ZEJULA First–Line Maintenance Dosing Guide

Indication

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 cases with a fatal outcome, have been reported in patients who received ZEJULA. In PRIMA, MDS/AML occurred in 6 out of 484 (1.2%) patients treated with ZEJULA, and in 3 out of 244 (1.2%) patients treated with placebo. The duration of therapy with ZEJULA in patients who developed secondary MDS/cancer therapy-related AML varied from 3.7 months to 2.5 years. All patients who developed secondary MDS/cancer therapy-related AML had received previous chemotherapy with platinum agents and/or other DNA-damaging agents, including radiotherapy. For suspected MDS/AML or prolonged hematological toxicities, refer the patient to a hematologist for further evaluation. Discontinue ZEJULA if MDS/AML is confirmed.

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).

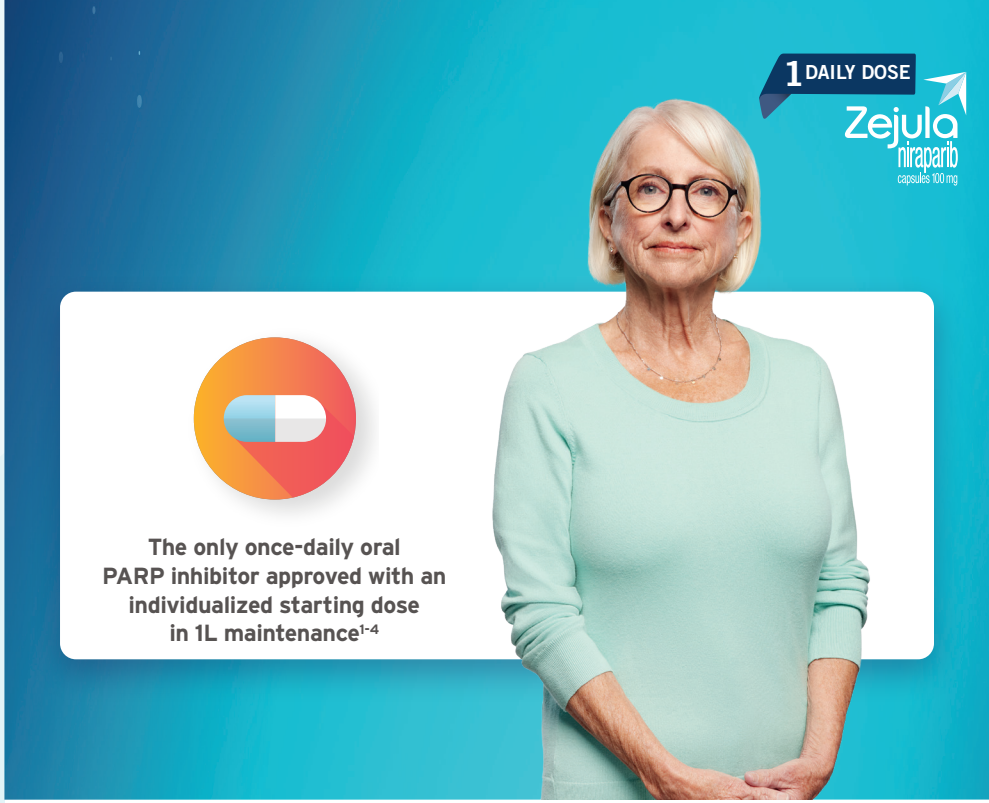
Please see additional Important Safety Information throughout, as well as the full Prescribing Information.

THE APPROVED STARTING DOSE FOR 1L MAINTENANCE IS BASED ON BASELINE WEIGHT AND PLATELET COUNT[1]

The only once-daily oral PARP inhibitor with an individualized starting dose[1-4]

	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]



Important Safety Information (continued)

Hematologic adverse reactions (continued)

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.

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.

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.

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%).

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 full Prescribing Information.

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

ZEJULA dose modifications to manage adverse reactions[1]

Dose Adjustments for Adverse Reactions[1]

Non-hematologic

- CTCAE ≥Grade 3 adverse reaction that persists despite medical management

Hematologic

- Hematologic ARs requiring transfusion
- Thrombocytopenia: platelet count <100,000/µL
- Grade ≥3 neutrophil count <1,000/µL
- Grade ≥3 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
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§

If myelodysplastic syndrome or acute myeloid leukemia (MDS/AML) is confirmed, discontinue ZEJULA.

*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. ‡This recommendation is per the PRIMA clinical study protocol.[5] §Monitor periodically. Schedule provided as an example.

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

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

1 DAILY DOSE
Zejula niraparib capsules 100 mg

Dose adjustment

FOR MODERATE HEPATIC IMPAIRMENT‖

Total bilirubin ≥1.5 x ULN to 3.0 x ULN and any AST level[1]

For patients with moderate hepatic impairment, reduce the starting dosage of ZEJULA to 200 mg once daily.[1]

Monitor patients for hematologic toxicity and reduce the dose further, if needed.

No dose adjustment necessary[1]

FOR FOOD

Food does not significantly affect the absorption of niraparib

FOR MILD/MODERATE RENAL IMPAIRMENT#

Mild: CLcr 60-89 mL/min
Moderate: CLcr 30-59 mL/min

FOR MILD HEPATIC IMPAIRMENT

Total bilirubin <1.5 x ULN and any AST level
OR
bilirubin ≤ULN and AST >ULN[1]

FOR AGE

≥65

≥65 years

‖There are no data in patients with severe hepatic impairment.
#There are no data in patients with severe renal impairment or end-stage renal disease undergoing hemodialysis.

Important Safety Information (continued)

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

Notes

1 DAILY DOSE
Zejula
niraparib
capsules 100 mg

RESPOND WITH ZEJULA, A CONVENIENT ONCE-DAILY MAINTENANCE TREATMENT[1]

The only once-daily oral PARPi monotherapy available for HRd patients in 1L maintenance[1-4]

ONCE-DAILY ORAL MONOTHERAPY

TAKEN WITH OR WITHOUT FOOD

TAKEN ANY TIME OF THE DAY

Bedtime administration may be a potential method for managing nausea

ZEJULA should be taken at approximately the same time each day.[1]

DRUG-DRUG INTERACTIONS

No specific drug-drug interactions have been reported*

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

- Store at room temperature (68-77 °F)

Visit **ZEJULAHCP.COM** to explore more dosing information.

Important Safety Information (continued)

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

1L = first-line; HRd = homologous recombination deficient; PARPi = poly (ADP-ribose) polymerase inhibitor.

References: 1. ZEJULA (niraparib). Prescribing Information. GlaxoSmithKline; 2022. **2.** González-Martín A, Pothuri B, Vergote I, et al; PRIMA/ENGOT-OV26/GOG-3012 Investigators. Niraparib in patients with newly diagnosed advanced ovarian cancer. *N Engl J Med*. 2019;381(25):2391-2402. doi:10.1056/NEJMoa1910962 **3.** Lynparza (olaparib). Prescribing Information. AstraZeneca Pharmaceuticals LP; 2022. **4.** Rubraca (rucaparib). Prescribing Information. Clovis Oncology, Inc; 2022. **5.** González-Martín A, et al. [supplementary appendix]. *N Engl J Med*. 2019;381(25):1-42. doi:10.1056/NEJMoa1910962

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1 DAILY DOSE
Zejula
niraparib
capsules 100 mg

Email attachment file name:
1LM Dosing Guide