Niraparib Treatment Management

Risk Minimization Measures for Non-Hematologic Adverse Reactions

Adverse Reaction	Risk Minimization Measure
Non-hematologic NCI-CTCAE Grade ≥3 adverse reaction where prophylaxis is not considered feasible or adverse reaction event persists despite treatment	Withhold niraparib until resolution of adverse reaction and/or for a maximum of 28 days. Resume niraparib at a reduced dose per Table above. For recurrence of Grade 3 (with no resolution to a baseline or Grade 1) and Grade 4 adverse reactions, niraparib should be discontinued.
NCI-CTCAE Grade ≥3 treatment-related adverse reaction event lasting more than 28 days while the participant is administered niraparib 100 mg/day	Discontinue medication.
Posterior Reversible Encephalopathy Syndrome (PRES)[a]: There have been reports of PRES in patients receiving niraparib.	Discontinue niraparib and treat specific symptoms including hypertension.

Abbreviation: NCI-CTCAE=National Cancer Institute-Common Terminology Criteria for Adverse Events; PRES=Posterior Reversible Encephalopathy Syndrome.

[a] PRES is a rare, reversible, neurological disorder which can present with rapidly evolving symptoms including seizures, headache, altered mental status, visual disturbance, or cortical blindness, with or without associated hypertension. A diagnosis of PRES requires confirmation by brain imaging, preferably MRI.

Risk Minimization Measures for Hematologic Adverse Reactions

Laboratory follow-up: Weekly blood draws for FBC will be monitored until the adverse reaction resolves, and to ensure safety of the new dose, weekly blood draws for FBC will also be required for an additional 4 weeks after the adverse reaction has been resolved to the specified levels, after which monitoring every 4 weeks may resume.

IMP discontinuation: For recurrence of NCI-CTCAE Grade 3 (with no resolution to a baseline or Grade 1) and NCI-CTCAE Grade 4 toxicity/adverse reaction, Niraparib should be discontinued.

Adverse Reaction	Risk Minimization Measure
Platelet count <100,000/µL	First occurrence: Withhold niraparib for a maximum of 28 days and monitor blood counts weekly until platelet counts return to ≥100,000 /µL. Resume niraparib at the same or reduced dose per Table above **(Niraparib Dose Reduction for Adverse Reactions)**. If nadir platelet count was <75,000/µL, resume at a reduced dose after recovery.
	Second occurrence: Withhold niraparib for a maximum of 28 days and monitor blood counts weekly until platelet counts return to ≥100,000/µL. Resume niraparib at a reduced dose per Table above. Discontinue niraparib if the platelet count has not returned to acceptable levels within 28 days of the dose interruption period or if the participant has already undergone dose reduction to 100 mg once daily.[a]
Neutrophil <1,000/µL or Haemoglobin <8 g/dL	Withhold niraparib for a maximum of 28 days and monitor blood counts weekly until neutrophil counts return to ≥1,500/µL or haemoglobin returns to ≥9 g/dL. Resume niraparib at a reduced dose per Table above. Discontinue niraparib if neutrophil or haemoglobin level has not returned to acceptable levels within 28 days of the dose interruption period, or if the participant has already undergone dose reduction to 100 mg once daily.[a]
Hematologic adverse reaction requiring red blood cell and/or platelet transfusion	For participants with platelet count ≤10,000/µL, platelet transfusion should be considered. If there are other risk factors such as co-administration of anticoagulation or antiplatelet drugs, consider interrupting these drugs and/or transfusion at a higher platelet count. RBC transfusion is at the discretion of the Investigator.

	Resume niraparib at a reduced dose.
MDS/AML	Any suspected case of MDS/AML reported while a participant is receiving treatment or followed for post-treatment assessments must be referred for evaluation to a local Haematologist to perform bone marrow aspirate and biopsy as per local standards of practice. The study site must receive a copy of the Haematologist's report of aspirate/biopsy findings, which must include a classification according to the WHO, and other sample testing reports related to MDS/AML. If a diagnosis of MDS/AML is confirmed by a Haematologist, the participant must permanently discontinue study treatment.

Abbreviations: AML=acute myeloid leukemia; CBC=complete blood count; MDS=myelodysplastic syndrome; NCI-CTCAE=National Cancer Institute - Common Terminology Criteria for Adverse Events; RBC=red blood cell; WHO=World Health Organization.

a If MDS/AML is confirmed, discontinue niraparib.