NIRAPARIB (Zejula) (relapsed disease)

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/)
Niraparib as maintenance treatment in patients with high grade 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 following a SECOND OR SUBSEQUENT platinum-based chemotherapy where the following criteria have been met:
2. Proven histological diagnosis of predominantly high grade serous or endometrioid ovarian, fallopian tube or primary peritoneal carcinoma.
3. Had germline and/or somatic (tumour) BRCA testing.
4. DOES NOT HAVE a documented deleterious or suspected deleterious BRCA mutation(s) in the germline or in the tumour.
5. Had disease which was sensitive to the penultimate line of platinum-based chemotherapy (i.e. the disease responded to the line of platinum-based chemotherapy preceding the most recent line of platinum-based chemotherapy).
6. Has recently completed a further line of platinum-based chemotherapy and has received a minimum of 4 cycles of platinum-based treatment.
7. Has responded to the recently completed SECOND OR SUBSEQUENT LINE platinum-based chemotherapy and has achieved a partial or complete response to treatment according to the definitions given below and there is no evidence of progressive disease on the post-treatment scan or a rising CA125 level.
-achieved a complete response at the end of the recent 2nd or subsequent line platinum-based chemotherapy i.e. has no measurable or non-measurable disease on the post-chemotherapy scan and the CA125 is normal or
- achieved a partial response at the end of the recent 2nd or subsequent line platinum-based chemotherapy i.e. has had a ≥30% reduction in measurable or non-measurable disease from the start of to the completion of the 2nd platinum-based chemotherapy or the patient has a complete remission on the post-chemotherapy CT scan but the CA125 has not decreased to within the normal range
8. Currently less than 8 weeks from the date of the last infusion of the last cycle of the recent 2nd or subsequent line platinum-based chemotherapy.
9. Not previously received any PARP inhibitor unless rucaparib via the CDF has had to be stopped within 3 months of its start solely as a consequence of dose-limiting toxicity and in the clear absence of disease progression. -the patient has never previously received a PARP inhibitor or
- the patient has previously received rucaparib via the CDF and this has had to be stopped within 3 months of its start solely as a consequence of dose-limiting toxicity and in the clear absence of disease progression.
10. Niraparib will be used as monotherapy.
11. ECOG performance status of either 0 or 1.Note: a patient with a performance status of 2 or more is not eligible for niraparib
12. Niraparib is to be continued until disease progression or unacceptable toxicity or patient choice to stop treatment.
13. A formal medical review as to whether maintenance treatment with niraparib should continue or not will be scheduled to occur at least by the start of the second cycle of treatment (in view of the potential need for dose reduction in the 2nd cycle of treatment).
14. No treatment breaks of more than 6 weeks beyond the expected cycle length are allowed (to allow any toxicity of current therapy to settle or intercurrent comorbidities to improve).
15. Niraparib is to be otherwise used as set out in its Summary of Product Characteristics

Niraparib as maintenance treatment in patients with high grade 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 platinum-sensitive disease and who are now in response following a SECOND platinum-based chemotherapy where the following criteria have been met:

2. Proven histological diagnosis of predominantly high grade serous or endometrioid ovarian, fallopian tube or primary peritoneal carcinoma.
3. Had germline and/or somatic (tumour) BRCA testing.
4. HAS a documented deleterious or suspected deleterious BRCA mutation(s) in the germline or in the tumour or in both.
- in the germline only or
- in the tumour (somatic tissue) only or- in both germline and somatic tissue.
5. HAS a documented deleterious or suspected deleterious BRCA 1 or BRCA 2 mutation(s)
6. Responded to initial (first line) platinum-based chemotherapy i.e. the recent FIRST relapse has occurred after a previous response to initial (first line) platinum-based treatment.
7. The patient has recently completed a SECOND platinum-based chemotherapy and has received a minimum of 4 cycles of platinum-based treatment.
8. This patient has responded to the recently completed SECOND platinum-based chemotherapy and has achieved a partial or complete response to treatment according to the definitions given below and there is no evidence of progressive disease on the post-treatment scan or a rising CA125 level.
- achieved a complete response at the end of the 2nd platinum-based chemotherapy i.e. has no measurable or non-measurable disease on the post-chemotherapy scan and the CA125 is normal or- achieved a partial response at the end of the 2nd platinum-based chemotherapy i.e. has had a ≥30% reduction in measurable or non-measurable disease from the start of to the completion of the 2nd platinum-based chemotherapy or the patient has a complete remission on the post-chemotherapy CT scan but the CA125 has not decreased to within the normal range.
9. Is currently less than 8 weeks from the date of the last infusion of the last cycle of the 2nd platinum-based chemotherapy.
10. Has not previously received any PARP inhibitor unless olaparib or rucaparib via the CDF has had to be stopped within 3 months of its start solely as a consequence of dose-limiting toxicity and in the clear absence of disease progression.
- the patient has never previously received a PARP inhibitor or
- the patient has previously received olaparib via the CDF and this has had to be stopped within 3 months of its start solely as a consequence of dose-limiting toxicity and in the clear absence of disease progression
- the patient has previously received rucaparib via the CDF and this has had to be stopped within 3 months of its start solely as a consequence of dose-limiting toxicity and in the clear absence of disease progression.
11. Niraparib will be used as monotherapy.
12. ECOG performance status of either 0 or 1. Note: a patient with a performance status of 2 or more is not eligible for niraparib.
13. Niraparib is to be continued until disease progression or unacceptable toxicity or patient choice to stop treatment.
14. A formal medical review as to whether maintenance treatment with niraparib should continue or not will be scheduled to occur at least by the start of the second cycle of treatment (in view of the potential need for dose reduction in the 2nd cycle of treatment).
15. No treatment breaks of more than 6 weeks beyond the expected cycle length are allowed (to allow any toxicity of current therapy to settle or intercurrent comorbidities to improve).
16. Niraparib is to be otherwise used as set out in its Summary of Product Characteristics

REGIMEN
NIRAPARIB 300mg orally once daily

CYCLE FREQUENCY AND NUMBER OF CYCLES
Daily for 28 days continuously until progression or toxicity

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

ANTI-EMETICS
Minimal risk all days

CONCURRENT MEDICATION REQUIRED

EXTRAVASATION AND TYPE OF LINE / FILTERS
Not applicable

INVESTIGATIONS
Blood results required before SACT administration
FBC, U&E and LFTs weekly for the first month then monthly for 10 months then periodically
Neutrophils x 10^9/L ≥1.5
Platelets x 10^9/L ≥100
Blood pressure weekly for 2 months then monthly for the first year then periodically
CA125 baseline and day 1 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