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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 adult patients:[1]

- 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:
    - 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

PQI Process:[1-7]

- 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 for 4 weeks, then monthly for 11 months, then periodically
    - Heart rate and BP monthly for 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	

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[8]
- 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 (e.g., ondansetron)
- Patient Assistance: NCODA Financial Assistance Tool

References:

1. ZEJULA® (niraparib) [package insert].
2. Mirza MR, Monk BJ, Herrstedt J, et al. Niraparib maintenance therapy in platinum-sensitive, recurrent ovarian cancer. *NEJM*. 2016; 375 (22): 2154 – 64.
3. Moore KN, Mirsa MR, Matulonia UA. The poly (ADP ribose) polymerase inhibitor niraparib: Management of toxicities. 2018; 149: 214 – 220.
4. National Comprehensive Cancer Network. Ovarian cancer. https://www.nccn.org/professionals/physician_gls/pdf/ovarian.pdf .
5. TESARO. Niraparib incidence and management of thrombocytopenia. TESARO Response letter; 2018.
6. TESARO. Retrospective analaysis of the NOVA trial to assess potential predictors for early dose modification. TESARO Response Letter; 2018.
7. Gonzalez A, Mirza MR, et al. A Prospective Evaluation of tolerability of niraparib dosing based upon baseline body weight and platelet count. Annals of Oncology (2018) 29 (suppl_8): vii332- vii358.10.1093/annonc/mdy285.
8. National Comprehensive Cancer Network. Antiemesis. https://www.nccn.org/professionals/physician_gls/pdf/antiemesis.pdf.