FOR YOUR ADULT PATIENTS WITH PLATINUM-RESPONSIVE ADVANCED OVARIAN CANCER[1]

1 DAILY DOSE

Zejula niraparib capsules 100 mg


# Proven efficacy in 1L maintenance regardless of biomarker status[1,2]

ZEJULA is the only once-daily oral PARP inhibitor monotherapy approved for all eligible first-line platinum responders with advanced ovarian cancer, regardless of biomarker status[1-4]

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

## Important Safety Information

**Myelodysplastic syndrome/acute myeloid leukemia** (MDS/AML), including some fatal cases, was reported in 15 patients (0.8%) out of 1,785 patients treated with ZEJULA monotherapy in clinical trials. The duration of therapy in patients who developed secondary MDS/cancer therapy-related AML varied from 0.5 months to 4.9 years. These patients had received prior chemotherapy with platinum agents and/or other DNA-damaging agents including radiotherapy. Discontinue ZEJULA if MDS/AML is confirmed.

**Please see additional Important Safety Information throughout, as well as the Prescribing Information.**

1L = first-line; PARP = poly (ADP-ribose) polymerase.

## The PRIMA trial assessed ZEJULA as 1L maintenance in patients with advanced ovarian cancer in response to platinum-based chemotherapy, regardless of biomarker status[1,2]

PRIMA was a randomized, double-blind, placebo-controlled phase 3 trial examining the efficacy and safety of ZEJULA in patients with newly diagnosed advanced ovarian cancer[1,2]

Patients with stage III–IV epithelial ovarian, fallopian tube, or primary peritoneal cancer at risk for recurrence after response to 1L platinum-based chemotherapy

2:1 Randomization* (N=733)

- ZEJULA† once daily (n=487)
- Placebo once daily (n=246)

**PRIMARY ENDPOINTS**

- Progression-free survival (PFS) in patients who had tumors with homologous recombination deficiency
- PFS in the overall population

## PRIMA enrolled a broad range of patients, including patients with poor prognoses[1,2,5–9]:

**Of patients in the overall population:**


HAD
**Residual Disease[9‡]**
AFTER PRIMARY DEBULKING SURGERY


HAD
**Stage IV Disease[1]**


HAD RECEIVED
**Neoadjuvant Chemotherapy[1,2]**

**Placebo: 8.2 Months[1]**
MEDIAN PFS IN OVERALL POPULATION

- 72% of patients on placebo estimated to have progressed or died within 2 years after diagnosis[2]

In PRIMA, HRd status was determined using the FDA-approved Myriad myChoice® CDx as either t*BRCA*m and/or GIS+ (GIS ≥42).[1,10]

*Patients were stratified based on neoadjuvant chemotherapy administered (yes or no), best response to first-line platinum therapy (CR or PR) and homologous-recombination (HR) status (deficient [HR-deficient], proficient [HR-proficient], or not determined).[1]

†Patients in PRIMA received a starting dose of either 200 mg or 300 mg based on their baseline body weight or platelet count (n=258), or a fixed starting dose of 300 mg per day (n=475) regardless of body weight or platelet count.[1]

‡Stage III and IV disease with visible residual tumor (>0 cm) after primary debulking surgery.[9]

### Important Safety Information (continued)

**Hematologic adverse reactions** (thrombocytopenia, anemia, neutropenia, and/or pancytopenia) have been reported in patients receiving ZEJULA. In PRIMA, the overall incidence of Grade ≥3 thrombocytopenia, anemia, and neutropenia were reported, respectively, in 39%, 31%, and 21% of patients receiving ZEJULA. Discontinuation due to thrombocytopenia, anemia, and neutropenia occurred, respectively, in 4%, 2%, and 2% of patients. In patients who were administered a starting dose of ZEJULA based on baseline weight or platelet count, Grade ≥3 thrombocytopenia, anemia, and neutropenia were reported, respectively, in 22%, 23%, and 15% of patients receiving ZEJULA. Discontinuation due to thrombocytopenia, anemia, and neutropenia occurred, respectively, in 3%, 3%, and 2% of patients. Do not start ZEJULA until patients have recovered from hematological toxicity caused by prior chemotherapy (≤Grade 1). Monitor complete blood counts weekly for the first month, monthly for the next 11 months, and periodically thereafter. If hematological toxicities do not resolve within 28 days following interruption, discontinue ZEJULA, and refer the patient to a hematologist for further investigations.

## ZEJULA significantly improved PFS in newly diagnosed patients who responded to platinum-based chemotherapy, regardless of biomarker status[1,2]

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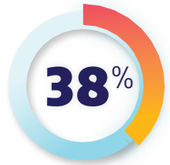
**Median PFS in the Overall Population** (N=733)

**13.8 months ZEJULA**
vs
**8.2 months placebo**




**Reduction in Risk of progression or death with ZEJULA vs placebo**
HR, 0.62 (95% CI, 0.50-0.76) *P*<0.0001

**The overall population consisted of[1]*:**

- HRd
  - *BRCA*m
  - *BRCA*wt
- HRp

*Patients with HRnd (n=111) were included in the overall population.[2]

## In the HRd population, ZEJULA doubled median PFS compared with placebo[1,2]

**Median PFS in the HRd Population** (n=373, 51% of overall study population)

**21.9 months ZEJULA**
vs
**10.4 months placebo**




**Reduction in Risk of progression or death with ZEJULA vs placebo**
HR, 0.43 (95% CI, 0.31-0.59) *P*<0.0001

**60% of patients in the HRd population were *BRCA*m[2]**

### Important Safety Information (continued)

**Hypertension and hypertensive crisis** have been reported in patients receiving ZEJULA. In PRIMA, Grade 3-4 hypertension occurred in 6% of patients receiving ZEJULA vs 1% of patients receiving placebo, with no reported discontinuations. Monitor blood pressure and heart rate at least weekly for the first two months, then monthly for the first year, and periodically thereafter during treatment with ZEJULA. Closely monitor patients with cardiovascular disorders, especially coronary insufficiency, cardiac arrhythmias, and hypertension. Manage hypertension with antihypertensive medications and adjustment of the ZEJULA dose, if necessary.

**Posterior reversible encephalopathy syndrome (PRES)** occurred in 0.1% of 2,165 patients treated with ZEJULA in clinical trials and has also been described in postmarketing reports. Monitor all patients for signs and symptoms of PRES, which include seizure, headache, altered mental status, visual disturbance, or cortical blindness, with or without associated hypertension. Diagnosis requires confirmation by brain imaging. If suspected, promptly discontinue ZEJULA and administer appropriate treatment. The safety of reinitiating ZEJULA is unknown.

**Embryo-fetal toxicity and lactation**: Based on its mechanism of action, ZEJULA can cause fetal harm. Advise females of reproductive potential of the potential risk to a fetus and to use effective contraception during treatment and for 6 months after receiving their final dose of ZEJULA. Because of the potential for serious adverse reactions from ZEJULA in breastfed infants, advise lactating women not to breastfeed during treatment with ZEJULA and for 1 month after receiving the final dose.

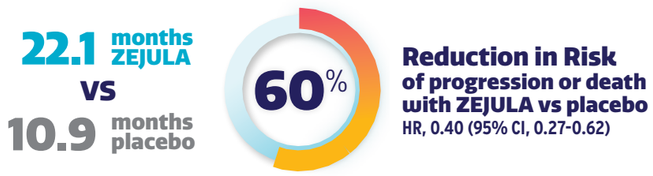
**Please see additional Important Safety Information throughout, as well as the Prescribing Information.**

1L = first-line; *BRCA* = breast cancer susceptibility gene; *BRCA*m = *BRCA*-mutated; *BRCA*wt = *BRCA* wild type; CI = confidence interval; CR = complete response; GIS = genomic instability score; HR = hazard ratio; HRd = homologous recombination deficient; HRnd = homologous recombination status not determined; HRp = homologous recombination proficient; PR = partial response; t*BRCA*m = tumor *BRCA*-mutated.

## 60% reduction in the risk of disease progression or death compared with placebo was observed in a prespecified exploratory analysis of the *BRCA*m subgroup[2,10,11]

This analysis is exploratory in nature and was not powered to detect a statistically significant treatment effect; therefore, results should be interpreted with caution.

**Median PFS in the *BRCA*m Population** (n=223)[2]




## 50% reduction in the risk of disease progression or death compared with placebo was observed in a prespecified exploratory analysis of the HRd *BRCA*wt subgroup[2,10,11]

This analysis is exploratory in nature and was not powered to detect a statistically significant treatment effect; therefore, results should be interpreted with caution.

**Median PFS in the HRd *BRCA*wt Population** (n=150)[2]


**The efficacy with ZEJULA was observed to be consistent in HRd subgroups, regardless of *BRCA* status[2,10,11]**

**Among the subgroup of patients with HRp (n=249)[2]**
- HR, 0.68 (95% CI, 0.49-0.94)

**Among the subgroup of patients with HRnd (n=111)[2]***
- HR, 0.85 (95% CI, 0.51-1.43)

*If test results were inconclusive or the test was not done, tumors were considered as homologous recombination status not determined (HRnd).[10]

### Important Safety Information (continued)

**Allergic reactions to FD&C Yellow No. 5 (tartrazine):** ZEJULA capsules contain FD&C Yellow No. 5 (tartrazine), which may cause allergic-type reactions (including bronchial asthma) in certain susceptible persons. Although the overall incidence in the general population is low, it is frequently seen in patients who also have aspirin hypersensitivity.

**References: 1.** ZEJULA (niraparib). Prescribing Information. GlaxoSmithKline; 2021. **2.** González-Martín A, et al. *N Engl J Med*. 2019;381(25):2391-2402. doi:10.1056/NEJMoa1910962 **3.** Lynparza (olaparib). Prescribing Information. AstraZeneca Pharmaceuticals LP; 2021. **4.** Rubraca (rucaparib). Prescribing Information. Clovis Oncology, Inc; 2020. **5.** Howlader N, et al, eds. *SEER Cancer Statistics Review. 1975-2017*. Bethesda, MD: National Cancer Institute. https://seer.cancer.gov/csr/1975_2017/, based on November 2019 SEER data submission, posted to the SEER website, April 2020. Accessed March 22, 2021. **6.** Horowitz NS, et al. *J Clin Oncol*. 2015;33(8):937-943. doi:10.1200/JCO.2014.56.3106 **7.** Chang S-J, et al. *Gynecol Oncol*. 2013;130(3):493-498. doi:10.1016/j.ygyno.2013.05.040 **8.** Davis A, et al. *Gynecol Oncol*. 2014;133(3):624-631. doi:10.1016/j.ygyno.2014.02.038 **9.** Data on file, GlaxoSmithKline. **10.** González-Martín A, et al. [supplementary appendix]. *N Engl J Med*. 2019;381(25):1-42. doi:10.1056/NEJMoa1910962 **11.** Monk BJ, et al. Presented at: Society of Gynecologic Oncology Annual Meeting on Women's Cancer Webinar Series; March 28-31, 2020.

*BRCA* = breast cancer susceptibility gene; *BRCA*m = *BRCA*-mutated; *BRCA*wt = *BRCA* wild type; CI = confidence interval; HR = hazard ratio; HRd = homologous recombination deficient; HRp = homologous recombination proficient; PFS = progression-free survival.

## A reduction in the risk of disease progression or death was observed with ZEJULA compared with placebo across multiple patient subgroups[1,2]

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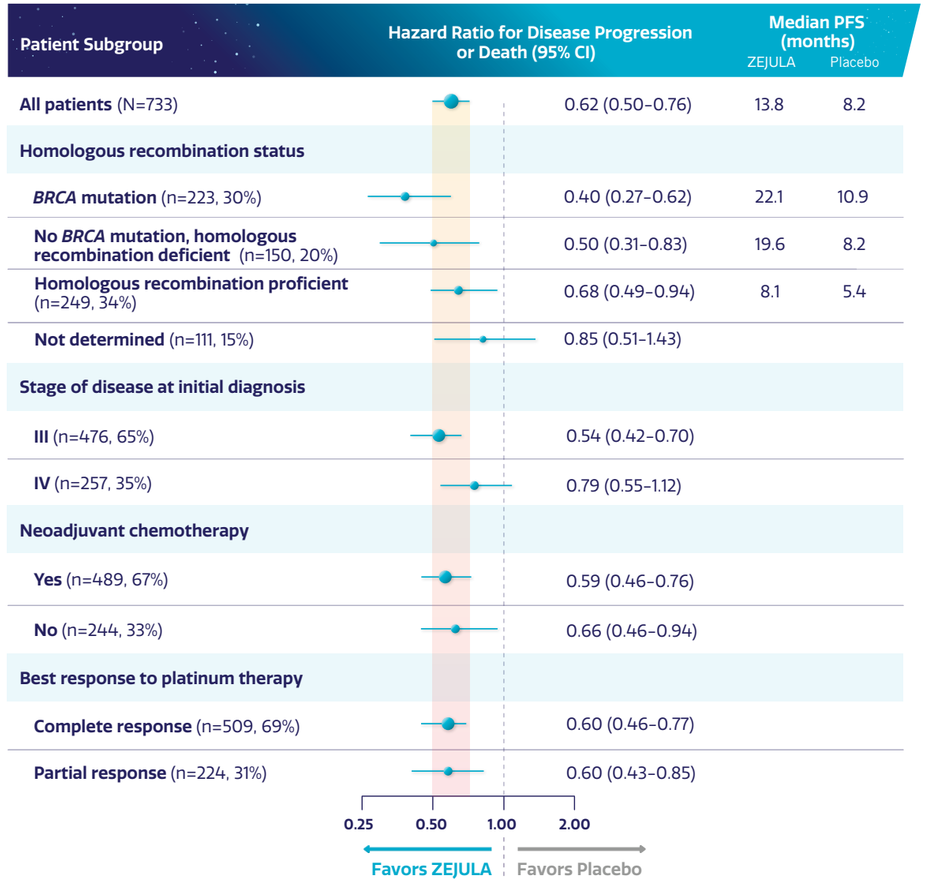
These prespecified subgroup analyses are exploratory in nature and were not powered to detect a statistically significant treatment effect; therefore, results should be interpreted with caution.[1,2]




At the time of the PFS analysis, limited overall survival data were available with 11% deaths in the overall population.[1]

### Important Safety Information (continued)

**The most common adverse reactions** (Grades 1-4) in ≥10% of all patients who received ZEJULA in PRIMA were thrombocytopenia (66%), anemia (64%), nausea (57%), fatigue (51%), neutropenia (42%), constipation (40%), musculoskeletal pain (39%), leukopenia (28%), headache (26%), insomnia (25%), vomiting (22%), dyspnea (22%), decreased appetite (19%), dizziness (19%), cough (18%), hypertension (18%), AST/ALT elevation (14%), and acute kidney injury (12%).

**References (continued): 12.** Mirza MR, et al. Poster presented at: American Society of Clinical Oncology Congress; May 29-31, 2020; virtual. **13.** Korach J, et al. *Int J Gynecol Cancer*. 2020;30(suppl 4):A125-A126. doi:10.1136/ijgc-2020-ESGO.220 **14.** Konstantinopoulos PA, et al. *J Clin Oncol*. 2020;38(11):1222-1245. doi:10.1200/JCO.19.02960 **15.** Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Ovarian Cancer Including Fallopian Tube Cancer and Primary Peritoneal Cancer V.1.2021. © National Comprehensive Cancer Network, Inc. 2021. All rights reserved. Accessed March 4, 2021. To view the most recent and complete version of the guideline, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.

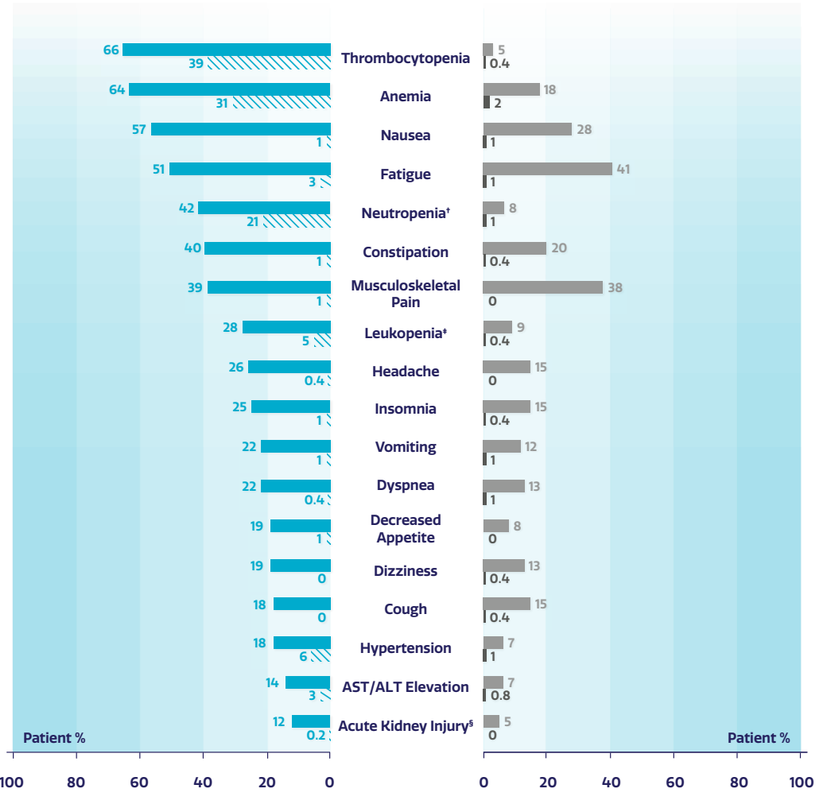
**Please see additional Important Safety Information throughout, as well as the Prescribing Information.**

## An established safety and tolerability profile, consistent with previous clinical trial experience[1,2]

### 12% of patients discontinued treatment with ZEJULA due to adverse events[2,10]

Adverse events resulting in discontinuation of ZEJULA in >1% of patients included thrombocytopenia (3.7%), anemia (1.9%), and nausea and neutropenia (1.2% each)[1]

**Adverse Reactions Reported in ≥10% of All Patients Receiving ZEJULA in PRIMA[1]***




### Side effects of ZEJULA may be managed with dose interruption and modification[1,2]

- In PRIMA, adverse events led to dose reduction or interruption in 80% of patients, most frequently from thrombocytopenia (56%), anemia (33%), and neutropenia (20%)[1]

### Monitoring complete blood counts, blood pressure, and heart rate helps identify the need to dose modify[1]

**BLOOD COUNTS**
**1X a week:** 1st month
**1X a month:** Rest of year
**1X every 2-3 months:** After year 1¶

**BLOOD PRESSURE AND HEART RATE**
**1X a week:** 1st and 2nd month
**1X a month:** Rest of year
**1X every 2-3 months:** After year 1¶

*All adverse reactions consist of grouped preferred terms except for nausea, vomiting, decreased appetite, headache and insomnia, which are single preferred terms.
†Includes neutropenia, neutropenic infection, neutropenic sepsis, febrile neutropenia.
‡Includes leukopenia, lymphocyte count decreased, lymphopenia, white blood cell count decreased.
§Includes blood creatinine increased, blood urea increased, acute kidney injury, renal failure, blood creatine increased.
‖CTCAE = Common Terminology Criteria for Adverse Evevvnts version 4.02.
¶Monitor periodically. Schedule provided as an example.

1L = first-line; ALT = alanine transaminase; AST = aspartate transaminase; *BRCA* = breast cancer susceptibility gene; *BRCA*m = *BRCA*-mutated; CI = confidence interval; HR = hazard ratio; HRd = homologous recombination deficient; PARP = poly (ADP-ribose) polymerase.

## ZEJULA, the only once-daily PARP inhibitor with an individualized starting dose in 1L maintenance[1–4]

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| | STARTING DOSE: | FIRST DOSE REDUCTION: | SECOND DOSE REDUCTION: | THIRD DOSE REDUCTION: |
|---|---|---|---|---|
| **If baseline weight: <170 lb** OR **platelets: <150,000/µL** | **200 mg/day** | 100 mg/day | discontinue | |
| **If baseline weight: ≥170 lb** AND **platelets: ≥150,000/µL** | **300 mg/day** | 200 mg/day | 100 mg/day | discontinue |

For patients with moderate hepatic impairment, reduce the starting dosage of ZEJULA to 200 mg once daily. Monitor patients for hematologic toxicity and reduce the dose further, if needed.[1]

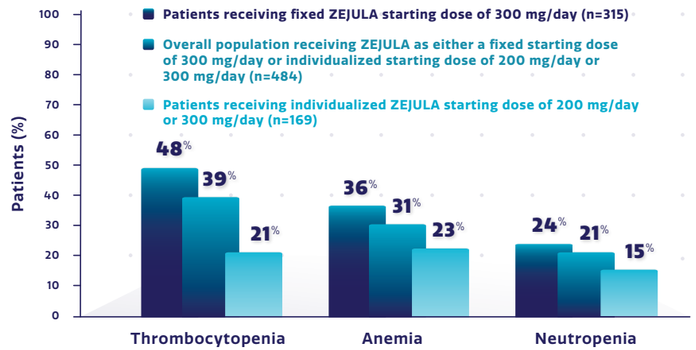
No specific drug-drug interactions have been reported with ZEJULA#

#No clinical drug interaction studies have been performed with ZEJULA.

## Lower rates of select hematologic adverse reactions and similar efficacy were observed with an individualized starting dose[1,12,13]**

PRIMA prospectively evaluated the safety and efficacy of an individualized starting dose of either 200 mg or 300 mg, selected based on baseline weight and platelet count, as well as a fixed starting dose of 300 mg[1]**

**Rates of Select Grade 3–4 Hematologic Adverse Reactions[1,12]**




**The individualized starting dose was shown to be effective in exploratory subgroup analyses** and is the approved starting dose for ZEJULA in first-line maintenance[1]**

- HR, 0.68 (95% CI, 0.48–0.97) in the overall population (n=258)
- HR, 0.39 (95% CI, 0.22–0.72) in the HRd population (n=130)

**In the *BRCA*m population (n=53)[13]****

- HR, 0.29 (95% CI, 0.128–0.667)

**These analyses are exploratory in nature, do not control for type 1 error, and are not powered to determine treatment effect in any subgroup.

In PRIMA, patients in the overall and individualized populations experienced the same rates of grade 3-4 leukopenia.[1]

### Important Safety Information (continued)

**Common lab abnormalities** (Grades 1-4) in ≥25% of all patients who received ZEJULA in PRIMA included: decreased hemoglobin (87%), decreased platelets (74%), decreased leukocytes (71%), increased glucose (66%), decreased neutrophils (66%), decreased lymphocytes (51%), increased alkaline phosphatase (46%), increased creatinine (40%), decreased magnesium (36%), increased AST (35%), and increased ALT (29%).

**Please see additional Important Safety Information throughout, as well as the Prescribing Information.**

FOR YOUR ADULT PATIENTS WITH ADVANCED OVARIAN CANCER IN COMPLETE OR PARTIAL RESPONSE TO PLATINUM-BASED CHEMOTHERAPY[1]

# ZEJULA for first–line maintenance[1]

## Proven efficacy regardless of biomarker status[1,2]

- **Overall population:** Median PFS of 13.8 months for ZEJULA vs 8.2 months for placebo (HR, 0.62; 95% CI, 0.50-0.76; *P*<0.0001)[1,2]
- **HRd population:** Median PFS of 21.9 months for ZEJULA vs 10.4 months for placebo (HR, 0.43; 95% CI, 0.31-0.59; *P*<0.0001)[1,2]

## Reduced risk of progression or death observed in exploratory subgroups[1,2]*

- ***BRCA*m population:** 60% reduction in risk of progression or death observed with ZEJULA vs placebo (HR, 0.40; 95% CI, 0.27-0.62)[2]
- **HRd *BRCA*wt population:** 50% reduction in risk of progression or death observed with ZEJULA vs placebo (HR, 0.50; 95% CI, 0.31-0.83)[2]

## Extends PARP inhibitor therapy to more women[1-4]

- No companion diagnostic required to initiate therapy[1]
- Biomarker testing may provide useful prognostic information and inform hereditary risk[1,4]

## Established safety and tolerability profile[1,2,10]

- 12% discontinuation rate due to adverse events[2,10]
- Lower rates of select grade 3-4 hematologic adverse reactions observed with an individualized starting dose compared with the overall study population[1,2]

## Convenient, once-daily, oral monotherapy[1]

- Can be taken any time of the day, with or without food. ZEJULA should be taken at approximately the same time each day[1]
- The only once-daily PARPi monotherapy available for HRd patients[1-4]

*These analyses are exploratory in nature and were not powered to detect a statistically significant treatment effect; therefore, results should be interpreted with caution.

## NCCN CLINICAL PRACTICE GUIDELINES IN ONCOLOGY (NCCN GUIDELINES®)

### Recommended Therapy Option for Certain Patients With Advanced Ovarian Cancer[15]

NCCN Guidelines® recommend niraparib (ZEJULA), an oral, once-daily PARP inhibitor, as an option for single-agent maintenance therapy in patients with advanced ovarian cancer who are in complete or partial response after surgery and 1L platinum-based chemotherapy†

†Not a recommended option if the patient has *BRCA1/2* wild type or unknown mutation status and had bevacizumab as part of primary treatment.

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## Select Important Safety Information: Summary of Warnings and Precautions

**Myelodysplastic syndrome/acute myeloid leukemia** (MDS/AML) occurred in patients exposed to ZEJULA, and some cases were fatal. Monitor patients for hematological toxicity and discontinue if MDS/AML is confirmed.

**Hematologic adverse reactions** (thrombocytopenia, anemia, neutropenia, and/or pancytopenia) have been reported in patients receiving ZEJULA. Do not start ZEJULA until patients have recovered from hematological toxicity caused by prior chemotherapy (≤ Grade 1). Monitor complete blood counts weekly for the first month, monthly for the next 11 months, and periodically thereafter for clinically significant changes. If hematological toxicities do not resolve within 28 days following interruption, discontinue ZEJULA.

**Hypertension and hypertensive crisis** have been reported in patients receiving ZEJULA. Monitor blood pressure and heart rate at least weekly for the first two months, then monthly for the first year, and periodically thereafter during treatment with ZEJULA. Manage hypertension with antihypertensive medications and adjustment of the ZEJULA dose, if necessary.

**Posterior reversible encephalopathy syndrome (PRES)** has occurred in patients treated with ZEJULA. Monitor all patients for signs and symptoms of PRES, which include seizure, headache, altered mental status, visual disturbance, or cortical blindness, with or without associated hypertension. Discontinue ZEJULA if PRES is confirmed.

**Embryo-fetal toxicity and lactation**: Based on its mechanism of action, ZEJULA can cause fetal harm. Advise females of reproductive potential of the potential risk to a fetus and to use effective contraception during treatment and for 6 months after receiving their final dose of ZEJULA. Because of the potential for serious adverse reactions from ZEJULA in breastfed infants, advise lactating women to not breastfeed during treatment with ZEJULA and for 1 month after receiving the final dose.

**Allergic reactions to FD&C Yellow No. 5 (tartrazine):** ZEJULA capsules contain FD&C Yellow No. 5 (tartrazine), which may cause allergic-type reactions (including bronchial asthma) in certain susceptible patients.

## Please see additional Important Safety Information throughout, as well as the Prescribing Information.

1L = first line; *BRCA* = breast cancer susceptibility gene; *BRCA*m = *BRCA*-mutated; *BRCA*wt = *BRCA* wild type; CI = confidence interval; HR = hazard ratio; HRd = homologous recombination deficient; NCCN = National Comprehensive Cancer Network; PARP = poly (ADP-ribose) polymerase; PFS = progression-free survival.

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