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Positive Quality Intervention: Niraparib (Zejula®): Dose Modifications Based on Weight and Platelet Counts

Description: The purpose of this PQI is to highlight key criteria for appropriate monitoring, dosing, and administration to improve the dispensing and management of patients taking niraparib.

Background: Niraparib is indicated for the maintenance treatment of patients with recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in a complete or partial response to platinum-based chemotherapy. Additional indication in patients with three or more prior chemotherapy regimens and whose cancer is associated with homologous recombination deficiency (HRD) positive status (BRCA+ or BRCA-with Genomic Instability Positive (GIS+) disease). Niraparib efficacy is particularly pronounced in patients with BRCA1/2 mutations but also yields therapeutic benefit in those without germline BRCA mutations. Discontinuation due to thrombocytopenia, anemia, and neutropenia occurred, respectively, in 3%, 1%, and 2% of patients. Retrospective analysis of the pivotal phase III NOVA clinical trial reveals most dose adjustments occurred within 3 months and did not appear to compromise efficacy.

PQI Process:

- Verify dose on initial fill—labeled starting dose is 300 mg once daily
  - **Consider starting at 200 mg daily for patients with baseline weight < 77 kg or baseline platelets < 150K**
  - In practice, it has been seen at starting doses of 100 mg once daily as well
- Ensure patients should start treatment with niraparib no later than 8 weeks after their most recent platinum-containing regimen
- Consider bevacizumab discontinuation before initiation of treatment with niraparib
- Ensure appropriate monitoring:
  - CBC weekly x 4 weeks, monthly x 11 months, then periodically
  - Heart rate and BP monthly x 12 months, then periodically

Dose Adjustments:

- Discontinue if adverse effect that has not resolved within 28 days or grade ≥ 3 while on 100 mg/day

Dose Adjustments for hematologic toxicity: ***MINIMUM dose 100 mg/day***

Platelets < 100 K *(Monitor CBC weekly until resolved)*	1st Occurrence: **HOLD*** until platelets ≥ 100 K • Resume same dose • However, if < 75K, reduce dose by 100 mg 2nd Occurrence: **HOLD*** until platelets ≥ 100K • Reduce by 100 mg/day
ANC < 1.0 or **Hg < 8 g/dL** *(Monitor CBC weekly until resolved)*	**HOLD*** until ANC ≥ 1.5 or Hg ≥ 9 g/dL • Reduce dose by 100 mg/day
** Hold for maximum of 28 days. Discontinue if not resolved within 28 days or if dose reduction needed beyond 100 mg/day*	

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Patient Centered Activities:

- Provide Oral Chemotherapy Education (OCE) Sheet
- Take once daily, with or without food
- Taking at bedtime may minimize nausea
    - Moderate to high emetogenic risk per NCCN guidelines
- Advise patients of warnings:
    - Myelodysplastic syndrome/acute myeloid leukemia
    - Bone marrow suppression
    - Cardiovascular effects (hypertension, tachycardia)
    - Embryo-fetal toxicity
- Consider weekly home blood pressure and heart rate monitoring
- Recommend and ensure patient has stool softeners/laxatives as needed for constipation
- Recommend and ensure patient has home antiemetic as needed for nausea/vomiting
    - Ex. 5HT-3 such as ondansetron
- Financial Assistance:
    - Quick start and bridge program
    - Commercially insured patients

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