# Niraparib Monotherapy

## INDICATIONS FOR USE:

| INDICATION | ICD10 | Regimen Code | Reimbursement Status |
|---|---|---|---|
| As monotherapy for the maintenance treatment of adult patients with **platinum sensitive relapsed:**<br>• high grade serous epithelial ovarian,<br>• fallopian tube or<br>• primary peritoneal cancer,<br>who are in response (complete response or partial response) to platinum-based chemotherapy | C56<br>C48<br>C57 | 00571a<br>00571b<br>00571c | CDS<br>1/3/2021 |
| As monotherapy for the maintenance treatment of adult patients with advanced epithelial (FIGO Stages III and IV)<br>• high grade ovarian<br>• fallopian tube or<br>• primary peritoneal cancer<br>who are in response (complete or partial) following completion of first-line platinum-based chemotherapy. | C56<br>C48<br>C57 | 00571d<br>00571e<br>00571f | CDS<br>1/4/2023 |

## TREATMENT:

*The starting dose of the drugs detailed below may be adjusted downward by the prescribing clinician, using their independent medical judgement, to consider each patient's individual clinical circumstances.*

Niraparib is taken once daily continuously until disease progression or unacceptable toxicity develops (1 cycle =28 days).

Recommended dosing for patients <77kg

| Drug | Dose | Route | Cycle |
|---|---|---|---|
| Niraparib | 200mg once daily | PO[a] | Continuous |
| [a]Capsules should be taken with or without food, swallowed whole with water and should not be chewed or crushed.<br>Bedtime administration may be a potential method for managing nausea.<br>If a patient misses a dose of niraparib, they should take their next dose at its scheduled time. | | | |

Recommended dosing for patients ≥77kg

| Drug | Dose | Route | Cycle |
|---|---|---|---|
| Niraparib | 300mg once daily [b] | PO[a] | Continuous |
| [a]Capsules should be taken with or without food, swallowed whole with water and should not be chewed or crushed.<br>Bedtime administration may be a potential method for managing nausea.<br>If a patient misses a dose of niraparib, they should take their next dose at its scheduled time.<br>[b] **First line maintenance indication**: for patients who weigh ≥ 77 kg and have baseline platelet count < 150,000/µL, the recommended starting dose is 200 mg | | | |

## ELIGIBILITY:

- Indications as above
- ECOG 0-1
- Adequate haematological and organ function

**Platinum sensitive relapsed indication:**

- Histologically confirmed relapsed ovarian cancer, fallopian tube cancer, or primary peritoneal cancer
- High grade serous histology only
- Completed their latest platinum containing chemotherapy regimen in the previous 8 weeks
- Completed at least two courses of platinum-based chemotherapy.
    - Following last regimen patients must have either
        1. CA125 in the normal range OR
        2. CA125 decrease by more than 90% during their last platinum regimen which is stable for at least 7 days (i.e., no increase >15%).

**First line maintenance indication:**

- Newly diagnosed advanced ovarian cancer
- High grade serous or endometrioid tumours
- Patients should have received a course of first-line platinum-based chemotherapy, which had resulted in a complete or partial response
    - Treatment should be commenced within 12 weeks after completion of the last dose of platinum based therapy
    - CA125 stable following completion of platinum treatment

## EXCLUSIONS:

- Hypersensitivity to niraparib or any of the excipients
- Breast-feeding during treatment and for 1 month after the last dose

## PRESCRIPTIVE AUTHORITY:

- The treatment plan must be initiated by a Consultant Medical Oncologist

## TESTS:

**Baseline tests:**

- FBC, renal and hepatic profile
- Blood pressure

**Regular tests:**

- FBC at 2 and 4 weeks followed by monthly monitoring for 1 year and then every 3 months thereafter.
- Blood pressure should be monitored at 2 weeks, followed by monthly monitoring for 6 months, then every 3 months thereafter
- Renal and hepatic profile monthly

**Disease monitoring:**

Disease monitoring should be in line with the patient's treatment plan and any other test/s as directed by the supervising Consultant.

## DOSE MODIFICATIONS:

- Any dose modification should be discussed with a Consultant.
- Treatment may be interrupted to manage adverse reactions. Dose reduction can be considered in these cases (Table 1).

**Table 1: Dose reduction for adverse events**

| Dose level | Dose reduction recommendation | |
|---|---|---|
| Starting dose | 200mg | 300mg |
| Dose -1 | 100mg | 200mg |
| Dose -2 | Discontinue | 100mg |
| Dose -3 | | Discontinue |

**Haematological:**

**Table 2: Recommended dose modifications in haematological toxicity**

| ANC ($x10^9$/L) | | Haemoglobin (g/dL) | Platelets ($X10^9$/L) | Dose |
|---|---|---|---|---|
| <1.0 | Or | <8 | | • Withhold niraparib for a maximum of 28 days and monitor blood counts weekly until recovery (ANC ≥1.5x$10^9$/L or haemoglobin ≥9g/dL).<br>• Resume niraparib at one reduced dose level<br>• 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 100 mg daily. |
| | | | < 100 | *1st occurrence*<br>• Withhold niraparib for a maximum of 28 days and monitor blood counts weekly until recovery to ≥100 x $10^9$/L.<br>• Resume niraparib at same or reduced dose level based on |

| | | |
|---|---|---|
| | | clinical evaluation.<br>• If platelets < 75 x$10^9$/L at any time resume niraparib at one reduced dose level.<br>*2nd occurrence*<br>• Withhold niraparib for a maximum of 28 days and monitor blood counts weekly until recovery to ≥100 x $10^9$/L.<br>• Resume niraparib at one reduced dose level<br>• 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 daily. |
| Haematologic adverse reaction requiring transfusion or haematopoietic growth factor support. | | • For patients with platelet count ≤ 10 x $10^9$/L, 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.<br>• Resume niraparib at a reduced dose. |
| Confirmed diagnosis of myelodysplastic syndrome (MDS) or acute myeloid leukaemia (AML). | | • Permanently discontinue niraparib. |

**Renal and Hepatic Impairment:**

**Table 3: Recommended dose modification in renal and hepatic impairment**

| **Renal Impairment** | **Hepatic Impairment** | | | | |
|---|---|---|---|---|---|
| No dose adjustment is necessary for patients with mild to moderate renal impairment.<br>There is no data in patients with severe renal impairment or end stage renal disease undergoing haemodialysis; use with caution in these patients. | | **AST** | | **Total Bilirubin** | |
| | Mild | >ULN | and | ≤ULN | No dose adjustment is needed. |
| | | Any | and | 1 – 1.5 x ULN | |
| | Moderate | Any | and | >1.5 – 3 x ULN | Recommended dose 200mg once daily. |
| | Severe | Any | and | >3 x ULN | There is no data in patients with severe hepatic impairment; use with caution in these patients. |

**Management of adverse events:**

**Table 4: Recommended dose modifications for adverse reactions**

| Adverse Reaction | Dose Modification |
|---|---|
| ≥ Grade 3* treatment-related adverse reaction where prophylaxis is not considered feasible or adverse reaction persists despite treatment | *1st occurrence*<br>• Withhold niraparib for a maximum of 28 days or until resolution of adverse reaction.<br>• Resume niraparib at one reduced dose level<br>*2nd occurrence*<br>• Withhold niraparib for a maximum of 28 days or until resolution of adverse reaction.<br>• Resume niraparib at one reduced dose level |
| ≥ Grade 3* treatment-related adverse reaction lasting more than 28 days while patient is administered niraparib 100mg/day | Discontinue treatment |

*CTCAE=Common Terminology Criteria for Adverse Events

## SUPPORTIVE CARE:

**EMETOGENIC POTENTIAL:** Moderate to high **(Refer to local policy)**.

**PREMEDICATIONS:** None recommended

**OTHER SUPPORTIVE CARE:**

- Prophylactic anti-emetics should be considered for the first 2 weeks of treatment as clinically indicated **(Refer to local policy).**

## ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS:

*The adverse effects listed are not exhaustive. Please refer to the relevant Summary of Product Characteristics for full details*.

- **Haematologic toxicity**: Haematologic toxicity (thrombocytopenia, anaemia, neutropenia) has been reported in patients treated with niraparib. If a patient develops severe persistent haematologic toxicity including pancytopenia that does not resolve within 28 days following interruption, niraparib should be discontinued. If a patient develops severe persistent haematologic toxicity that does not resolve within 28 days following interruption, niraparib should be discontinued. Due to the risk of thrombocytopenia, anticoagulants and medicinal products known to reduce the thrombocyte count should be used with caution.
- **Myelodysplastic syndrome/acute myeloid leukaemia**: Cases of Myelodysplastic syndrome/acute myeloid leukaemia (MDS/AML) have been reported in clinical studies with niraparib. If MDS and/or AML are confirmed while on treatment with niraparib, treatment should be discontinued and the patient treated appropriately.
- **Hypertension:** Hypertension, including hypertensive crisis, has been reported with the use of niraparib. Pre-existing hypertension should be adequately controlled before starting niraparib treatment. Blood pressure should be monitored frequently as stated above. Hypertension should be medically managed with antihypertensive medicinal products as well as adjustment of the niraparib

dose. Niraparib should be discontinued in case of hypertensive crisis or if medically significant hypertension cannot be adequately controlled with antihypertensive therapy.

- **Posterior reversible encephalopathy syndrome (PRES):** There have been reports of Posterior Reversible Encephalopathy Syndrome (PRES) in patients receiving niraparib. In case of PRES, it is recommended to discontinue niraparib and to treat specific symptoms including hypertension. The safety of reinitiating niraparib therapy in patients previously experiencing PRES is not known
- **Pregnancy/contraception:** Niraparib should not be used during pregnancy or in women of childbearing potential not willing to use reliable contraception during therapy and for 6 months after receiving the last dose of Niraparib. A pregnancy test should be performed on all women of childbearing potential prior to treatment.
- **Pneumonitis:** Pneumonitis has been reported in a small number of patients receiving niraparib. Reports of pneumonitis had no consistent clinical pattern and were confounded by a number of pre-disposing factors (cancer and/or metastases in lungs, underlying pulmonary disease, smoking history, and/or previous chemotherapy and radiotherapy). If patients present with new or worsening respiratory symptoms such as dyspnoea, cough and fever, or an abnormal chest radiologic finding is observed, niraparib treatment should be interrupted and prompt investigation initiated. If pneumonitis is confirmed, niraparib treatment should be discontinued and the patient treated appropriately.
- **Lactose**: Niraparib hard capsules contain lactose monohydrate. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.
- **Tartrazine (E 102):** This medicinal product contains tartrazine (E 102), which may cause allergic reactions.

## DRUG INTERACTIONS:

- Current drug interaction databases should be consulted for more information.

## REFERENCES:


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2. Berek et al. Safety and dose modification for patients receiving niraparib. Annals of oncology 29:1784-1792, 2018
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https://www.hse.ie/eng/services/list/5/cancer/profinfo/chemoprotocols/nccp-classification-document-for-systemic-anti-cancer-therapy-sact-induced-nausea-and-vomiting.pdf

6. Niraparib (Zejula®) Summary of product characteristics. Last updated: December2020. Accessed Febuary 2023. Available at: https://www.ema.europa.eu/en/documents/product-information/zejula-epar-product-information_en.pdf

| Version | Date | Amendment | Approved By |
|---|---|---|---|
| 1 | 01/03/2021 | | Dr Dearbhaile Collins |
| 2 | 08/07/2021 | Update of hepatic dose modifications as per SPC update | Dr Dearbhaile Collins |
| 3 | 12/04/2022 | Reviewed.<br>Updated treatment table.<br>Updated emetogenic potential. | Dr Dearbhaile Collins |
| 4 | 01/04/2023 | Added new indication and split treatment table into two tables based on weight. | Dr Dearbhaile Collins |
| 5 | 26/04/2023 | Amended treatment table and eligibility section | Dr Dearbhaile Collins |

Comments and feedback welcome at oncologydrugs@cancercontrol.ie.