NIRAPARIB (Zejula) (second or subsequent line maintenance)

INDICATION (ICD10) C56

Check the most recent Blueteq eligibility criteria before prescribing. Blueteq registration required. (www.england.nhs.uk/publication/national-cancer-drugs-fund-list/) (NIR1) (NIR2)

1. Niraparib as maintenance treatment in patients with high grade predominantly high grade serous or high grade endometrioid or high grade clear cell epithelial ovarian, fallopian tube or primary peritoneal carcinoma who have a deleterious or suspected deleterious germline and/or somatic BRCA mutation and who have a recent FIRST RELAPSE of platinumsensitive disease (responded to initial (first line) platinum-based chemotherapy), not previously received any PARP inhibitor and who are now achieved a partial or complete response has no evidence of progressive disease on the post-treatment scan or a rising CA125 level, following a SECOND minimum of 4 cycles platinumbased chemotherapy. PS 0 or 1. (TA784)

4. Niraparib as maintenance treatment in patients with high grade serous or high grade endometrioid or high grade clear cell epithelial ovarian, fallopian tube or primary peritoneal carcinoma who do NOT have a deleterious or suspected deleterious germline and/or somatic BRCA mutation and who have a recent FIRST OR SUBSEQUENT relapse of platinum-sensitive disease and who are now in response has no evidence of progressive disease on the post-treatment scan or a rising CA125 level, following penultimate SECOND OR SUBSEQUENT platinum-based chemotherapy, not previously received any PARP inhibitor. PS 0 or 1. (TA784**)**

REGIMEN

Second or subsequent line maintenance will commence maintenance niraparib monotherapy within 8 weeks from the date of the last infusion of the last cycle of 2nd or subsequent platinum based chemotherapy.

Days 1 to 28	**NIRAPARIB**	300mg*	oral	once daily

*may start on 200mg and increase dose

CYCLE FREQUENCY AND NUMBER OF CYCLES

Daily for 28 days continuously until progression or toxicity

ADMINISTRATION

Available as 100mg tablets
Swallow whole with or without food, preferably at night.

ANTI-EMETICS

Minimal risk all days

EXTRAVASATION AND TYPE OF LINE / FILTERS

Not applicable

INVESTIGATIONS

Blood results required before SACT administration

FBC, U&E including Mg^{++} (>0.4) and LFTs Neutrophils x 10^9/L ≥1.0 provided patient is well Platelets ≥100x10^9/L	Baseline, weekly for the first month then monthly for 10 months then periodically
Blood pressure	baseline then weekly for 2 months then monthly for the first year then periodically
Serum creatinine	baseline and every cycle
CA125	baseline and every 3rd cycle
Virology	before cycle 1 if not previously checked
Weight	baseline and every cycle

MAIN TOXICITES AND ADVERSE REACTIONS

Niraparib	Arthralgia Cardiac disorders Diarrhoea, constipation Hypertension Infections Photosensitivity

INTERACTIONS WHICH MAY REQUIRE DOSE MODIFICATIONS

(not exhaustive list check SPC/BNF/Stockleys)

Niraparib	-

DOSE MODIFICATIONS

When dose reduction is necessary, the niraparib dose may be reduced to 200mg once daily and further to 100mg once daily.

Haematological

Niraparib

Haematologic adverse reaction requiring transfusion or GCSF	• For patients with platelet count ≤100, platelet transfusion should be considered. If there are other risk factors for bleeding such as co-administration of anticoagulation or antiplatelet medicinal products, consider interrupting these substances and/or transfusion at a higher platelet count. • Resume niraparib at a reduced dose.
Platelet count ≤100	First occurrence: • Withhold niraparib for a maximum of 28 days and monitor blood counts weekly until platelet counts return to ≥100. • Resume niraparib at same or reduced dose based on clinical evaluation. • If platelet count is <75 at any time, resume at a reduced dose. Second occurrence: • Withhold niraparib for a maximum of 28 days and monitor blood counts weekly until platelet counts return to ≥100. • Resume niraparib at a reduced dose. • Discontinue niraparib if the platelet count has not returned to acceptable levels within 28 days of the dose interruption period, or if the patient has already undergone dose reduction to 100mg once daily.
Neutrophil <1.0 or Haemoglobin <8g/dL	• Withhold niraparib for a maximum of 28 days and monitor blood counts weekly until neutrophil counts return to ≥1.5 or haemoglobin returns to ≥9 g/dL. • Resume niraparib at a reduced dose. • Discontinue niraparib if neutrophils and/or haemoglobin have not returned to acceptable levels within 28 days of the dose interruption period, or if the patient has already undergone dose reduction to 100mg once daily.
Confirmed diagnosis of myelodysplastic syndrome or acute myeloid leukaemia	Permanently discontinue niraparib.

Non-haematogical

Niraparib

≥Grade 3 toxicity where prophylaxis is not considered feasible or adverse reaction persists despite treatment	First occurrence: • Withhold niraparib for a maximum of 28 days or until resolution of adverse reaction. • Resume niraparib at a reduced dose (200mg/day). Second occurrence: • Withhold niraparib for a maximum of 28 days or until resolution of adverse reaction. • Resume niraparib at a reduced dose (100mg/day).
≥Grade 3 toxicity lasting more than 28 days while patient is administered niraparib 100mg/day	Discontinue treatment

Hepatic impairment
Niraparib
No dose adjustment is needed in patients with mild hepatic impairment AST >ULN and total bilirubin ≤ULN or any AST and bilirubin >1.0–1.5xULN.
Patients with moderate hepatic impairment any AST and bilirubin >1.5-3xULN the recommended starting dose of niraparib is 200mg once daily.
No data in patients with severe hepatic impairment (any AST and bilirubin >3xULN); use with caution in these patients

Renal impairment
Niraparib
No dose adjustment is necessary for patients with mild to moderate renal impairment.
No data in patients with severe renal impairment or end stage renal disease undergoing haemodialysis; use with caution in these patients.

REFERENCES
1. Mirza, M et al; NEJM 2016; 375: 2154-2164

Assessments

	Pre	Cycle 1	Cycle 2	Cycle 3	Cycle 4	Ongoing
Clinical assessment	X		Pre cycle		Pre cycle	Every cycle
SACT assessment (PS and toxicities)	X	X	X	X	X	Every cycle
FBC	X	X	X	X	X	weekly for the first month then monthly for 10 months then periodically
U&E, calcium & LFT	X	X	X	X	X	weekly for the first month then monthly for 10 months then periodically
CA125	X			X		Every 3rd cycle
CT scan	X					At cycle 6, Inform consultant team if not booked
Informed consent	X					Verbal each cycle
Height	X					
Weight recorded	X	X	X	X	X	Every cycle