutated Advanced Ovarian Cancer Receiving Lynparza

<table>
<thead>
<tr>
<th>Laboratory Parameter*</th>
<th>Grades 1-4 N=223</th>
<th>Grades 3-4 N=223</th>
</tr>
</thead>
<tbody>
<tr>
<td>Decrease in hemoglobin</td>
<td>90</td>
<td>15</td>
</tr>
<tr>
<td>Decrease in absolute neutrophil count</td>
<td>25</td>
<td>7</td>
</tr>
<tr>
<td>Decrease in platelets</td>
<td>30</td>
<td>3</td>
</tr>
<tr>
<td>Decrease in lymphocytes</td>
<td>56</td>
<td>17</td>
</tr>
<tr>
<td>Mean corpuscular volume elevation</td>
<td>57</td>
<td>-</td>
</tr>
<tr>
<td>Increase in creatinine*</td>
<td>30</td>
<td>2</td>
</tr>
</tbody>
</table>

* Patients were allowed to enter clinical studies with laboratory values of Grade 1.

The following adverse reactions and laboratory abnormailities have been identified in ≥10 to <20% of the 223 patients receiving Lynparza and not included in the table: cough, constipation, dysgeusia, peripheral edema, back pain, dizziness, headache, urinary tract infection, dyspnea, and rash.

The following adverse reactions and laboratory abnormalities have been identified in ≥1% to <10% of the 223 patients receiving Lynparza and not included in the table: leukopenia, stomatitis, peripheral neuropathy, pyrexia, hypomagnesemia, hyperglycemia, anxiety, depression, insomnia, dysuria, urinary incontinence, vulvovaginal disorder, dry skin/eczema, pruritus, hypertension, venous thrombosis (including pulmonary embolism), and hot flush.

Table 3 presents adverse reactions reported in ≥20% of patients from a randomized trial of Lynparza 400 mg twice daily as maintenance monotherapy compared to placebo in patients with platinum sensitive, relapsed, high-grade serous ovarian cancer following treatment with 2 or more platinum-containing regimens. Table 4 presents the laboratory abnormalities in patients from this randomized trial. Of the 96 patients with gBRCA-mutation, 53 received Lynparza, and 43 received placebo. The median duration on treatment with Lynparza was 11.1 months for patients with a gBRCA-mutation compared to 4.4 months for patients with gBRCA-mutation on placebo.

Adverse reactions led to dose interruptions in 26% of those receiving Lynparza and 7% of those receiving placebo; dose reductions in 15% of Lynparza and 5% of placebo patients; and discontinuation in 9% of Lynparza and 0% in placebo patients. One (2%) patient on Lynparza died as a result of an adverse reaction.

The following adverse reactions are discussed elsewhere in the labeling:
- Myelodysplastic Syndrome/Acute Myeloid Leukemia [see Warnings and Precautions (5.1)]
- Pneumonitis [see Warnings and Precautions (5.2)]
7.1 Anticancer Agents
Clinical studies of Lynparza in combination with other myelosuppressive anticancer agents, including DNA damaging agents, indicate a potentiation and prolongation of myelosuppressive toxicity.

7.2 Drugs that may Increase Olaparib Plasma Concentrations
Olaparib is primarily metabolized by CYP3A. In patients (N=57), co-administration of irinotecan, a strong CYP3A inhibitor, increased AUC of olaparib by 2.2-fold. A moderate CYP3A inhibitor, fluorouracil, is predicted to increase the AUC of olaparib by approximately 50%.

Avoid concomitant use of strong CYP3A inhibitors (e.g., phenytoin, rifampicin, carbamazepine, St. John’s Wort) and moderate CYP3A4 inducers (e.g., bosentan, efavirenz, etravirine, modalfinil, nefazodone). If a moderate CYP3A inhibitor cannot be avoided, be aware of a potential for decreased efficacy of Lynparza [see Clinical Pharmacology (12.3)].

8 USE IN SPECIFIC POPULATIONS
8.1 Pregnancy
Risk Summary
Based on findings in animals and its mechanism of action [see Clinical Pharmacology (12.1)], 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 400 mg twice daily [see Data]. 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 2-4%; and the risk for spontaneous abortion is approximately 15-20% in clinically recognized pregnancies.

Data
Animal Data
In a fertility and early embryonic development study in female rats, olaparib was administered orally for 14 days before mating through to day 6 of pregnancy, which resulted in increased post-implantation loss at a dose level of 15 mg/kg/day (with maternal systemic exposures approximately 11% of the human exposure (AUC\text{0-24h}) at the recommended dose).

An embryo-fetal development study, pregnant rats received oral doses of 0.05 and 0.5 mg/kg/day olaparib during the period of organogenesis. A dose of 0.5 mg/kg/day (with maternal systemic exposures approximately 0.3% of human exposure (AUC\text{0-24h}) at the recommended dose) caused embryo-fetal toxicities including increased post-implantation loss and major malformations of the eyes (anophthalmia, microphthalmia), vertebrae/ribs (extra rib or ossification center; fused or absent neural arches, ribs, and sternebrae), skull (fused exoccipital) and diaphragm (hernia). Additional abnormalities or variants included incomplete or absent ossification (vertebrae/sternebrae, ribs, limbs) and other findings in the vertebrae/sternebrae, pelvic girdle, lung, thymus, liver, ureter and umbilical artery. Some findings noted above in the eyes, ribs and ureter were observed at a dose of 0.05 mg/kg/day olaparib at lower incidence.

8.2 Lactation
Risk Summary
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 infants from Lynparza, advise a lactating woman not to breastfeed during treatment with Lynparza and for one month after receiving the last dose.

8.3 Females and Males of Reproductive Potential
Contraception
Females
Lynparza can cause fetal harm when administered to a pregnant woman [see Use in Specific Populations (8.1)]. Advise females of reproductive potential to use highly effective contraception during treatment with Lynparza and for at least 6 months following the last dose.

8.4 Pediatric Use
The safety and efficacy of Lynparza have not been established in pediatric patients.

8.5 Geriatric Use
In clinical studies of Lynparza enrolling 735 patients with advanced solid tumors [the majority (69%) of whom had ovarian cancer] who received Lynparza 400 mg twice daily as monotherapy, 148 (20%) of patients were aged ≥65 years. The safety profile was similar irrespective of age with the exception of AEs of CTCAE ≥3 which were reported more frequently in patients aged ≥65 years (53.4%) than those <65 years (43.4%). No individual adverse event or System Organ Class accounted for this observed difference.

Table 3 Adverse Reactions Reported in ≥20% of Patients with gBRCA-Mutated Ovarian Cancer in the Randomized Trial

<table>
<thead>
<tr>
<th>Adverse Reactions</th>
<th>Lynparza N=53</th>
<th>Placebo N=43</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Grades 1-4 %</td>
<td>Grades 3-4 %</td>
</tr>
<tr>
<td>Blood and Lymphatic disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anemia</td>
<td>25</td>
<td>4</td>
</tr>
<tr>
<td>Gastrointestinal disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abdominal pain/discomfort</td>
<td>47</td>
<td>0</td>
</tr>
<tr>
<td>Decreased appetite</td>
<td>25</td>
<td>0</td>
</tr>
<tr>
<td>Nausea</td>
<td>75</td>
<td>2</td>
</tr>
<tr>
<td>Vomiting</td>
<td>32</td>
<td>4</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>28</td>
<td>4</td>
</tr>
<tr>
<td>Dyspepsia</td>
<td>25</td>
<td>0</td>
</tr>
<tr>
<td>Dysgeusia</td>
<td>21</td>
<td>0</td>
</tr>
<tr>
<td>General disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fatigue (including asthenia, lethargy)</td>
<td>68</td>
<td>6</td>
</tr>
<tr>
<td>Infections and infestations</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nasopharyngitis/Pharyngitis/URI</td>
<td>43</td>
<td>0</td>
</tr>
</tbody>
</table>
| Musculoskeletal and Connective tissue disorders
  Arthralgia/Musculoskeletal pain        | 32            | 4            | 21            | 0            |               |              |
  Myalgia                               | 25            | 2            | 12            | 0            |               |              |
  Back pain                             | 25            | 6            | 21            | 0            |               |              |
| Nervous system disorder               | Headache      | 25           | 0             | 19           | 2             |              |
| Respiratory, Thoracic, Mediastinal disorders
  Cough                                 | 21            | 0            | 14            | 0            |               |              |
| Skin and Subcutaneous Tissue          | Dermatitis/Rash | 25           | 0             | 14           | 0             |              |

Table 4 Laboratory Abnormalities in ≥25% Patients with gBRCA-Mutated Ovarian Cancer in the Randomized Trial

<table>
<thead>
<tr>
<th>Laboratory parameter</th>
<th>Lynparza N=53</th>
<th>Placebo N=43</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Grades 1-4 %</td>
<td>Grades 3-4 %</td>
</tr>
<tr>
<td>Decrease in hemoglobin</td>
<td>85</td>
<td>8</td>
</tr>
<tr>
<td>Decrease in absolute neutrophil count</td>
<td>32</td>
<td>8</td>
</tr>
<tr>
<td>Decrease in platelets</td>
<td>26</td>
<td>6</td>
</tr>
<tr>
<td>Mean corpuscular volume elevation</td>
<td>85</td>
<td>-</td>
</tr>
<tr>
<td>Increase in creatinine*</td>
<td>26</td>
<td>0</td>
</tr>
</tbody>
</table>

* Patients were allowed to enter clinical studies with laboratory values of Grade 1.

Avoid grapefruit and Seville oranges during Lynparza treatment [see Dosage and Administration (2.4) and Clinical Pharmacology (12.3)].
8.6 Hepatic Impairment

No adjustment to the starting dose is required in patients with mild hepatic impairment. A 1.2-fold increase in mean exposure (AUC) was observed in patients with mild hepatic impairment (based on Child-Pugh classification A) compared to patients with normal hepatic function. There are no data in patients with moderate or severe hepatic impairment [see Clinical Pharmacology (12.3)].

8.7 Renal Impairment

A 1.2-fold increase in mean exposure (AUC) was observed in patients with mild renal impairment (CLcre = 51-80 mL/min) compared to patients with normal renal function (CLcre >80 mL/min). No dose adjustment to the starting dose is required in patients with mild renal impairment, but patients should be monitored closely for toxicity. A 1.4-fold increase in AUC was observed in patients with moderate renal impairment (CLcre = 31-50 mL/min) compared to patients with normal renal function (CLcre >80 mL/min). For patients with moderate renal impairment, reduce the dose of Lynparza to 300 mg twice daily [see Dosage and Administration (2.5)]. There are no data in patients with severe renal impairment or end-stage disease (CLcre ≤30 mL/min) [see Clinical Pharmacology (12.3)].

10 OVERDOSAGE

There is no specific treatment in the event of Lynparza overdose, and symptoms of overdose are not established. In the event of an overdose, physicians should follow general supportive measures and should treat symptomatically.

11 DESCRIPTION

Olaparib is an inhibitor of the mammalian polyadenosine 5′-diphosphoribose polymerase (PARP) enzyme. The chemical name is 4-[[3-[[4-cyclopropylcarbonyl]piperezin-1-y]carbonyl]-4-fluorophenyl]methyl]phenazin-1(2H)-one and it has the following chemical structure:

\[
\text{C}_{26}\text{H}_{28}\text{N}_{2}\text{O}_{4}
\]

The empirical formula for Lynparza is C_{26}H_{28}N_2O_4 and the relative molecular mass is 434.46.

Olaparib is a crystalline solid, is non-chiral and shows pH-independent low solubility of approximately 0.1 mg/mL across the physiological pH range.

Lynparza is available in 50 mg capsules for oral administration. Each capsule contains olaparib as the active ingredient and the following inactive ingredients:

- Capsule content: lauroyl polyoxylglycerides
- Capsule shell: hypromellose, titanium dioxide, gelatin gum, potassium acetate
- Capsule printing ink: shellac, ferrisosferic oxide

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Lynparza is an inhibitor of poly (ADP-ribose) polymerase (PARP) enzymes, including PARP1, PARP2, and PARP3. PARP enzymes are involved in normal cellular homeostasis, such as DNA transcription, cell cycle regulation, and DNA repair. Olaparib has been shown to inhibit growth of select tumor cell lines in vitro and decrease tumor growth in mouse xenograft models of human cancer both as monotherapy or following platinum-based chemotherapy. Increased cytotoxicity and anti-tumor activity following treatment with olaparib were noted in cell lines and mouse tumor models with deficiencies in BRCA.

In vitro studies have shown that olaparib-induced cytotoxicity may involve inhibition of PARP enzymatic activity and increased formation of PARP-DNA complex, resulting in disruption of cellular homeostasis and cell death.

12.3 Pharmacokinetics

**Absorption**

Following oral administration of olaparib via the capsule formulation, absorption is rapid with peak plasma concentrations typically achieved between 1 to 3 hours after dosing. On multiple dosing there is no marked accumulation (accumulation ratio of 1.4 – 1.5 for twice daily dosing), with steady state exposures achieved within 3 to 4 days. Limited data suggest that the systemic exposure (AUC) of olaparib increases less than proportionally with dose over the dose range of 100 to 400 mg, but the PK data were variable across trials.

Co-administration with a high fat meal slowed the rate (Tmax delayed by 2 hours) of absorption, but did not significantly alter the extent of olaparib absorption (mean AUC increased by approximately 20%).

**Distribution**

Olaparib had a mean (± standard deviation) apparent volume of distribution at steady state of 167 ± 196 L after a single 400 mg dose of olaparib. In vitro protein binding of olaparib at plasma concentrations achieved following dosing at 400 mg twice daily is approximately 82%.
14 CLINICAL STUDIES
The efficacy of Lynparza was investigated in a single-arm study in patients with deleterious or suspected deleterious germline BRCA-mutated (gBRCAm) advanced cancers (Study 1). A total of 137 patients with measurable, gBRCAm-associated ovarian cancer treated with three or more prior lines of chemotherapy were enrolled. All patients received Lynparza at a dose of 400 mg twice daily as monotherapy until disease progression or intolerable toxicity. Objective response rate (ORR) and duration of response (DOR) were assessed by the investigator according to RECIST v1.1.

The median age of the patients was 58 years, the majority were Caucasian (94%) and 93% had an ECOG PS of 0 or 1. Deleterious or suspected deleterious, germline BRCA-mutation status was verified retrospectively in 97% (59/61) of the patients for whom blood samples were available by the companion diagnostic BRACAnalysis CDxTM, which is FDA approved for selection of patients for Lynparza treatment.

Efficacy results from Study 1 are summarized in Table 5.

Table 5 Overall Response and Duration of Response in Patients with gBRCA-mutated Advanced Ovarian Cancer Who Received 3 or More Prior Lines of Chemotherapy in Study 1

<table>
<thead>
<tr>
<th></th>
<th>N=137</th>
</tr>
</thead>
<tbody>
<tr>
<td>Objective Response Rate (95% CI)</td>
<td>34% (26, 42)</td>
</tr>
<tr>
<td>Complete Response</td>
<td>2%</td>
</tr>
<tr>
<td>Partial Response</td>
<td>32%</td>
</tr>
<tr>
<td>Median DOR in months (95% CI)</td>
<td>7.9 (5.6, 9.6)</td>
</tr>
</tbody>
</table>

16 HOW SUPPLIED/STORAGE AND HANDLING
16.1 How Supplied
Lynparza 50 mg is a white, opaque, hard capsule, marked in black ink with: “OLAPARIB 50 mg” on the cap and AstraZeneca logo on the body; available in:
Bottles of 112 capsules NDC 0310-0657-58

16.2 Storage
Store at 25°C (77°F), excursions permitted to 15°C-30°C (59°F-86°F) [see USP Controlled Room Temperature]

Lynparza should not be exposed to temperatures greater than 40°C or 104°F. Do not take Lynparza if it is suspected of having been exposed to temperatures greater than 40°C or 104°F.

17 PATIENT COUNSELING INFORMATION
Advise the patient to read the FDA-approved patient labeling (Medication Guide).

• Dosing Instructions: Inform patients on how to take Lynparza [see Dosage and Administration (2.2)]. Lynparza should be taken twice daily with or without food. Instruct patients that if they miss a dose of Lynparza, not to take an extra dose to make up for the one that they missed. They should take their next normal dose at the usual time. Each capsule should be swallowed whole. Do not chew, dissolve, or open the capsule. Patient should not take Lynparza with grapefruit or Seville oranges.

• MDS/AML: Advise patients to contact their healthcare provider if they experience weakness, feeling tired, fever, weight loss, frequent infections, bruising, bleeding easily, breathlessness, blood in urine or stool, and/or laboratory findings of low blood cell counts, or a need for blood transfusions. This may be a sign of hematological toxicity or a more serious uncommon bone marrow problem called ‘myelodysplastic syndrome’ (MDS) or ‘acute myeloid leukemia’ (AML) which have been reported in patients treated with Lynparza [see Warnings and Precautions (5.1)].

• Pneumonitis: Advise patients to contact their healthcare provider if they experience any new or worsening respiratory symptoms including shortness of breath, fever, cough, or wheezing [see Warnings and Precautions (5.2)].

• Embryo-Fetal Toxicity: Advise females to inform their healthcare provider if they are pregnant or become pregnant. Inform female patients of the risk to a fetus and potential loss of the pregnancy [see Use in Specific Populations (8.1)]. Advise females of reproductive potential to use effective contraception during treatment with Lynparza and for 6 months after receiving the last dose [see Warnings and Precautions (5.3) and Use in Specific Populations (8.1, 8.3)].

• Lactation: Advise patients not to breastfeed while taking Lynparza and for one month after receiving the last dose [see Use in Special Populations (8.2)].

• Nausea/vomiting: Advise patients that mild or moderate nausea and/or vomiting is very common in patients receiving Lynparza and that they should contact their healthcare provider who will advise on available antiemetic treatment options.
**What is the most important information I should know about Lynparza?**

Lynparza may cause serious side effects that can lead to death, including:

**Bone marrow problems called Myelodysplastic Syndrome (MDS) or Acute Myeloid Leukemia (AML).** Some people who have ovarian cancer or who have received previous treatment with chemotherapy, radiotherapy or certain other medicines for their cancer have developed MDS or AML during treatment with Lynparza. If you develop MDS or AML, your healthcare provider will stop treatment with Lynparza.

Symptoms of low blood cell counts are common during treatment with Lynparza, but can be a sign of serious bone marrow problems, including MDS or AML. Symptoms may include:

- weakness
- blood in urine or stool
- weight loss
- shortness of breath
- fever
- feeling very tired
- frequent infections
- bruising or bleeding more easily

Your healthcare provider will do blood tests to check your blood cell counts:

- before treatment with Lynparza
- every month during treatment with Lynparza
- weekly if you have low blood cell counts that last a long time. Your healthcare provider may stop treatment with Lynparza until your blood cell counts improve.

**Lung problems (pneumonitis).** Tell your healthcare provider if you have any new or worsening symptoms of lung problems, including shortness of breath, fever, cough, or wheezing. Your healthcare provider may do a chest x-ray if you have any of these symptoms. Your healthcare provider may temporarily stop treatment or completely stop treatment if you develop pneumonitis.

Tell your healthcare provider if you have any of the symptoms above during treatment with Lynparza.

**What is Lynparza?**

Lynparza is a prescription medicine used to treat women with advanced ovarian cancer who:

- have received previous treatment with 3 or more prior chemotherapy medicines or a combination of chemotherapy medicines for their cancer, and
- have a certain type of abnormal inherited BRCA gene.

Your healthcare provider will perform a test to make sure that Lynparza is right for you.

It is not known if Lynparza is safe and effective in children.

**What should I tell my healthcare provider before taking Lynparza?**

Before you take Lynparza, tell your healthcare provider about all of your medical conditions including if you:

- have lung or breathing problems
- have liver problems
- have kidney problems
- are pregnant or plan to become pregnant. Lynparza can harm your unborn baby and may cause loss of pregnancy (miscarriage).
  - If you are able to become pregnant, your healthcare provider may do a pregnancy test before you start treatment with Lynparza.
  - Females who are able to become pregnant should use effective birth control (contraception) during treatment with Lynparza and for 6 months after receiving the last dose of Lynparza.
  - Talk to your healthcare provider about birth control methods that may be right for you.
  - Tell your healthcare provider right away if you become pregnant.
- are breastfeeding or plan to breastfeed. It is not known if Lynparza passes into your breast milk. Do not breastfeed during treatment with Lynparza and for 1 month after receiving the last dose of Lynparza. Talk to your healthcare provider about the best way to feed your baby during this time.

**Tell your healthcare provider about all the medicines you take,** including prescription and over-the-counter medicines, vitamins, and herbal supplements. Taking Lynparza and certain other medicines may affect how Lynparza works and may cause side effects.
**How should I take Lynparza?**

- Take Lynparza exactly as your healthcare provider tells you.
- Your healthcare provider may temporarily stop treatment with Lynparza or change your dose of Lynparza if you have side effects.
- Take Lynparza by mouth 2 times a day. Each dose should be taken 12 hours apart.
- Take Lynparza with or without food.
- Swallow Lynparza capsules whole. Do not chew, dissolve, or open the capsules.
- Do not take Lynparza capsules if they look damaged or show signs of leakage.
- If you miss a dose of Lynparza, take your next dose at your usual scheduled time. Do not take an extra dose to make up for a missed dose.
- If you take too much Lynparza, call your healthcare provider or go to the nearest emergency room right away.

**What should I avoid while taking Lynparza?**

- Avoid grapefruit, grapefruit juice and Seville oranges during treatment with Lynparza. Grapefruit and Seville oranges may increase the level of Lynparza in your blood.

**What are the possible side effects of Lynparza?**

Lynparza may cause serious side effects.

See “What is the most important information I should know about Lynparza?”

The most common side effects of Lynparza are:

- nausea or vomiting. Tell your healthcare provider if you get nausea or vomiting. Your healthcare provider may prescribe medicines to treat these symptoms.
- tiredness or weakness
- diarrhea
- indigestion or heartburn
- headache
- loss of appetite
- changes in the way food tastes
- changes in kidney function blood test
- sore throat or runny nose
- upper respiratory infection
- cough
- pain in the joints, muscles, and back
- rash
- pain or discomfort in the stomach area

These are not all the possible side effects of Lynparza. For more information, ask your healthcare provider or pharmacist. Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

**How should I store Lynparza?**

- Store Lynparza at room temperature, between 68°F to 77°F (20°C to 25°C).
- Do not store Lynparza at temperatures greater than 104°F (40°C). Do not take Lynparza if you think it may have been stored at a temperature greater than 104°F (40°C).

Keep Lynparza and all medicines out of the reach of children.

**General information about the safe and effective use of Lynparza**

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not use Lynparza for a condition for which it was not prescribed. Do not give Lynparza to other people, even if they have the same symptoms you have. It may harm them. If you would like more information, talk with your healthcare provider. You can ask your healthcare provider or pharmacist for information about Lynparza that is written for health professionals.

**What are the ingredients in Lynparza?**

**Active ingredient:** olaparib

**Inactive ingredients:**
Capsule contains: lauroyl polyoxyglycerides
Capsule shell contains: hypromellose, titanium dioxide, gellan gum, potassium acetate
Capsule printing ink contains: shellac, ferrosoferric oxide

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