National Community Oncology Dispensing Association, Inc.
PASSION FOR PATIENTS

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Positive Quality Intervention: Niraparib dose adjustment based on weight and platelet counts

Description of PQI: Summary of dosing, administration, and clinical experience to ease the dispensing and management of 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. Niraparib is a highly selective PARP inhibitor. It induces synthetic lethality by taking advantage of deficient homologous recombination repair, leading DNA damage and cell death. This effect is particularly pronounced in patients with BRCA1/2 mutations but also yields therapeutic benefit in those without germline BRCA mutations.

The phase 3 ENGOT-OV16/NOVA trial demonstrated median progression-free survival of 21 months with niraparib vs. 5.5 months with placebo in patients with germline BRCA mutations. In patients without germline BRCA mutations, niraparib treated patients had 12.9 months progression-free survival vs. 3.8 months with placebo.

Adverse events resulting in dose modification are common (69% of patients) within the first three months of treatment. However, patients typically stabilize after dose reduction, and generally niraparib treatment is very tolerable on their individualized dose. Discontinuation due to thrombocytopenia, anemia, and neutropenia occurred, respectively, in 3%, 1%, and 2% of patients. There was ≥ 1% new incidence of thrombocytopenia of any grade after month 3 with dose modification.

Baseline body weight < 77 kg ***or*** *baseline platelet count < 150K was predictive of grade 3 or 4 thrombocytopenia necessitating a dose reduction to 200 mg daily.* Only 17% of patients with either of these characteristics at baseline were able to remain on 300 mg dose by month 4. Dose reductions did not appear to compromise the primary endpoint of progression-free survival (PFS) in BRCA mutated patients.

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Common grades 1 – 4 adverse effects:

- Nausea 74%
- Thrombocytopenia 61%
- Fatigue 57%
- Anemia 50%
- Constipation 40%
- Vomiting 34%
- Abdominal pain/distension 33%

PQI Process:

- Verify dose on initial fill—labeled starting dose is 300 mg once daily
  - In practice, it has been seen at starting doses of 100 or 200 mg once daily as well
  - May consider starting at 200 mg daily for patients with baseline weight < 77 kg or baseline platelets < 150K.
- Ensure bevacizumab has been discontinued before initiation of treatment
- Ensure appropriate monitoring
  - CBC weekly x 4 weeks, monthly x 11 months, then periodically
  - Heart rate and BP monthly x 11 months, then periodically

Dose Adjustments:

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

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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 • If < 75K, Resume at same dose *or* reduce 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.*	

Dose Adjustments for non-hematologic toxicity: For any grade ≥ 3 adverse effect not responding to supportive care or prophylaxis, hold until resolved.

Patient-Centered Activities:

- Counseling points—
  - 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 at least weekly home blood pressure and heart rate monitoring
- Recommend stool softeners/laxatives as needed for constipation
- Recommend home antiemetic as needed for nausea/vomiting
  - Ex. 5HT-3 such as: Ondansetron

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Financial Assistance:

- Quick start and bridge program—offers 15 day supply while awaiting insurance authorization (up to 5 refills)
- Commercially insured patients
  - $0 copay, up to $26,000 per year
- Government, uninsured, or under-insured
  - Patient assistance program to provide free medication
  - Form must be completed by patient and prescriber
- Foundation assistance (subject to availability)—examples include: Patient Access Network Foundation, Patient Advocate Foundation, Cancer Care, Healthwell

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