HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use LYNPARZA safely and effectively. See full prescribing information for LYNPARZA.

LYNPARZA® (olaparib) tablets, for oral use
Initial U.S. Approval: 2014

---------- **INDICATIONS AND USAGE** ----------
Lynparza is a poly (ADP-ribose) polymerase (PARP) inhibitor indicated:
- for the maintenance treatment of adult patients with recurrent epithelial ovarian, fallopian tube or primary peritoneal cancer, who are in a complete or partial response to platinum-based chemotherapy. (1.1)
- for the treatment of adult patients with deleterious or suspected deleterious germline *BRCA*-mutated advanced ovarian cancer who have been treated with three or more prior lines of chemotherapy. Select patients for therapy based on an FDA-approved companion diagnostic for Lynparza. (1.2, 2.3)

---------- **DOSAGE AND ADMINISTRATION** ----------
- To avoid substitution errors and overdose, **do not substitute Lynparza tablets with Lynparza capsules** on a milligram-to-milligram basis due to differences in the dosing and bioavailability of each formulation. (2.1)
- Recommended tablet dose is 300 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 or dose reduction. (2.4)
- For moderate renal impairment (CLcr 31-50 mL/min), reduce dose to 200 mg twice daily. (2.6)

---------- **DOSAGE FORMS AND STRENGTHS** ----------
Tablets: 150 mg, 100 mg (3)

---------- **CONTRAINDICATIONS** ----------
None (4)

---------- **WARNINGS AND PRECAUTIONS** ----------
- Myelodysplastic Syndrome/Acute Myeloid Leukemia (MDS/AML): Occurred in <1.5% of patients exposed to Lynparza monotherapy and the majority of events had a fatal outcome. Monitor patients for hematological toxicity at baseline and monthly thereafter. Discontinue if MDS/AML is confirmed. (5.1)
- Pneumonitis: Occurred in <1% of patients exposed to Lynparza, and some cases were fatal. Interrupt treatment if pneumonitis is suspected. Discontinue if pneumonitis is confirmed. (5.2)
- Embryo-Fetal Toxicity: Lynparza can cause fetal harm. Advise females of reproductive potential of the potential risk to a fetus and to use effective contraception. (5.3, 8.1, 8.3)

---------- **ADVERSE REACTIONS** ----------
- Most common adverse reactions (≥20%) in clinical trials were anemia, nausea, fatigue (including asthenia), vomiting, nasopharyngitis/upper respiratory tract infection/influenza, diarrhea, arthralgia/myalgia, dysgeusia, headache, dyspepsia, decreased appetite, constipation. and stomatitis. (6.1)
- Most common laboratory abnormalities (≥25%) were decrease in hemoglobin, increase in mean corpuscular volume, decrease in lymphocytes, decrease in leukocytes, decrease in absolute neutrophil count, increase in serum creatinine 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 or moderate CYP3A inhibitors. If the inhibitor cannot be avoided, reduce the olaparib dose. (2.5, 7.2)
- CYP3A Inducers: Avoid concomitant use of strong or moderate CYP3A inducers as decreased efficacy can occur. (7.3, 12.3)

---------- **USE IN SPECIFIC POPULATIONS** ----------
Lactation: Advise women not to breastfeed. (8.2)

See 17 for PATIENT COUNSELING INFORMATION and MEDICATION GUIDE

Revised: 8/2017

FULL PRESCRIBING INFORMATION: CONTENTS*

*Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

1.1 Maintenance Treatment of Recurrent Ovarian Cancer

Lynparza is indicated for the maintenance treatment of adult patients with recurrent epithelial ovarian, fallopian tube or primary peritoneal cancer, who are in a complete or partial response to platinum-based chemotherapy.

1.2 Advanced *gBRCA*-mutated Ovarian Cancer After 3 or More Lines of Chemotherapy

Lynparza is indicated for the treatment of adult patients with deleterious or suspected deleterious germline *BRCA*-mutated (*gBRCAm*) advanced ovarian cancer who have been treated with three or more prior lines of chemotherapy. Select patients for therapy based on an FDA-approved companion diagnostic for Lynparza.

2 DOSAGE AND ADMINISTRATION

2.1 Important Administration Instructions

Lynparza is also available as a 50 mg capsule. **DO NOT substitute Lynparza tablets (100 mg and 150 mg) with Lynparza capsules (50 mg)** on a milligram-to-milligram basis due to differences in the dosing and bioavailability of each formulation *[see Clinical Pharmacology (12.3)]*. Refer to the full prescribing information for Lynparza capsules for specific capsule dosing.

2.2 Recommended Dosing

The recommended dose of Lynparza is 300 mg (two 150 mg tablets) taken orally twice daily, with or without food, for a total daily dose of 600 mg. The 100 mg tablet is available for dose reduction.

Continue treatment until disease progression or unacceptable toxicity.

If a patient misses a dose of Lynparza, instruct patient to take their next dose at its scheduled time.

Swallow tablets whole. Do not chew, crush, dissolve, or divide tablet *[see How Supplied/Storage and Handling (16.2)]*.

2.3 Patient Selection for *gBRCA*-mutated Advanced Ovarian Cancer

Select patients for the treatment of advanced ovarian cancer with Lynparza based on the presence of deleterious or suspected deleterious *BRCA*-mutations *[see Indications and Usage (1.2) and Clinical Studies (14.2)]*. Information on FDA-approved tests for the detection of *BRCA*-mutations is available at http://www.fda.gov/companiondiagnostics.

2.4 Dose Adjustments for Adverse Reactions

To manage adverse reactions, consider interruption of treatment or dose reduction.

The recommended dose reduction is to 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.

2.5 Dose Modifications for Use with CYP3A Inhibitors

Avoid concomitant use of strong or moderate CYP3A inhibitors and consider alternative agents with less CYP3A inhibition. If a strong CYP3A inhibitor must be co-administered, reduce the Lynparza dose to 100 mg (one 100 mg tablet) taken twice daily (equivalent to a total daily dose of 200 mg). If a moderate CYP3A inhibitor must be co-administered, reduce the Lynparza dose to 150 mg (one 150 mg tablet) taken twice daily (equivalent to a total daily dose of 300 mg) *[see Drug Interactions (7.2) and Clinical Pharmacology (12.3)]*.

2.6 Dose Modifications for Patients with Renal Impairment

Patients with mild renal impairment (CLcr 51-80 mL/min as estimated by Cockcroft-Gault equation) 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 200 mg (two 100 mg tablets) twice daily, for a total daily dose of 400 mg. The pharmacokinetics of Lynparza 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

Tablets:

- 150 mg: green to green/grey, oval, bi-convex, film-coated, with debossment ‘OP150’ on one side and plain on the reverse side.
- 100 mg: yellow to dark yellow, oval, bi-convex, film-coated, with debossment ‘OP100’ on one side and plain on the reverse side.

4 CONTRAINDICATIONS

None.

5 WARNINGS AND PRECAUTIONS

5.1 Myelodysplastic Syndrome/Acute Myeloid Leukemia

Overall, the incidence of Myelodysplastic Syndrome/Acute Myeloid Leukemia (MDS/AML) in patients treated with Lynparza monotherapy in clinical trials, including long-term follow up, was <1.5% (21/1680) and the majority of events had a fatal outcome. Of these, 19/21 patients had a documented *BRCA* mutation, 1 patient had *gBRCA* wildtype and in 1 patient the *BRCA* mutation status was unknown. Additional cases of MDS/AML have been documented in patients treated with Lynparza in combination studies. 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 received 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 bone marrow dysplasia.

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.

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, 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.

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 300 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.

Adverse reactions presented below were reported from clinical trials in 782 patients with ovarian cancer (555 received Lynparza, 227 received placebo).

Maintenance Treatment of Recurrent Ovarian Cancer

SOLO-2

The safety of Lynparza for the maintenance treatment of patients with platinum sensitive *gBRCAm* ovarian cancer was investigated in SOLO-2. This study was a placebo-controlled, double-blind study in which 294 patients received either Lynparza 300 mg (2 x 150 mg tablets) twice daily (n=195) or placebo tablets twice daily (n=99) until disease progression or unacceptable toxicity. The median duration of study treatment was 19.4 months for patients who received Lynparza and 5.6 months for patients who received placebo. Dose interruptions due to an adverse reaction of any grade occurred in 45% of patients receiving Lynparza and 18% of those receiving placebo; dose reductions due to an adverse reaction occurred in 27% of Lynparza patients and 3% of placebo patients. The most frequent adverse reactions leading to dose interruption or reduction of Lynparza were anemia (22%), neutropenia (9%), and fatigue/asthenia (8%). Discontinuation occurred in 11% of Lynparza patients and 2% in placebo patients.

Table 1 summarizes the adverse reactions that occurred in at least 20% of patients who received Lynparza in SOLO-2. Table 2 presents the laboratory abnormalities that occurred in at least 25 % of patients who received Lynparza in SOLO-2.

Table 1 Adverse Reactions[a] in SOLO-2 (≥20% of Patients who Received Lynparza)

Adverse Reactions	Lynparza tablets n=195		Placebo n=99	
	Grades 1-4 %	Grades 3-4 %	Grades 1-4 %	Grades 3-4 %
Blood and lymphatic disorders				
Anemia[b]	44	20	9	2
Gastrointestinal disorders				
Nausea	76	3	33	0
Vomiting	37	3	19	1
Diarrhea	33	2	22	0
Stomatitis[c]	20	1	16	0
Infections and Infestations				
Nasopharyngitis/ URI/ sinusitis/ rhinitis/ influenza	36	0	29	0
General disorders and administration site conditions				
Fatigue including asthenia	66	4	39	2
Metabolism and nutrition disorders				
Decreased appetite	22	0	11	0
Musculoskeletal and connective tissue disorder				
Arthralgia/myalgia	30	0	28	0
Nervous system disorders				
Dysgeusia	27	0	7	0
Headache	26	1	14	0

[a] Graded according to the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE), version 4.0.

[b] Represents grouped term consisting of anemia, hematocrit decreased, hemoglobin decreased, iron deficiency, mean cell volume increased and red blood cell count decreased.

[c] Represents grouped term consisting of abscess oral, aphthous ulcer, gingival abscess, gingival disorder, gingival pain, gingivitis, mouth ulceration, mucosal infection, mucosal inflammation, oral candidiasis, oral discomfort, oral herpes, oral infection, oral mucosal erythema, oral pain, oropharyngeal discomfort, and oropharyngeal pain.

In addition, the adverse reactions observed in SOLO-2 that occurred in <20% of patients receiving Lynparza were neutropenia, rash, cough, dyspepsia, leukopenia, hypomagnesemia, dizziness, thrombocytopenia, increase in creatinine, lymphopenia and edema.

Table 2 Laboratory Abnormalities Reported in ≥25% of Patients in SOLO-2

Laboratory Parameter[a]	Lynparza tablets n=195		Placebo n=99	
	Grades 1-4 %	Grades 3-4 %	Grades 1-4 %	Grades 3-4 %
Increase in mean corpuscular volume[b]	89	-	52	-
Decrease in hemoglobin	83	17	69	0
Decrease in leukocytes	69	5	48	1
Decrease in lymphocytes	67	11	37	1
Decrease in absolute neutrophil count	51	7	34	3
Increase in serum creatinine	44	0	29	0
Decrease in platelets	42	2	22	1

[a] Patients were allowed to enter clinical studies with laboratory values of CTCAE Grade 1.
[b] Represents the proportion of subjects whose mean corpuscular volume was > upper limit of normal (ULN).

Study 19

The safety of Lynparza capsules as maintenance monotherapy was also evaluated in patients with platinum sensitive ovarian cancer who had received 2 or more previous platinum containing regimens in Study 19, a randomized, placebo-controlled, double-blind, multi-center study in which 264 patients received Lynparza 400 mg twice daily (n=136) or placebo (n=128). At the time of final analysis, the median duration of exposure was 8.7 months in patients who received Lynparza and 4.6 months in patients who received placebo.

Adverse reactions led to dose interruptions in 35% of those receiving Lynparza and 10% of those receiving placebo; dose reductions in 26% of Lynparza and 4% of placebo; and discontinuation in 6% of Lynparza and 2% in placebo.

Table 3 summarizes the adverse reactions that occurred in at least 20% of patients who received Lynparza in Study 19. Table 4 presents the laboratory abnormalities that occurred in at least 25% of patients from Study 19.

Table 3 Adverse Reactions[a] in Study 19 (≥20% of Patients who Received Lynparza)

Adverse Reactions	Lynparza capsules n=136		Placebo n=128	
	Grades 1-4 %	Grades 3-4 %	Grades 1-4 %	Grades 3-4 %
Blood and lymphatic disorders				
Anemia[b]	23	7	7	1
Gastrointestinal disorders				
Nausea	71	2	36	0
Vomiting	35	2	14	1
Diarrhea	28	2	25	2
Constipation	22	1	12	0
General disorders and administration site conditions				
Fatigue (including asthenia)	63	9	46	3
Infections and infestations				
Respiratory tract infection	22	2	11	0
Metabolism and nutrition disorders				
Decreased appetite	21	0	13	0
Nervous system disorders				
Headache	21	0	13	1

[a] Graded according to NCI CTCAE 4.0.
[b] Represents grouped terms of related terms that reflect the medical concept of the adverse reaction.

In addition, the adverse reactions in Study 19 that occurred in <20% of patients receiving Lynparza were dyspepsia, stomatitis, dysgeusia, dizziness, increase in creatinine, neutropenia, thrombocytopenia, leukopenia, lymphopenia, dyspnea, pyrexia and edema.

Table 4 Laboratory Abnormalities Reported in ≥25% of Patients in Study 19

Laboratory Parameter[a]	Lynparza capsules n=136		Placebo n=129	
	Grades 1-4 %	Grades 3-4 %	Grades 1-4 %	Grades 3-4 %
Decrease in hemoglobin	82	8	58	1
Increase in mean corpuscular volume[b]	82	-	51	-
Decrease in leukocytes	58	4	37	2
Decrease in lymphocytes	52	10	32	3
Decrease in absolute neutrophil count	47	7	40	2
Increase in serum creatinine	45	0	14	0
Decrease in platelets	36	4	18	0

[a] Patients were allowed to enter clinical studies with laboratory values of CTCAE Grade 1.
[b] Represents the proportion of subjects whose mean corpuscular volume was > ULN.

Treatment of Advanced *gBRCAm* Ovarian Cancer After 3 or More Lines of Chemotherapy

Pooled data

Treatment with Lynparza (capsule formulation) as monotherapy was studied in 223 patients (pooled from 6 studies) with *gBRCAm* advanced ovarian cancer who had received 3 or more prior lines of

chemotherapy. Adverse reactions led to dose interruption in 40% of patients, dose reduction in 4% of patients, and discontinuation in 7% of patients. 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 capsules in these patients was 5.2 months.

Table 5 presents adverse reactions reported in ≥20% of patients and Table 6 presents laboratory abnormalities that occurred in at least 25% of patients from the pooled studies.

Table 5 Adverse Reactions Reported in Pooled Data (≥20% of Patients who Received Lynparza)

Adverse Reactions	3 or more lines of prior Chemotherapy	
	Grades 1-4 n=223 %	Grades 3-4 n=223 %
Blood and Lymphatic disorders		
Anemia	34	18
Gastrointestinal disorders		
Decreased appetite	22	1
Nausea	64	3
Vomiting	43	4
Diarrhea	31	1
Dyspepsia	25	0
General disorders		
Fatigue/asthenia	66	8
Infections and infestations		
Nasopharyngitis/URI	26	0
Musculoskeletal and Connective Tissue disorders		
Arthralgia/musculoskeletal pain	21	0
Myalgia	22	0

Table 6 Laboratory Abnormalities Reported ≥25% of Patients in Pooled Data

Laboratory Parameter[a]	3 or more lines of prior Chemotherapy	
	Grades 1-4 n=223 (%)	Grades 3-4 n=223 (%)
Decrease in hemoglobin	90	15
Decrease in absolute neutrophil count	25	7
Decrease in platelets	30	3
Decrease in lymphocytes	56	17
Mean corpuscular volume elevation	57	-
Increase in creatinine	30	2

[a] Patients were allowed to enter clinical studies with laboratory values of CTCAE Grade 1.

The following adverse reactions and laboratory abnormalities 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, and venous thrombosis (including pulmonary embolism).

6.2 Postmarketing Experience

The following adverse reactions have been identified during post-approval use of Lynparza capsules. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Immune System Disorders: Hypersensitivity (rash/dermatitis).

7 DRUG INTERACTIONS

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 itraconazole, a strong CYP3A inhibitor, increased AUC of olaparib by 170%. A moderate CYP3A inhibitor, fluconazole, is predicted to increase the AUC of olaparib by 121%.

Avoid concomitant use of strong CYP3A inhibitors such as itraconazole, telithromycin, clarithromycin, ketoconazole, voriconazole, nefazodone, posaconazole, ritonavir, lopinavir/ritonavir, indinavir, saquinavir, nelfinavir, boceprevir, and telaprevir. Avoid use of moderate CYPA inhibitors such as amprenavir, aprepitant, atazanavir, ciprofloxacin, crizotinib, darunavir/ritonavir, diltiazem, erythromycin, fluconazole, fosamprenavir, imatinib, and verapamil. If the strong or moderate CYP3A inhibitors must be co-administered, reduce the dose of Lynparza *[see Dosage and Administration (2.5)]*.

Avoid grapefruit, grapefruit juice, Seville oranges, and Seville orange juice during Lynparza treatment since they are CYP3A inhibitors *[see Dosage and Administration (2.5) and Clinical Pharmacology (12.3)]*.

7.3 Drugs That May Decrease Olaparib Plasma Concentrations

In patients (N=22), co-administration of rifampicin, a strong CYP3A inducer, decreased AUC of olaparib by 87%. A moderate CYP3A inducer, efavirenz, is predicted to decrease the AUC of olaparib by approximately 60%.

Avoid concomitant use of strong CYP3A inducers such as phenytoin, rifampicin, carbamazepine, and St. John's Wort. Avoid concomitant use of moderate CYP3A4 inducers such as bosentan, efavirenz, etravirine, modafinil, and nafcillin. If a moderate CYP3A inducer cannot be avoided, there is 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 300 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 7% of the human exposure ($AUC_{0\text{-}24h}$) at the recommended dose).

In 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 0.18% of human exposure ($AUC_{0\text{-}24h}$) 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

Pregnancy Testing

Pregnancy testing is recommended for females of reproductive potential prior to initiating treatment with Lynparza.

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 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 482 patients with advanced solid tumors who received Lynparza tablets 300 mg twice daily as monotherapy, 135 (28%) patients were aged ≥65 years. There appeared to be no major difference in the safety profile of patients treated with olaparib aged <65 years versus ≥65 years, nor within the age categories of 65 to 74 years, 75 to 84 years. No patients were aged ≥85 years.

8.6 Hepatic Impairment

No adjustment to the starting dose is required in patients with mild hepatic impairment. A 15% 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

No adjustment to the starting dose is required in patients with mild renal impairment, but patients should be monitored closely for toxicity. A 24% increase in mean exposure (AUC) was observed in patients with mild renal impairment (CLcr = 51-80 mL/min) compared to patients with normal renal function (CLcr

>80 mL/min). A 44% increase in AUC was observed in patients with moderate renal impairment (CLcr 31-50 mL/min) compared to patients with normal renal function (CLcr >80 mL/min). For patients with moderate renal impairment, reduce the dose of Lynparza to 200 mg twice daily *[see Dosage and Administration (2.6)]*. There are no data in patients with severe renal impairment or end-stage disease (CLcr ≤30 mL/min) *[see Clinical Pharmacology (12.3)]*.

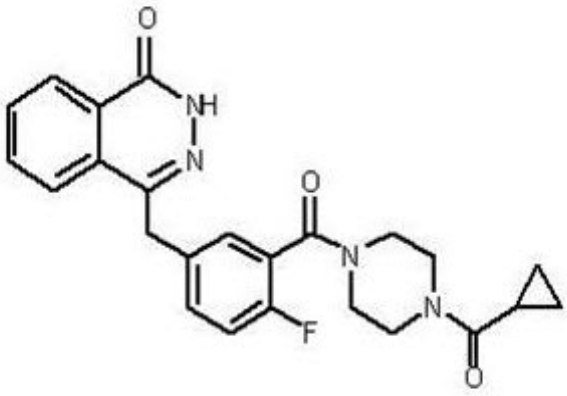
10 OVERDOSAGE

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 the patient symptomatically.

11 DESCRIPTION

Olaparib is an inhibitor of the mammalian polyadenosine 5'-diphosphoribose polymerase (PARP) enzyme.

The chemical name is 4-[(3-{[4-(cyclopropylcarbonyl)piperazin-1-yl]carbonyl}-4-fluorophenyl)methyl]phthalazin-1(2*H*)-one and it has the following chemical structure:



The empirical molecular formula for Lynparza is $C_{24}H_{23}FN_4O_3$ and the relative molecular mass is 434.46.

Olaparib is a crystalline solid, is non-chiral and shows pH-independent low solubility across the physiological pH range.

Lynparza tablets for oral administration contain 100 mg or 150 mg of olaparib. Inactive ingredients in the tablet core are copovidone, mannitol, colloidal silicon dioxide and sodium stearyl fumarate. The tablet coating consists of hypromellose, polyethylene glycol 400, titanium dioxide, ferric oxide yellow and ferrosoferric oxide (150 mg tablet only).

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 functions, such as DNA transcription 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 and non-BRCA proteins involved in the homologous recombination repair (HRR) of DNA damage and correlated with platinum response. *In vitro* studies have shown that olaparib-induced cytotoxicity may involve inhibition of PARP enzymatic activity and increased formation of PARP-DNA complexes, resulting in DNA damage and cancer cell death.

12.2 Pharmacodynamics

Cardiac Electrophysiology

The effect of olaparib on cardiac repolarization was assessed in 119 patients following a single dose of 300 mg and in 109 patients following multiple dosing of 300 mg twice daily. No clinically relevant effect of olaparib on QT interval was observed.

12.3 Pharmacokinetics

Lynparza is available as a tablet and capsule formulation. The oral bioavailability of the tablet formulation is higher than the capsule formulation. Population pharmacokinetic analyses have shown that the steady state exposure (AUC) following 300 mg tablet twice daily was 77% higher compared to that following 400 mg capsule twice daily. The olaparib geometric mean AUC and C_{max} following a single 300 mg tablet dose were 42.0 μg*h/mL (n=204) and 5.8 μg/mL (n=204), respectively, and the steady state geometric mean AUC and C_{max} following 300 mg tablet twice daily were 49.0 μg*h/mL (n=227) and 7.7 μg/mL (n=227), respectively. Olaparib showed time-dependent PK that the steady state clearance decreased by 15% after multiple dosing.

Absorption

Following oral administration of olaparib, absorption is rapid with median peak plasma concentrations typically achieved 1.5 hours after dosing. An AUC mean accumulation ratio of 1.8 is observed at steady state following multiple dosing of 300 mg tablets twice daily.

Systemic exposure (single dose AUC) to olaparib increases approximately proportionally with doses over the dose range of 25 mg to 450 mg, C_{max} increased slightly less than proportionally for the same dose range.

Co-administration of a high fat meal with olaparib slowed the rate (t_{max} delayed by 2.5 hours) of absorption, but did not significantly alter the extent of olaparib absorption (mean AUC increased by approximately 8%).

Distribution

Olaparib had a mean (± standard deviation) apparent volume of distribution of 158 ± 136 L after a single 300 mg dose of olaparib. The *in vitro* protein binding of olaparib is approximately 82%.

Metabolism

In vitro, CYP3A4/5 were shown to be the enzymes primarily responsible for the metabolism of olaparib.

Following oral dosing of ^{14}C-olaparib to female patients, unchanged olaparib accounted for the majority of the circulating radioactivity in plasma (70%). It was extensively metabolized with unchanged drug accounting for 15% and 6% of radioactivity in urine and feces, respectively. The majority of the metabolism is attributable to oxidation reactions with a number of the components produced undergoing subsequent glucuronide or sulfate conjugation.

Excretion

A mean (± standard deviation) terminal plasma half-life of 14.9 ± 8.2 hours and apparent plasma clearance of 7.4 ± 3.9 L/h were observed after a single 300 mg dose of olaparib.

Following a single dose of ^{14}C-olaparib, 86% of the dosed radioactivity was recovered within a 7-day collection period, 44% via the urine and 42% via the feces. The majority of the material was excreted as metabolites.

Drug Interactions

Based on the data from a drug-interaction trial (N=57), the AUC and C_{max} of olaparib increased by 170% and 42%, respectively, when olaparib was administered in combination with itraconazole, a strong CYP3A inhibitor. Simulations suggested that a moderate CYP3A inhibitor (fluconazole) may increase the AUC and C_{max} of olaparib by 121% and 14%, respectively.

Based on the data from a drug-interaction trial (N=22), the AUC and C_{max} of olaparib decreased by 87% and 71%, respectively, when olaparib was administered in combination with rifampicin, a strong CYP3A inducer. Simulations suggested that a moderate CYP3A inducer (efavirenz) may decrease the AUC and C_{max} of olaparib by approximately 60% and 31%, respectively.

In vitro studies have shown that olaparib is both an inhibitor and inducer of CYP3A and an inducer of CYP2B6. Olaprib is predicted to be a weak CYP3A inhibitor in humans. *In vitro* studies also indicated that olaparib is an inhibitor of UGT1A1, BCRP, OATP1B1, OCT1, OCT2, OAT3, MATE1 and MATE2K. The clinical relevance of these findings is unknown. *In vitro*, olaparib is a substrate of, and inhibits, the efflux transporter P-gp. The potential for olaparib to induce P-gp has not been evaluated.

Pharmacokinetics in Specific Populations

Hepatic Impairment

In a hepatic impairment trial, the mean AUC increased by 15% and the mean C_{max} by 13% when olaparib was dosed in patients with mild hepatic impairment (Child-Pugh classification A; N=9) compared with

patients with normal hepatic function (N=13). Mild hepatic impairment had 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 moderate or severe hepatic impairment.

Renal Impairment

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).

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenicity studies have not been conducted with olaparib.

Olaparib was clastogenic in an *in vitro* chromosomal aberration assay in mammalian Chinese hamster ovary (CHO) cells and in an *in vivo* rat bone marrow micronucleus assay. This clastogenicity is consistent with genomic instability resulting from the primary pharmacology of olaparib and indicates potential for genotoxicity in humans. Olaparib was not mutagenic in a bacterial reverse mutation (Ames) test.

In a fertility study, female rats received oral olaparib at doses of 0.05, 0.5, and 15 mg/kg/day for at least 14 days before mating through the first week of pregnancy. There were no adverse effects on mating and fertility rates at doses up to 15 mg/kg/day (maternal systemic exposures approximately 7% of the human exposure (AUC_{0-24h}) at the recommended dose).

In a male fertility study, olaparib had no effect on mating and fertility in rats at oral doses up to 40 mg/kg/day following at least 70 days of olaparib treatment (with systemic exposures of approximately 5% of the human exposure (AUC_{0-24h}) at the recommended dose).

14 CLINICAL STUDIES

14.1 Maintenance Treatment of Recurrent Ovarian Cancer

The efficacy of Lynparza was investigated in two randomized, placebo-controlled, double-blind, multi-center studies in patients with recurrent ovarian cancers who were in response to platinum-based therapy.

SOLO-2

SOLO-2 (NCT01874353) was a double-blind, placebo-controlled trial in which patients (N=295) with germline *BRCA*-mutated *(gBRCAm)* ovarian, fallopian tube, or primary peritoneal cancer were randomized (2:1) to receive Lynparza tablets 300 mg orally twice daily or placebo until unacceptable toxicity or progressive disease. Randomization was stratified by response to last platinum chemotherapy (complete versus partial) and time to disease progression in the penultimate platinum-based chemotherapy

prior to enrollment (6-12 months versus > 12 months). All patients had received at least two prior platinum-containing regimens and were in response (complete or partial) to their most recent platinum-based regimen. All patients had a deleterious or suspected deleterious germline *BRCA*-mutation as detected either by a local test (n= 236) or central Myriad CLIA test (n=59), subsequently confirmed by BRAC Analysis CDx (n= 286).

The major efficacy outcome was investigator-assessed progression-free survival (PFS) evaluated according to Response Evaluation Criteria in Solid Tumors (RECIST), version 1.1. Additional endpoints included overall survival (OS).

The median age of patients treated with Lynparza was 56 years (range: 28 to 83) and 56 years (range: 39 to 78) among patients treated with placebo. ECOG performance score was 0 in 83% of patients receiving Lynparza and 78% of patients receiving placebo. Of all patients, 89% were White, 17% were enrolled in the U.S. or Canada, 47% were in complete response to their most recent platinum-based regimen, and 40% had a progression-free interval of 6-12 months since their penultimate platinum regimen. Prior bevacizumab therapy was reported for 17% of those treated with Lynparza and 20% of those receiving placebo. Approximately 44% of patients on the Lynparza arm and 37% on placebo had received three or more lines of platinum-based treatment.

SOLO-2 demonstrated a statistically significant improvement in investigator-assessed PFS in patients randomized to Lynparza as compared with placebo (Table 7 and Figure 1). Results from a blinded independent review were consistent. At the time of the analysis of PFS, overall survival (OS) data were not mature with 24% of events.

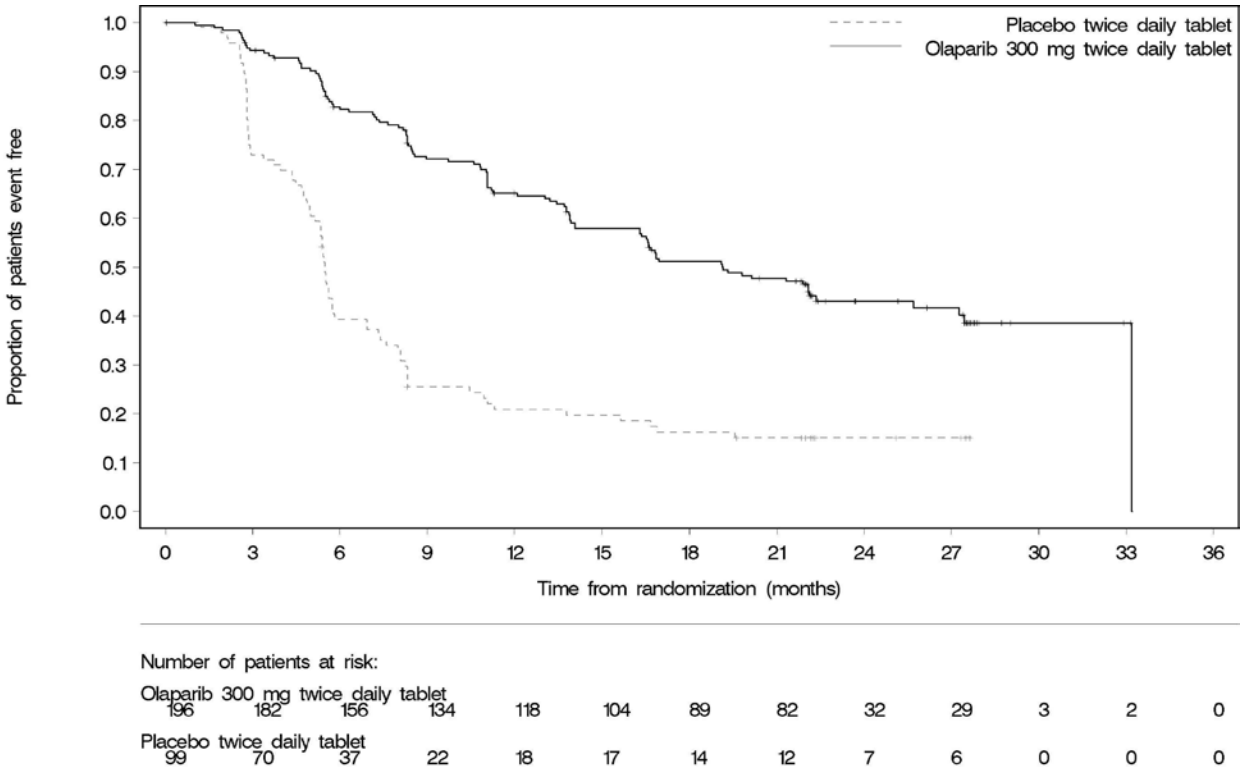
Table 7 Efficacy Results – SOLO-2 (Investigator Assessment)

	Lynparza tablets (n=196)	**Placebo (n=99)**
Progression-Free Survival		
Number of events (%)	107 (54.6%)	80 (80.8%)
Median, months	19.1	5.5
Hazard ratio[a] (95% CI)	0.30 (0.22, 0.41)	
p-value[b]	<0.0001	

[a] Hazard ratio from the stratified proportional hazards model, stratified by response to last platinum chemotherapy (complete versus partial) and time to disease progression in the penultimate platinum-based chemotherapy prior to enrollment.

[b] The p-value is derived from a stratified log-rank test.

Figure 1: Kaplan-Meier Curves of Investigator-Assessed Progression-Free Survival – SOLO-2



Study 19

Study 19 (NCT00753545) was a double-blind, placebo-controlled trial in which patients (N=265) with platinum-sensitive ovarian cancer who had received 2 or more previous platinum-containing regimens were randomized (1:1) to receive Lynparza capsules 400 mg orally twice daily or placebo until unacceptable toxicity or progressive disease. Randomization was stratified by response to last platinum chemotherapy (CR versus PR), time to disease progression in the penultimate platinum-based chemotherapy (6-12 months versus > 12 months), and descent (Jewish versus non-Jewish). The major efficacy outcome measure of the study was investigator-assessed PFS evaluated according to RECIST, version 1.0.

The median age of patients treated with Lynparza (n=136) was 58 years (range: 21 to 89) and 59 years (range 33 to 84) among patients treated with placebo (n=129). ECOG performance status was 0 in 81% of patients receiving Lynparza and 74% of patients receiving placebo. Of all patients, 97% were White, 19% were enrolled in the US or Canada, 45% were in complete response following their most recent platinum chemotherapy regimen, and 40% had a progression-free interval of 6-12 months since their penultimate platinum. Prior bevacizumab therapy was reported for 13% of patients receiving Lynparza and 16% of patients receiving placebo. A retrospective analysis for germline BRCA mutation status, some performed

using the Myriad test, indicated that 36% (n=96) of patients from the ITT population had deleterious *gBRCA* mutation, including 39% (n=53) of patients on Lynparza and 33% (n=43) of patients on placebo.

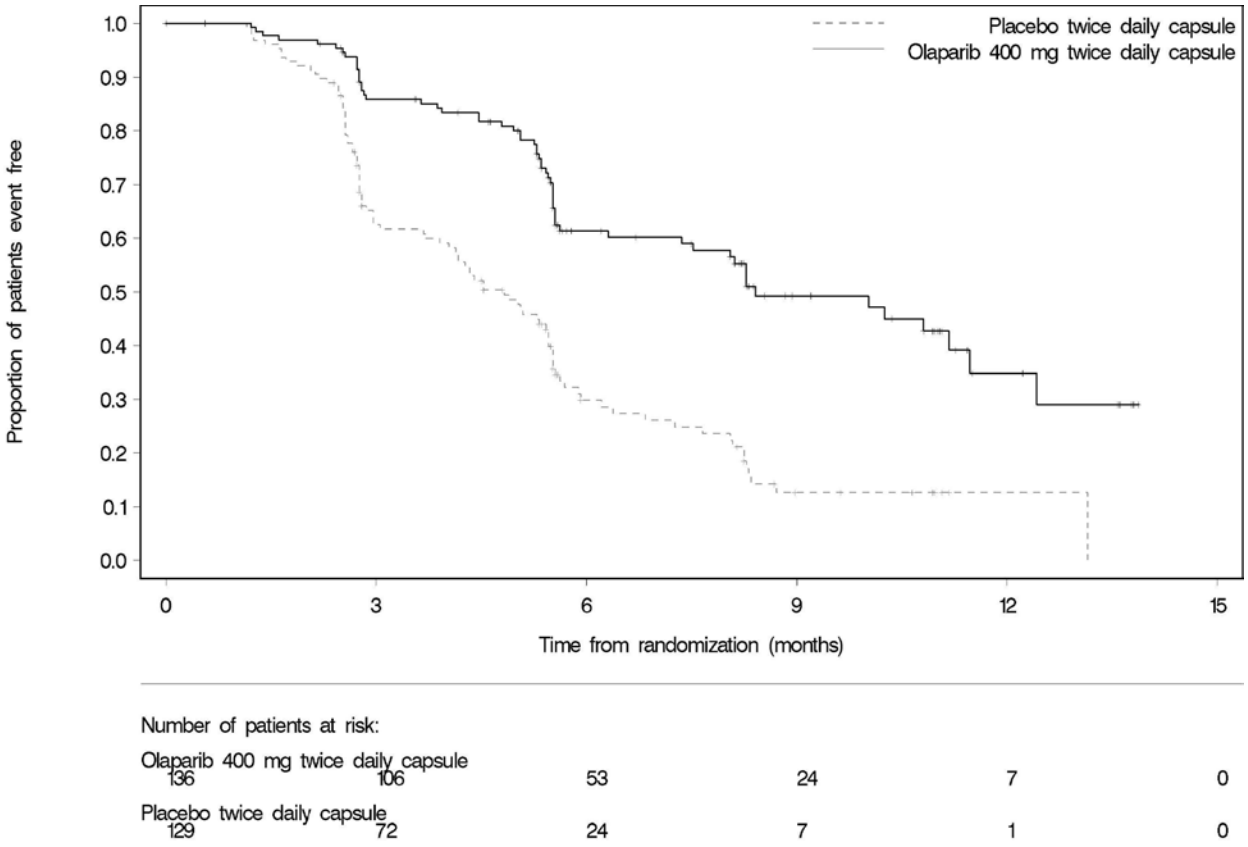
Study 19 demonstrated a statistically significant improvement in investigator-assessed PFS in patients treated with Lynparza versus placebo (Table 8 and Figure 2).

Table 8 Efficacy Results - Study 19 (Investigator Assessment)

	Lynparza capsules (n=136)	**Placebo (n=129)**
Progression-Free Survival		
Number of events (%)	60 (44%)	94 (73%)
Median, months	8.4	4.8
Hazard ratio[a] (95% CI)	0.35 (0.25, 0.49)	
p-value[b]	<0.0001	
Overall Survival[c]		
Number of events (%)	98 (72%)	112 (87%)
Median, months	29.8	27.8
Hazard ratio (95% CI)	0.73 (0.55, 0.95)	

[a] Hazard ratio is derived from a stratified proportional hazards model, stratified by response to last platinum chemotherapy, time to disease progression in the penultimate platinum-based chemotherapy and Jewish and non-Jewish descent.
[b] The p-value is derived from a stratified log-rank test.
[c] Without adjusting for multiple analyses.

Figure 2: Kaplan-Meier Curves of Investigator-Assessed Progression-Free Survival – Study 19



14.2 Advanced *gBRCA*-mutated Ovarian Cancer Treated with 3 or More Prior Lines of Chemotherapy

The efficacy of Lynparza was also investigated in a single-arm study of patients with deleterious or suspected deleterious *gBRCAm* advanced cancers. A total of 137 patients with measurable, advanced *gBRCAm* ovarian cancer treated with three or more prior lines of chemotherapy were enrolled. All patients received Lynparza capsules 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, version 1.0.

The median age of the patients was 58 years, the majority were White (94%) and 93% had an ECOG PS of 0 or 1. Deleterious or suspected deleterious *gBRCAm* status was verified retrospectively in 97% (59/61) of the patients for whom blood samples were available by the BRAC Analysis CDx™. Efficacy results are summarized in Table 9.

Table 9 Overall Response and Duration of Response in Patients with *gBRCA*-mutated Advanced Ovarian Cancer Who Received 3 or More Lines of Chemotherapy

	n=137
Objective Response Rate (95% CI)	34% (26, 42)
Complete Response	2%
Partial Response	32%
Median DOR in months (95% CI)	7.9 (5.6, 9.6)

16 HOW SUPPLIED/STORAGE AND HANDLING

16.1 How Supplied

Lynparza is available as 150 mg and 100 mg tablets.

- 150 mg tablets: green to green/grey, oval, bi-convex film-coated tablet, with debossment 'OP150' on one side and plain on the reverse, are available in:
    - Bottles of 60 tablets (NDC 0310-0679-60) and
    - Bottles of 120 tablets (NDC 0310-0679-12).
- 100 mg tablets: yellow to dark yellow, oval, bi-convex, film-coated tablet, with debossment 'OP100'on one side and plain on the reverse, are available in:
    - Bottles of 60 tablets (NDC 0310-0668-60) and
    - Bottles of 120 tablets (NDC 0310-0668-12).

16.2 Storage

Store at 20ºC to 25ºC (68°F to 77°F), excursions permitted to 15ºC to 30ºC (59ºF to 86ºF) [see USP Controlled Room Temperature]. Store in original bottle to protect from moisture.

17 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Medication Guide).

- Administration Instructions: Inform patients that Lynparza should be taken twice daily with or without food. Instruct patients that if they miss a dose of Lynparza, they should take their next normal dose at the usual time. Swallow each tablet whole. Do not chew, crush, dissolve, or divide tablet. Do not take more than 4 tablets daily *[see Dosage and Administration (2.2)]*. Inform patients to avoid grapefruit, grapefruit juice, Seville oranges, and Seville orange juice while taking Lynparza *[see Drug Interactions (7.3)]*.
- Inform patients **not** to substitute Lynparza tablets (100 mg and 150 mg) with Lynparza capsules (50 mg) on a milligram-to-milligram basis due to differences in the dosing and bioavailability of each formulation *[see Dosage and Administration (2.1)]*.
- 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 Specific 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.

Medication Guide
Lynparza (Lin-par-zah)
(olaparib)
tablets

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

Lynparza may cause serious side effects, including:

Bone marrow problems called Myelodysplastic Syndrome (MDS) or Acute Myeloid Leukemia (AML). Some people who have ovarian cancer and who have received previous treatment with chemotherapy, radiotherapy or certain other medicines for their cancer have developed MDS or AML during treatment with Lynparza. MDS or AML may lead to death. 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
- weight loss
- fever
- frequent infections
- blood in urine or stool
- shortness of breath
- feeling very tired
- 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. Pneumonitis may lead to death.

What is Lynparza?

Lynparza is a prescription medicine used for:

- the maintenance treatment of adults with ovarian cancer, fallopian tube cancer, or primary peritoneal cancer, when the cancer has come back. Lynparza is used after the cancer has responded to treatment with platinum-based chemotherapy.
- the treatment of adults who have a certain type of abnormal inherited BRCA gene advanced ovarian cancer, **and** have received treatment with 3 or more prior types of chemotherapy medicines. 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 tablets exactly as your healthcare provider tells you.
- Your healthcare provider may temporarily stop treatment with Lynparza or change your dose of Lynparza if you experience side effects.
- Lynparza comes as tablets and capsules. Lynparza tablets and capsules are **not** the same. If your healthcare provider prescribes Lynparza tablets for you, **do not** take Lynparza capsules. **Do not** take more than 4 Lynparza tablets in 1 day. If you have any questions about Lynparza, talk to your healthcare provider or pharmacist.
- Take Lynparza by mouth 2 times a day.
- Each dose should be taken about 12 hours apart.
- Swallow Lynparza tablets whole. Do not chew, crush, dissolve, or divide the tablets.
- Take Lynparza with or without food.
- 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 hospital emergency room right away.

What should I avoid while taking Lynparza?

- Avoid grapefruit, grapefruit juice, Seville oranges and Seville orange juice during treatment with Lynparza since they 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
- headache
- changes in kidney function blood test
- low number of platelets
- changes in the way food tastes
- loss of appetite
- low number of red or white blood cells
- mouth sores
- respiratory infections

These are not all the possible side effects of Lynparza.
Call your healthcare provider 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).
- Store Lynparza in the original bottle to protect it from moisture.

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.

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:

Tablet contains: copovidone, mannitol, colloidal silicon dioxide and sodium stearyl fumarate

Tablet coating contains: hypromellose, polyethylene glycol 400, titanium dioxide, ferric oxide yellow and ferrosoferric oxide (150 mg tablet only)

Distributed by:
AstraZeneca Pharmaceuticals LP
Wilmington, DE 19850
For more information, call 1-800-236-9933 or go to www.Lynparza.com.

This Medication Guide has been approved by the U.S. Food and Drug Administration. Issued: 8/2017