1 DAILY DOSE

Zejula
niraparib
capsules 100 mg

ZEJULA | Dosing Guide

Indications

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.
- 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.
- for the treatment of adult patients with advanced ovarian, fallopian tube, or primary peritoneal cancer who have been treated with three or more prior chemotherapy regimens and whose cancer is associated with homologous recombination deficiency (HRD) positive status defined by either:
  - a deleterious or suspected deleterious *BRCA* mutation, or
  - genomic instability and who have progressed more than six months after response to the last platinum-based chemotherapy.

Select patients for therapy based on an FDA-approved companion diagnostic for ZEJULA.

Important Safety Information

Myelodysplastic Syndrome/Acute Myeloid Leukemia (MDS/AML), including some fatal cases, was reported in 15 patients (0.8%) out of 1785 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 accompanying Prescribing Information.

Recommended ZEJULA starting dose by indication[1]

1L Maintenance Treatment for Newly Diagnosed Advanced Ovarian Cancer*	2L+ Maintenance Treatment for Recurrent Ovarian Cancer† and 4L+ Late-Line Treatment Following 3 Prior Lines of Chemotherapy‡
200 mg taken orally once daily for: • Patients weighing <170 lb **OR** • Platelet count of <150,000/µL	**300 mg taken orally once daily**
300 mg taken orally once daily for: • Patients weighing ≥170 lb **AND** • Platelet count of ≥150,000/µL	

*Patients should start maintenance treatment with ZEJULA no later than 12 weeks after their most recent platinum-containing regimen.

†Patients should start maintenance treatment with ZEJULA no later than 8 weeks after their most recent platinum-containing regimen.

‡Treated with 3 or more prior chemotherapy regimens.

Important Safety Information (continued)

Hematologic adverse reactions (thrombocytopenia, anemia, and neutropenia) have been reported in patients receiving ZEJULA. The overall incidence of Grade ≥3 thrombocytopenia, anemia, and neutropenia were reported, respectively, in 39%, 31%, and 21% of patients receiving ZEJULA in PRIMA; 29%, 25%, and 20% of patients receiving ZEJULA in NOVA; and 28%, 27%, and 13% of patients receiving ZEJULA in QUADRA. Discontinuation due to thrombocytopenia, anemia, and neutropenia occurred, respectively, in 4%, 2%, and 2% of patients in PRIMA; 3%, 1%, and 2% of patients in NOVA; and 4%, 2%, and 1% of patients in QUADRA. In patients who were administered a starting dose of ZEJULA based on baseline weight or platelet count in PRIMA, 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.

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1L MAINTENANCE TREATMENT FOR ADVANCED OVARIAN CANCER

Overall Population[1,2]

13.8 MONTHS ZEJULA — **Median PFS** HR=0.62; 95% CI; 0.50-0.76; *P*<0.0001 — **VS** — 8.2 MONTHS Placebo

HRd Population[1,2]

21.9 MONTHS ZEJULA — **Median PFS** HR=0.43; 95% CI, 0.31-0.59, *P*<0.0001 — **VS** — 10.4 MONTHS Placebo

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.

Study Design: PRIMA, a randomized, double-blind, placebo-controlled phase 3 trial, evaluated the safety and efficacy of ZEJULA in women (N=733) with newly diagnosed advanced epithelial ovarian, fallopian tube, or primary peritoneal cancer following CR or PR to 1L platinum-based chemotherapy. Patients were randomized 2:1 to receive ZEJULA or placebo once daily. The primary endpoint was PFS in patients who had tumors that were HRd and then in the overall population, as determined on hierarchical testing. PFS was measured from time of randomization to time of disease progression or death.[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)

Hypertension and hypertensive crisis have been reported in patients receiving ZEJULA. Grade 3-4 hypertension occurred in 6% of patients receiving ZEJULA vs 1% of patients receiving placebo in PRIMA, with no reported discontinuations. Grade 3-4 hypertension occurred in 9% of patients receiving ZEJULA vs 2% of patients receiving placebo in NOVA, with discontinuation occurring in <1% of patients. Grade 3-4 hypertension occurred in 5% of ZEJULA-treated patients in QUADRA, with discontinuation occurring in <0.2% of patients. 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.

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

1L, first-line; 2L, second-line; 4L, fourth-line; CI, confidence interval; CR, complete response; HR, hazard ratio; HRd, homologous recombination deficient; PFS, progression-free survival; PR, partial response.

The approved starting dose for 1L maintenance is based on baseline weight and platelet count[1]

ZEJULA Recommended Dose Modifications for Adverse Reactions[1]

STARTING DOSE

If baseline weight: <170 lb **or** platelets: <150,000/µL

200 mg/day

FIRST DOSE REDUCTION:
100 mg/day

SECOND DOSE REDUCTION:
discontinue

If baseline weight: ≥170 lb **and** platelets: ≥150,000/µL

300 mg/day

FIRST DOSE REDUCTION:
200 mg/day

SECOND DOSE REDUCTION:
100 mg/day

THIRD DOSE REDUCTION:
discontinue

Important Safety Information (continued)

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.

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

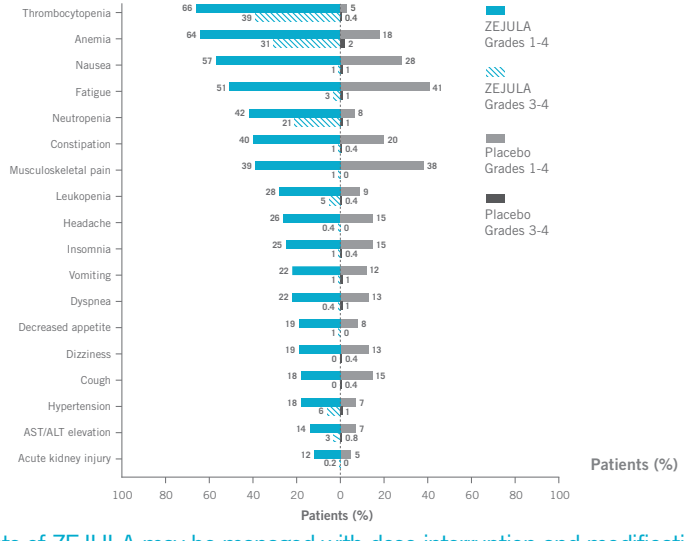
1 DAILY DOSE
Zejula niraparib capsules 100 mg

The safety and tolerability profile is well characterized and consistent with previous clinical trial experience[1,2]

12% of patients discontinued treatment with ZEJULA due to adverse events[2,3]

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)

Adverse Reactions Reported in ≥10% of All Patients Receiving ZEJULA in PRIMA: Grades 1-4 (N=728)[1]



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

- Adverse events led to dose interruptions or reduction in 80% of patients, most frequently from thrombocytopenia (56%), anemia (33%), and neutropenia (20%)
- No specific drug-drug interactions have been reported with ZEJULA*

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

Important Safety Information (continued)

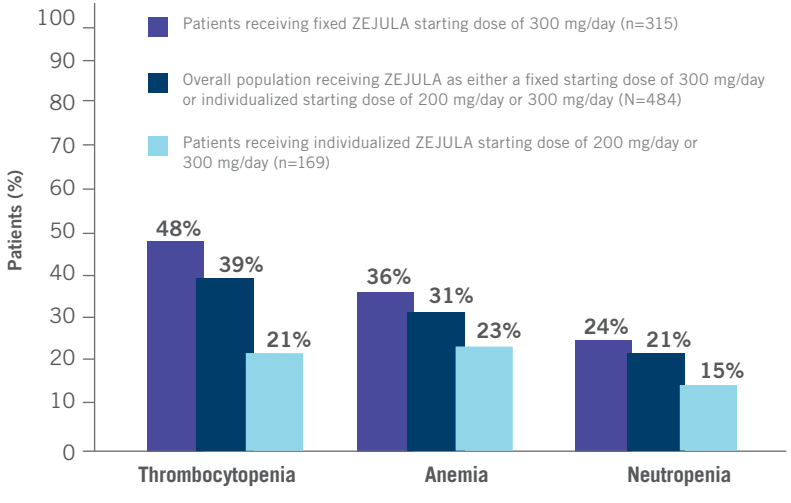
First-line Maintenance Advanced Ovarian Cancer
Most common adverse reactions (Grades 1-4) in ≥10% of all patients who received ZEJULA in PRIMA were thrombocytopenia (66%), anemia (64%), nausea (57%), fatigue (51%), neutropenia (42%), constipation (40%), musculoskeletal pain (39%), leukopenia (28%), headache (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%).

1L, first-line; ALT, alanine transaminase; AST, aspartate transaminase.

Lower rates of select hematologic adverse reactions were observed with an individualized starting dose[1]

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 Grades 3-4 Hematologic Adverse Reactions[1,4]



In PRIMA, patients in the overall and individualized populations experienced the same rates of grades 3-4 leukopenia.

The individualized starting dose was shown to be effective in exploratory subgroup analyses* and is the approved starting dose for ZEJULA in 1L 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)

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

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%).

In a prespecified exploratory analysis, relative dose intensity was similar in patients in the fixed and individualized starting dose subgroups[1,4]

A prespecified dose-exposure analysis of the individualized starting dose regimen was performed on the overall safety population who received ZEJULA (N=484), which included the fixed starting dose (n=315) and the individualized starting dose (n=169).

Dose Exposure and Intensity in the PRIMA Safety Population[4]

Parameter	Overall (N=484)	Fixed Starting Dose (n=315)	Individualized Starting Dose (n=169)
Median treatment exposure months (range)	11.1 (0-29)	11.5 (0-29)	11 (0-16)
Median dose intensity mg/day	181.3	181.8	178.6
Median relative intensity %	62.6	60.6	66.4
Overall dose interruptions %	79.5	84.1	71.0
Overall dose reductions %	74.8	79.7	65.7
Discontinuations due to TEAE %	12.0	11.1	13.6

Dose intensity (mg/day) was defined as sum of the daily doses actually consumed divided by overall treatment exposure (converted to days), and was summarized as a continuous variable.

Relative dose intensity (%) was defined as dose intensity (mg/day) divided by intended dose intensity (mg/day), where intended dose intensity was the intended starting dose of 300 or 200 mg/day and was summarized as a continuous variable.

This prespecified dose-exposure analysis was exploratory in nature; therefore, results should be interpreted with caution. No conclusions about efficacy should be made.

Important Safety Information (continued)

Maintenance Recurrent Ovarian Cancer: Most common adverse reactions (Grades 1-4) in ≥10% of patients who received ZEJULA in NOVA were nausea (74%), thrombocytopenia (61%), fatigue/asthenia (57%), anemia (50%), constipation (40%), vomiting (34%), neutropenia (30%), insomnia (27%), headache (26%), decreased appetite (25%), nasopharyngitis (23%), rash (21%), hypertension (20%), dyspnea (20%), mucositis/stomatitis (20%), dizziness (18%), back pain (18%), dyspepsia (18%), leukopenia (17%), cough (16%), urinary tract infection (13%), anxiety (11%), dry mouth (10%), AST/ALT elevation (10%), dysgeusia (10%), palpitations (10%).

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

1L, first-line; CI, confidence interval; HR, hazard ratio; HRd, homologous recombination deficient; TEAE, treatment-emergent adverse event.

ZEJULA IS THE ONLY ONCE-DAILY PARP INHIBITOR FOR OVARIAN CANCER[1,5,6]

1 DAILY DOSE

Zejula niraparib capsules 100 mg

2L MAINTENANCE TREATMENT FOR RECURRENT OVARIAN CANCER

g*BRCA*mut[1]

21 MONTHS ZEJULA	Median PFS HR=0.26; 95% CI, 0.17-0.41, *P*<0.0001 VS	5.5 MONTHS Placebo

non-g*BRCA*mut[1]

9.3 MONTHS ZEJULA	Median PFS HR=0.45; 95% CI, 0.34-0.61, *P*<0.0001 VS	3.9 MONTHS Placebo

ZEJULA 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.

Study Design: NOVA, a phase 3, double-blind, placebo-controlled trial, evaluated the safety and efficacy of ZEJULA in women (N=553) with advanced epithelial ovarian, fallopian tube, or primary peritoneal cancer following CR or PR to second-line or later platinum-based chemotherapy. Patients were randomized to receive ZEJULA or placebo once daily. The primary endpoint was PFS, as assessed by an independent review. NOVA separately evaluated PFS in both the g*BRCA*mut and non-g*BRCA*mut cohorts. PFS was measured from time of randomization to time of disease progression or death. At the time of the PFS analysis, limited overall survival data were available, with 17% of survival events occurring in the study.[1,7,8]

Important Safety Information (continued)

Common lab abnormalities (Grades 1-4) in ≥25% of patients who received ZEJULA in NOVA included: decrease in hemoglobin (85%), decrease in platelet count (72%), decrease in white blood cell count (66%), decrease in absolute neutrophil count (53%), increase in AST (36%) and increase in ALT (28%).

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

2L, second-line; CI, confidence interval; CR, complete response; g*BRCA*mut, germline *BRCA*-mutated; HR, hazard ratio; non-g*BRCA*mut, not germline *BRCA*-mutated; PARP, poly (ADP-ribose) polymerase; PFS, progression-free survival; PR, partial response.

ZEJULA is the only once-daily PARP inhibitor with 1 capsule strength for ease of dose modification[1,5,6]

The approved starting dose of ZEJULA for 2L maintenance is 300 mg once daily[1]

ZEJULA Recommended Dose Modifications for Adverse Reactions[1]

STARTING DOSE

300 mg/day

FIRST DOSE REDUCTION:

200 mg/day

SECOND DOSE REDUCTION:

100 mg/day

THIRD DOSE REDUCTION:

discontinue

Important Safety Information (continued)

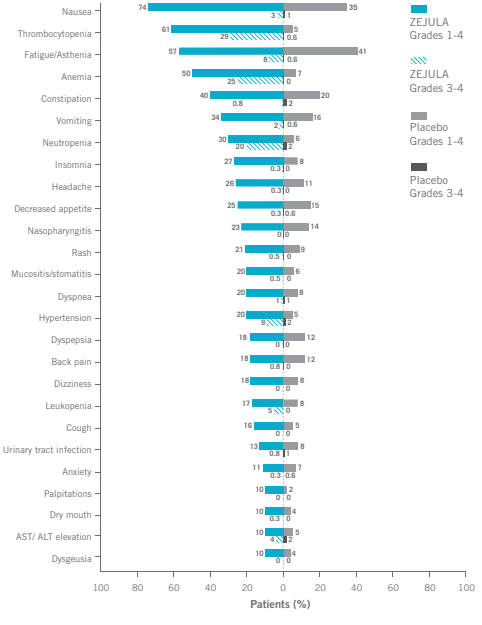
Treatment of Advanced HRD+ Ovarian Cancer

Most common adverse reactions (Grades 1-4) in ≥10% of patients who received ZEJULA in QUADRA were nausea (67%), fatigue (56%), thrombocytopenia (52%), anemia (51%), vomiting (44%), constipation (36%), abdominal pain (34%), musculoskeletal pain (29%), decreased appetite (27%), dyspnea (22%), insomnia (21%), neutropenia (20%), headache (19%), diarrhea (17%), acute kidney injury (17%), urinary tract infection (15%), hypertension (14%), cough (13%), dizziness (11%), AST/ALT elevation (11%), blood alkaline phosphatase increased (11%).

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

The side effect profile of ZEJULA is well characterized[1]

Adverse Reactions Reported in ≥10% of Patients Receiving ZEJULA in NOVA: Grades 1-4 (N=546)[1]



NOVA safety population: ZEJULA, n=367; placebo, n=179.

- Adverse reactions led to dose reduction or interruption in 69% of patients, most frequently from thrombocytopenia (41%) and anemia (20%)[1]
- No on-treatment deaths were reported during the trial[7]

Important Safety Information (continued)

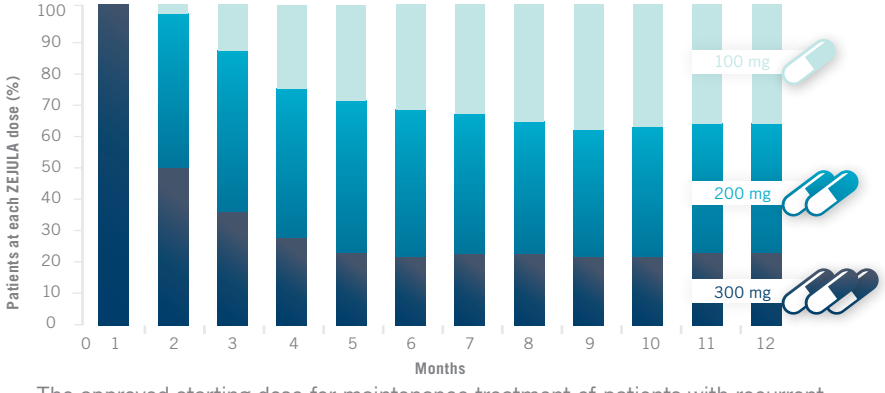
Common lab abnormalities (Grades 1-4) in ≥25% of patients who received ZEJULA in QUADRA included: decreased hemoglobin (83%), increased glucose (66%), decreased platelets (60%), decreased lymphocytes (57%), decreased leukocytes (53%), decreased magnesium (46%), increased alkaline phosphatase (40%), increased gamma glutamyl transferase (40%), increased creatinine (36%), decreased sodium (34%), decreased neutrophils (34%), increased aspartate aminotransferase (29%), and decreased albumin (27%).

2L, second-line; ALT, alanine transaminase; AR, adverse reaction; AST, aspartate transaminase; PARP, poly (ADP-ribose) polymerase.

After dose modification, 200 mg was the most commonly administered dose in NOVA[9,10]

Dose reductions primarily occurred within the first few months of NOVA[9]

ZEJULA Dose Level by Month on Treatment in the NOVA Trial



The approved starting dose for maintenance treatment of patients with recurrent ovarian cancer is 300 mg once daily.[1]

Important Safety Information (continued)

Myelodysplastic Syndrome/Acute Myeloid Leukemia (MDS/AML), including some fatal cases, was reported in 15 patients (0.8%) out of 1785 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.

Hematologic adverse reactions (thrombocytopenia, anemia and neutropenia) have been reported in patients receiving ZEJULA. The overall incidence of Grade ≥3 thrombocytopenia, anemia and neutropenia were reported, respectively, in 39%, 31%, and 21% of patients receiving ZEJULA in PRIMA; 29%, 25%, and 20% of patients receiving ZEJULA in NOVA; and 28%, 27%, and 13% of patients receiving ZEJULA in QUADRA. Discontinuation due to thrombocytopenia, anemia, and neutropenia occurred, respectively, in 4%, 2%, and 2% of patients in PRIMA; 3%, 1%, and 2% of patients in NOVA; and 4%, 2%, and 1% of patients in QUADRA. In patients who were administered a starting dose of ZEJULA based on baseline weight or platelet count in PRIMA, 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.

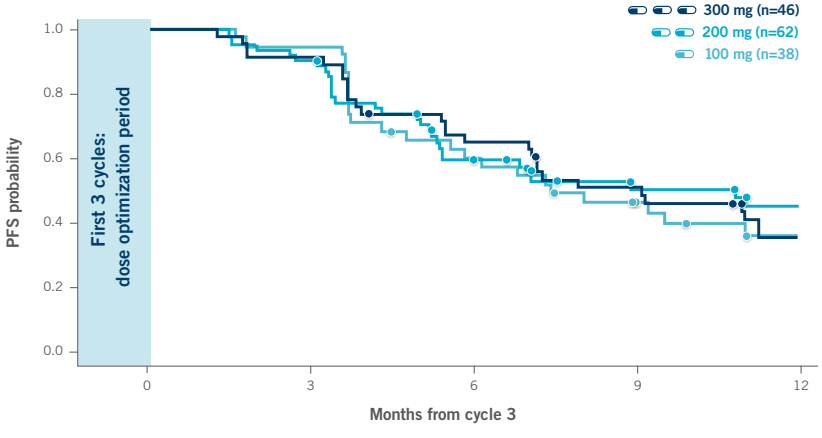
1 DAILY DOSE

Zejula niraparib capsules 100 mg

An exploratory subgroup analysis of NOVA suggested that efficacy was not compromised by dose reduction[11]

Estimated PFS probability by dose level measured after cycle 3 in *BRCA*– subgroup[11]*

This analysis is exploratory in nature; it does not control for Type 1 error and is not powered to determine treatment effect in any subgroup



- Confidence intervals for efficacy by dose curves are overlapping
- Interrupt and reduce dose at the first sign of unacceptable toxicity[1]

*Censored subjects are indicated by circles.

Important Safety Information (continued)

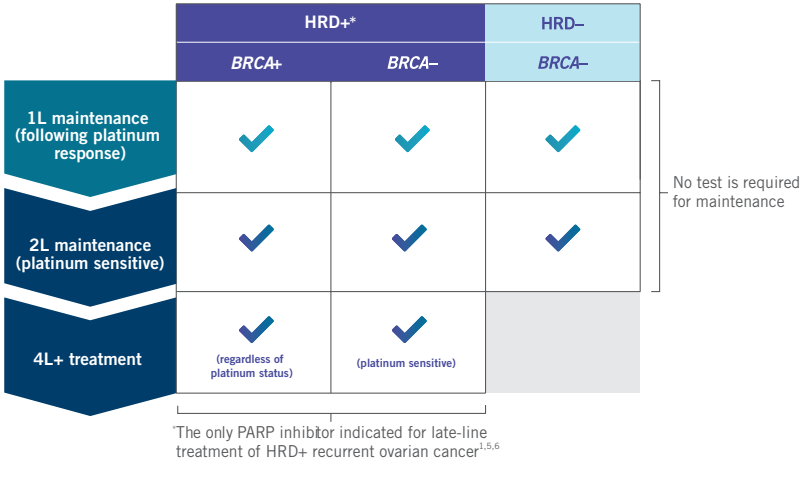
Do not start ZEJULA until patients have recovered from hematological toxicity caused by prior chemotherapy (≤ Grade 1). Monitor complete blood counts weekly for the first month, monthly for the next 11 months, and periodically thereafter. If hematological toxicities do not resolve within 28 days following interruption, discontinue ZEJULA, and refer the patient to a hematologist for further investigations.

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

2L, second-line; *BRCA*, breast cancer susceptibility gene; *BRCA*–, not *BRCA*-mutated; PFS, progression-free survival.

THE ONLY PARP INHIBITOR INDICATED FOR LATE-LINE TREATMENT OF HRD+ ADVANCED OVARIAN CANCER[1,5,6]

FDA-approved indications for ZEJULA[1]



*In QUADRA, HRD positive status (HRD+) was determined using the Myriad myChoice® CDx as either t*BRCA*+ and/or GIS+ (genomic instability score [GIS] ≥42).[1]

1 DAILY DOSE

Zejula niraparib capsules 100 mg

4L+ TREATMENT FOR ADVANCED HRD+ OVARIAN CANCER

8.3 MONTHS **Median duration of response[1]** in the indicated population: 95% CI, 6.5-NE N=98

24% **ORR** 95% CI, 16-34 N=98[1,12]

ZEJULA is indicated for the treatment of adult patients with advanced ovarian, fallopian tube, or primary peritoneal cancer who have been treated with three or more prior chemotherapy regimens and whose cancer is associated with homologous recombination deficiency (HRD) positive status defined by either:

- **a deleterious or suspected deleterious *BRCA* mutation, or**
- **genomic instability and who have progressed more than six months after response to the last platinum-based chemotherapy**

Select patients for therapy based on an FDA-approved companion diagnostic for ZEJULA.

Study Design: QUADRA, a single-arm, phase 2 trial of patients (N=463) with advanced ovarian cancer who have been treated with 3 or more prior lines of chemotherapy. The FDA-indicated population is for HRD+ patients with either *BRCA*+ tumors, regardless of platinum status, or *BRCA*– tumors with genomic instability (GIS+) and who had progressed more than 6 months after the last platinum-based chemotherapy. Those with prior exposure to PARP inhibitors were excluded. Patients received ZEJULA 300 mg once daily continuously for 28-day cycles until disease progression or unacceptable toxicity.[1,13]

Important Safety Information (continued)

Hypertension and hypertensive crisis have been reported in patients receiving ZEJULA. Grade 3-4 hypertension occurred in 6% of patients receiving ZEJULA vs 1% of patients receiving placebo in PRIMA, with no reported discontinuations. Grade 3-4 hypertension occurred in 9% of patients receiving ZEJULA vs 2% of patients receiving placebo in NOVA, with discontinuation occurring in <1% of patients. Grade 3-4 hypertension occurred in 5% of ZEJULA-treated patients in QUADRA, with discontinuation occurring in <0.2% of patients. 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.

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

1L, first-line; 2L, second-line; 4L+, fourth-line or later; *BRCA*+, breast cancer susceptibility gene mutated; *BRCA*–, not *BRCA*-mutated; CI, confidence interval; FDA, US Food and Drug Administration; GIS+, genomic instability score; HRD, homologous recombination deficiency; HRD+, HRD positive; HRD–, HRD negative; NE, not estimable; ORR, overall response rate; PARP, poly (ADP-ribose) polymerase; t*BRCA*+, tumor *BRCA*-mutated.

ZEJULA is the only once-daily PARP inhibitor with 1 capsule strength for ease of dose modification[1,5,6]

The approved starting dose of ZEJULA for 4L+ treatment of advanced ovarian cancer is 300 mg once daily[1]

ZEJULA Recommended Dose Modifications for Adverse Reactions

STARTING DOSE

300 mg/day

FIRST DOSE REDUCTION:

200 mg/day

SECOND DOSE REDUCTION:

100 mg/day

THIRD DOSE REDUCTION:

discontinue

Important Safety Information (continued)

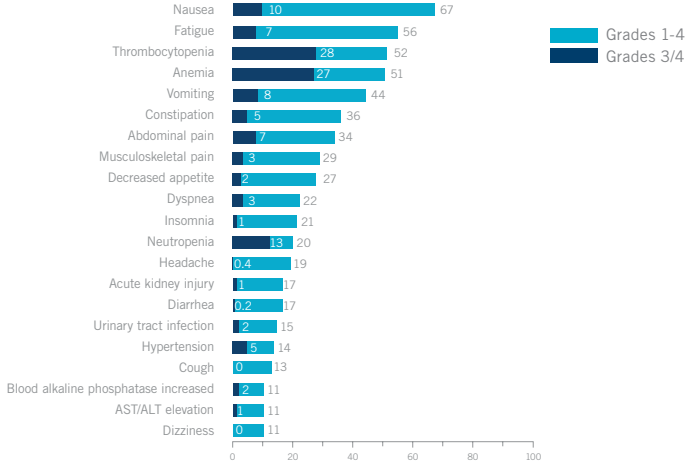
Embryo-Fetal Toxicity and Lactation: Based on its mechanism of action, ZEJULA can cause fetal harm. Advise females of reproductive potential of the potential risk to a fetus and to use effective contraception during treatment and for 6 months after receiving their final dose of ZEJULA. Because of the 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.

Adverse reactions in QUADRA were consistent with previous clinical findings in NOVA[1]

1 DAILY DOSE

Zejula niraparib capsules 100 mg

Adverse Reactions Reported in ≥10% of Patients Receiving ZEJULA in QUADRA: Grades 1-4 (N=463)[1]



Adverse reactions in QUADRA led to[1]

Dose reduction or interruption, 73%

Most frequently from:

- Thrombocytopenia, 40%
- Anemia, 21%
- Neutropenia, 11%
- Nausea, 13%
- Vomiting, 11%
- Fatigue, 9%
- Abdominal pain, 5%

Discontinuation, 21%

Important Safety Information (continued)

First-line Maintenance Advanced Ovarian Cancer

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%).

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

4L+, fourth-line or later; ALT, alanine transaminase; AST, aspartate transaminase; HRD, homologous recombination deficiency; PARP, poly (ADP-ribose) polymerase.

ZEJULA dose modifications to manage adverse reactions[1]

Non-hematologic

- Grade ≥3 (CTCAE) when prophylaxis is not considered feasible or when ARs persist despite treatment

Hematologic

- Hematologic ARs requiring transfusion
- Thrombocytopenia: platelet count <100,000/µL
- Grade ≥3 neutropenia: neutrophil count <1000/µL
- Grade ≥3 anemia: hemoglobin count <8 g/dL

Interrupt treatment for up to 28 days*

Resume at reduced dose following resolution

Obtain CBC weekly

↓

Resume at same† or reduced dose following resolution

↓

Continue CBC weekly for an additional 4 weeks

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

Blood counts

1st month	Rest of year	After year 1, monitor periodically
1× A WEEK	1× A MONTH	1× EVERY 2-3 MONTHS‡

Blood pressure and heart rate

1st and 2nd month	Rest of year	After year 1, monitor periodically
1× A WEEK	1× A MONTH	1× EVERY 2-3 MONTHS‡

*If hematological toxicities do not resolve within 28 days following interruption, discontinue ZEJULA and refer the patient to a hematologist for further investigation.
†Resume at the same dose only for the first occurrence of thrombocytopenia if platelets are >75,000/µL.
‡Schedule provided as an example.

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%).

No starting dose adjustment is necessary for special populations or conditions[1]

1 DAILY DOSE
Zejula niraparib capsules 100 mg

No Dose Adjustment Necessary[1]

For Food	For Mild/Moderate Renal Impairment§	For Mild Hepatic Impairment‖	For Age
Food does not significantly affect the absorption of niraparib	Mild: CLcr 60-89 mL/min Moderate: CLcr 30-59 mL/min	>1 - ≤1.5 x ULN total bilirubin¶ OR >ULN AST with normal bilirubin¶	≥65 years

ZEJULA: Once-daily oral dosing[1]

Can Be Taken at Any Time of Day

Patients should take their dose at approximately the same time each day

Bedtime administration may be a potential method for managing nausea

Drug-Drug Interactions

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

Storage Requirement

ZEJULA should be stored at room temperature (68°F-77°F)

§There are no data in patients with severe renal impairment or end-stage renal disease undergoing hemodialysis.
‖There are no data in patients with moderate to severe hepatic impairment.
#No clinical drug interaction studies have been performed with ZEJULA.
¶As defined by the National Cancer Institute – Organ Dysfunction Working Group (NCI-ODWG) criteria.

Important Safety Information (continued)

Maintenance Recurrent Ovarian Cancer
Most common adverse reactions (Grades 1-4) in ≥10% of patients who received ZEJULA in NOVA were nausea (74%), thrombocytopenia (61%), fatigue/asthenia (57%), anemia (50%), constipation (40%), vomiting (34%), neutropenia (30%), insomnia (27%), headache (26%), decreased appetite (25%), nasopharyngitis (23%), rash (21%), hypertension (20%), dyspnea (20%), mucositis/stomatitis (20%), dizziness (18%), back pain (18%), dyspepsia (18%), leukopenia (17%), cough (16%), urinary tract infection (13%), anxiety (11%), dry mouth (10%), AST/ALT elevation (10%), dysgeusia (10%), palpitations (10%)

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

AST, aspartate transaminase; CBC, complete blood count; CLcr, creatinine clearance; CTCAE, Common Terminology Criteria for Adverse Events; ULN, upper limit of normal.

Consider ZEJULA for your eligible patients

- The convenience of once-daily, oral dosing with 1 capsule strength for easy dose adjustment[1]
- Low discontinuation rates due to adverse reactions were observed with ZEJULA as maintenance treatment[1]
- In 1L maintenance, lower rates of select Grade 3-4 hematologic adverse reactions were observed with individualized dosing[1,4]

View more dosing information.
Visit ZEJULA.COM/HCP/DOSING

Important Safety Information (continued)

Common lab abnormalities (Grades 1-4) in ≥25% of patients who received ZEJULA in NOVA included: decrease in hemoglobin (85%), decrease in platelet count (72%), decrease in white blood cell count (66%), decrease in absolute neutrophil count (53%), increase in AST (36%) and increase in ALT (28%).

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

1L, first-line.

References: 1. ZEJULA (niraparib). Prescribing Information. GlaxoSmithKline; 2020. **2.** González-Martín A, Pothuri B, Vergote I, et al; for the PRIMA/ENGOT-OV26/GOG-3012 Investigators. Niraparib in patients with newly diagnosed advanced ovarian cancer. *N Engl J Med.* 2019;381(25):2391-2402. **3.** González-Martín A, Pothuri B, Vergote I, et al; for the PRIMA/ENGOT-OV26/GOG-3012 Investigators. Niraparib in patients with newly diagnosed advanced ovarian cancer [supplementary appendix]. *N Engl J Med.* 2019;381(25):2391-2402. **4.** Mirza MR, González-Martín A, Graybill W, et al. Evaluation of an individualized starting dose of niraparib in the PRIMA/ENGOT-OV26/GOG-3012 study. Poster presented at: American Society of Clinical Oncology Congress; May 29-31, 2020; virtual. **5.** Lynparza (olaparib). Prescribing Information. AstraZeneca Pharmaceuticals LP; 2020. **6.** Rubraca (rucaparib) Prescribing Information. Clovis Oncology, Inc; 2020. **7.** Mirza MR, Monk BJ, Herrstedt J, et al; for the ENGOT-OV16/NOVA Investigators. Niraparib maintenance therapy in platinum-sensitive, recurrent ovarian cancer. *N Engl J Med.* 2016;375(22):2154-2164. **8.** Mirza MR, Monk BJ, Oza AM, et al. ENGOT-OV16/NOVA trial: niraparib maintenance therapy in patients with recurrent ovarian cancer. Presented at: 41st European Society for Medical Oncology Congress; October 7-11, 2016; Copenhagen, Denmark. **9.** Berek JS, Matulonis UA, Peen U, et al. Safety and dose modification for patients receiving niraparib. *Ann Oncol.* 2018;29(8):1784-1792. **10.** Data on file, GlaxoSmithKline. **11.** Wang J, Zhang Z-Y, Mirza MR, et al. The exposure-response relationship of niraparib in patients with g*BRCA*mut and non-g*BRCA*mut: results from the ENGOT-OV16/NOVA trial. Poster presented at: Annual Congress of the European Society for Medical Oncology; September 8-12, 2017; Madrid, Spain. **12.** Moore KN, Secord AA, Geller MA, et al. QUADRA: a phase 2, open-label, single-arm study to evaluate niraparib in patients with relapsed ovarian cancer in the 4th or later line of therapy: results from the *BRCA*mut subset. Poster presented at: European Society for Medical Oncology Annual Meeting; October 19-23, 2018; Munich, Germany. **13.** Moore KN, Secord AA, Geller MA, et al. Niraparib monotherapy for late-line treatment of ovarian cancer (QUADRA): a multicentre, open-label, single-arm, phase 2 trial. *Lancet Oncol.* 2019;20(5):636-648.

NRPBROC200014 September 2020
Produced in USA. 0002-0007-94