Niraparib (Capsules) Monotherapy

Note:

- **There are two formulations of niraparib, capsules and tablets**
- **From 1st March 2024, Niraparib capsules will no longer be available to order**

- **This regimen is for treatment with niraparib capsules only**
- **Niraparib capsules can be taken without regard to meals**
- **For information relating to the tablet formulation, see regimen NCCP 00862 Niraparib (Tablets) Monotherapy**

INDICATIONS FOR USE:

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

*This is for post 2012 indications only

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 can be taken without regard to meals. Capsules should be swallowed whole with water and should not be chewed or crushed. Bedtime administration may be a potential method for managing nausea. 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 can be taken without regard to meals. . Capsules should be swallowed whole with water and should not be chewed or crushed. Bedtime administration may be a potential method for managing nausea. If a patient misses a dose of niraparib, they should take their next dose at its scheduled time. [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 weekly during the first month of treatment followed by monthly monitoring for the next 10 months of treatment and periodically after this time.
- 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 ≥1.5x10^9/L or haemoglobin ≥9g/dL). • Resume niraparib at one reduced dose level • 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* • Withhold niraparib for a maximum of 28 days and monitor blood counts weekly until recovery to ≥100 x 10^9/L. • Resume niraparib at same or reduced dose level based on clinical evaluation. • If platelets < 75 x10^9/L at any time resume niraparib at one reduced dose level. *2nd occurrence* • Withhold niraparib for a maximum of 28 days and monitor blood counts weekly until recovery to ≥100 x 10^9/L. • Resume niraparib at one reduced dose level • 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. • 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	
CrCl (mL/min)	**Dose**	**Level**	**Dose**
≥ 30 ml/min	No dose adjustment is needed	Mild	No dose adjustment is needed
< 30 ml/min	No need for dose adjustment is expected	Moderate and severe	66% of the original dose
Haemodialysis	No need for dose adjustment is expected		
Renal and hepatic dose modifications from Giraud et al 2023			

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* • Withhold niraparib for a maximum of 28 days or until resolution of adverse reaction. • Resume niraparib at one reduced dose level *2nd occurrence* • Withhold niraparib for a maximum of 28 days or until resolution of adverse reaction. • 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:

1. Mirza MR et al. Niraparib Maintenance Therapy in Platinum-Sensitive, Recurrent Ovarian Cancer. N Engl J Med. 2016 Dec 1; 375(22):2154-2164. doi: 10.1056/NEJMoa1611310. Including supplementary material.
2. Berek et al. Safety and dose modification for patients receiving niraparib. Annals of oncology 29:1784-1792, 2018
3. Wu XH et al. Niraparib maintenance therapy in patients with platinum-sensitive recurrent ovarian cancer using an individualized starting dose (NORA): a randomized, double-blind, placebo-controlled phase III trial. Ann Oncol. 2021 Apr;32(4):512-521. doi: 10.1016/j.annonc.2020.12.018. Available at https://pubmed.ncbi.nlm.nih.gov/33453391/
4. Gonzalez-Martin A, et al. Niraparib in patients with newly diagnosed advanced ovarian cancer. N Engl J Med 2019; 381:2391-2402
5. Giraud E L, Lijster B D, et al. Dose recommendations for anticancer drugs in patients with renal or hepatic impairment: an update. Available at: https://pubmed.ncbi.nlm.nih.gov/37269847/NCCP
6. NCCP Classification Document for Systemic AntiCancer Therapy (SACT) Induced Nausea and Vomiting. V5 2023. Available at: 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
7. Niraparib (Zejula®) Summary of product characteristics.. Accessed March 2024 2024. Last updated 08/01/2024. 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. Updated treatment table. 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
5b	11/04/2024	Updated title to include capsules as tablet formulation now available	NCCP
6	03/05/2024	Modified note under title of regimen.	Dr Dearbhaile Collins

		Administration instructions in the treatment tables have been updated to align with the SPC. Updated regular tests section. Updated renal and hepatic dose modifications in line with Giraud et al, 2023.	

Comments and feedback welcome at oncologydrugs@cancercontrol.ie.