Niraparib and Abiraterone acetate (Akeega®) and prednisoLONE Therapy

INDICATIONS FOR USE:

INDICATION	ICD10	Regimen Code	HSE approved reimbursement status*
Niraparib in combination with abiraterone acetate (Akeega®) and predniSONE/prednisoLONE for the treatment of adults with metastatic castration resistant prostate cancer (mCRPC) and BRCA1/2 mutations (germline and/or somatic) in whom chemotherapy is not clinically indicated.	C61	00848	CDS 01/11/2023

* This applies to 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 patients individual clinical circumstances.

Niraparib/abiraterone (Akeega®) is administered as a single oral daily dose until disease progression or unacceptable toxicity.

Medical castration with a gonadotropin-releasing hormone (GnRH) analogue should be continued during treatment in patients not surgically castrated.

Drug	Dose	Route	Cycle
Niraparib/abiraterone (Akeega®)	200mg/1000mg once daily [1]	PO[2,3]	Continuous
predniSONE or prednisoLONE	10mg daily	PO with food	Continuous

[1] Niraparib/abiraterone (Akeega®) tablets are commonly available in two presentations:

- Akeega® 50mg/500mg film-coated tablets
- Akeega® 100mg/500mg film-coated tablets

The starting dose of 200mg/ 1000mg would comprise of two tablets of the 100mg/ 500mg strength. Niraparib/abiraterone (Akeega®) tablets should be taken as a single daily dose at approximately the same time every day.

[2]Niraparib/abiraterone (Akeega®) tablets should be taken on an empty stomach, at least 1 hour before or 2 hours after a meal. For optimal absorption, the tablets must be swallowed whole with water, they must not be broken, crushed, or chewed.

[3]Women who are or may become pregnant should wear gloves when handling the tablets.

If a dose of either niraparib/abiraterone (Akeega®), predniSONE or prednisoLONE is missed, it should be taken as soon as possible on the same day with a return to the normal schedule the following day. Extra tablets must not be taken to make up for the missed dose.

ELIGIBILITY:

- Indication as above
- BRCA 1/2 mutation (germline and/or somatic) as demonstrated by an accurate and validated test method
- Metastatic prostate cancer in the setting of castrate levels of testosterone ≤50 ng/dL on a GnRHa or bilateral orchiectomy
- ECOG status 0-2
- Adequate haematological function

CAUTION:

- Patients with a history of cardiovascular disease
- Hypertension should be adequately controlled before treatment is commenced
- Clinically significant heart disease (LVEF < 50% at baseline)

EXCLUSIONS:

- Hypersensitivity to niraparib, abiraterone, predniSONE or prednisoLONE or any of the excipients
- Prior treatment with a PARP inhibitor
- Symptomatic brain metastases
- History or current diagnosis of myelodysplastic syndrome (MDS)/acute myeloid leukemia (AML)
- Severe hepatic impairment
- Abiraterone with predniSONE or prednisoLONE is contraindicated in combination with Ra-223
- Active or symptomatic viral hepatitis
- History of adrenal dysfunction

PRESCRIPTIVE AUTHORITY:

The treatment plan must be initiated by a Consultant Medical Oncologist

TESTS:

Baseline tests:

- FBC, renal and liver profile
- Confirmation of BRCA 1/2 mutation (germline and/or somatic) using a validated test method
- Blood pressure
- Blood glucose
- Echocardiogram and ECG (and consider Echocardiogram) if clinically indicated or history of cardiac problems

Regular tests:

- FBC weekly for the first month, then every two weeks for the next two months, then monthly thereafter for the first year, then every 2nd month for remainder of treatment
- Serum aminotransferases and total bilirubin every two weeks for the first three months, followed by monthly thereafter for the first year and then every 2nd month for the duration of treatment
  - If starting lower strength dose of niraparib/abiraterone (Akeega®) after dose interruption, liver tests every two weeks for six weeks, before resuming regular monitoring
- Renal profile
- Blood pressure weekly for the first two months, followed by monthly for the first year and then every other month for the duration of treatment
- Blood glucose as clinically indicated
- ECG as clinically indicated
- Cardiovascular assessment as clinically indicated

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

Table 1: Recommended dose reductions for niraparib/abiraterone (Akeega®) for adverse reactions

Dose level	Dose recommendation for haematological toxicity	Dose recommendation for hepatotoxicity
First dose reduction	2 x 50mg/500mg niraparib/abiraterone (Akeega®) tablets	1 x 100mg/500mg niraparib/abiraterone (Akeega®) tablets
Second dose reduction	Consider discontinuation	Discontinue

Haematological:

Table 2: Dose modification of niraparib/abiraterone (Akeega®) for neutropenia and thrombocytopenia

Grade	Dose
1	• No dose adjustment, consider weekly monitoring
2	• At least weekly monitoring and consider withholding niraparib/abiraterone (Akeega®) until recovery to Grade 1 or baseline[1] • Resume niraparib/abiraterone (Akeega®) with recommendation of weekly monitoring for 28 days after restarting dose
≥3	**1st occurrence:** • Withhold niraparib/abiraterone (Akeega®) and monitor at least weekly until recovery to Grade 1 or baseline[1] • Then resume niraparib/abiraterone (Akeega®) or, if warranted, reduce by one dose level (Refer to Table 1 for recommended dose reductions for haematological toxicity) • Weekly monitoring of blood counts is recommended for 28 days after restarting full dose or starting reduced dose[2] **2nd occurrence:** • Withhold niraparib/abiraterone (Akeega®) and monitor at least weekly until recovery to Grade 1 • Resume treatment, reducing by one dose level (Refer to Table 1 for recommended dose reductions for haematological toxicity) • Weekly monitoring is recommended for 28 days after resuming treatment with reduced dose[2] • If patient was already on reduced dose, consider treatment discontinuation **3rd occurrence:** • Permanently discontinue treatment
[1] During niraparib/abiraterone (Akeega®) treatment interruption, abiraterone acetate and predniSONE/prednisoLONE may be considered to maintain daily dose of abiraterone acetate.	
[2] When starting the lower strength dose (two tablets) after dose interruption, liver function should be monitored every two weeks for six weeks due to risk of increased abiraterone exposure, before resuming regular monitoring.	

Table 3: Dose modification of niraparib/abiraterone (Akeega®) for anaemia

Grade	Dose
1	• No change, consider weekly monitoring
2	• At least weekly monitoring for 28 days, if baseline anaemia was Grade ≤ 1
≥3	**1st occurrence:** • Withhold niraparib/abiraterone (Akeega®) [1] and provide supportive management with monitoring at least weekly until recovered to Grade ≤ 2 If anaemia persists, based on clinical judgement, consider reducing by one dose level[2] (Refer to Table 1 for recommended dose reductions for haematological toxicity) **2nd occurrence:** • Withhold niraparib/abiraterone (Akeega®), provide supportive management and monitor at least weekly until recovered to Grade ≤ 2 • Resume treatment, reducing by one dose level (Refer to Table 1 for recommended dose reductions for haematological toxicity)

	• Weekly monitoring is recommended for 28 days after resuming treatment with reduced dose[2] • If patient was already on reduced dose, consider treatment discontinuation **3rd occurrence:** • Consider discontinuing treatment based on clinical judgment
[1] During niraparib/abiraterone (Akeega®) treatment interruption, abiraterone acetate and predniSONE/prednisoLONE may be considered to maintain daily dose of abiraterone acetate.	
[2] When starting the lower strength dose (two tablets) after dose interruption, liver function should be monitored every two weeks for six weeks due to risk of increased abiraterone exposure, before resuming regular monitoring.	

Renal and Hepatic Impairment:

Table 4: Dose modification of niraparib/abiraterone (Akeega®) in renal and hepatic impairment

Renal Impairment		**Hepatic Impairment**	
Mild	No dose adjustment necessary.	**Mild (Child-Pugh Class A)**	No dose adjustment is necessary for patients with pre-existing mild hepatic impairment.
Moderate	No dose adjustment necessary although close monitoring of safety events should be conducted in patients with moderate renal impairment due to the potential for increased niraparib exposure.	**Moderate (Child-Pugh Class B)**	There are no data on the clinical safety and efficacy when administered to patients with moderate hepatic impairment. No dose adjustment can be predicted. Use of niraparib/abiraterone (Akeega®) should be cautiously assessed in patients, in whom the benefit clearly should outweigh the possible risk.
Severe renal impairment or end stage renal disease undergoing haemodialysis	There are no data. Niraparib/abiraterone (Akeega®) may only be used in patients with severe renal impairment if the benefit outweighs the potential risk, and the patient should be carefully monitored for renal function and adverse events.	**Severe (Child-Pugh Class C)**	There are no data on the clinical safety and efficacy when administered to patients with moderate hepatic impairment. Contraindicated in patients with severe hepatic impairment.
Source – niraparib/abiraterone (Akeega®) SmPC			

Management of adverse events:

Table 5: Dose Modification of niraparib/abiraterone (Akeega®) for Adverse Events

Adverse reactions	Recommended dose modification
Non-haematological adverse reactions Grade ≥ 3	• Treatment should be interrupted and appropriate medical management should be instituted • Treatment with niraparib/abiraterone (Akeega®) should not be reinitiated until symptoms of the toxicity have resolved to Grade 1 or baseline
Hepatotoxicity: • **Grade ≥ 3 (ALT or AST > 5 x ULN)**	• Treatment with niraparib/abiraterone (Akeega®) should be interrupted and liver function closely monitored • Re-treatment may take place only after return of liver function tests to the patient's baseline and at a reduction of one dose level[1] (Refer to Table 1 for recommended dose reductions for **hepatotoxicity**) • If hepatotoxicity recurs at the reduced dose level, treatment with niraparib/abiraterone (Akeega®) should be discontinued
• **Severe hepatotoxicity (ALT or AST 20 x ULN)**	• Permanently discontinue treatment
• **Concurrent elevation of ALT > 3 x ULN and total bilirubin > 2 x ULN (in the absence of biliary obstruction or other causes)**	• Permanently discontinue treatment
[1]For patients being re-treated, serum transaminases should be monitored at a minimum of every two weeks for three months and monthly thereafter.	

Hypokalemia Management:
Patients with pre-existing hypokalaemia or those that develop hypokalaemia while treated with abiraterone, consider maintaining the patient's potassium level at ≥4.0mM.

SUPPORTIVE CARE:

EMETOGENIC POTENTIAL

- As outlined in NCCP Classification Document for Systemic Anti Cancer Therapy (SACT) Induced Nausea and Vomiting - Available on the NCCP website

Niraparib/abiraterone (Akeega®): Moderate to high **(Refer to local policy).**

For information:
Within NCIS regimens, anti-emetics have been standardised by the Medical Oncologists and Haemato-oncologists and information is available in the following document:

- NCCP Supportive Care Antiemetic Medicines for **Inclusion in NCIS** (Medical Oncology) - Available on the NCCP website
- NCCP Supportive Care Antiemetic Medicines for **Inclusion in NCIS** (Haemato-oncology) - Available on the NCCP website

PREMEDICATIONS: Not usually required

OTHER SUPPORTIVE CARE:

- During treatment and for four months after the last dose of niraparib/abiraterone acetate:
  - A condom is required if the patient is engaged in sexual activity with a pregnant woman
  - If the patient is engaged in sex with a woman of childbearing potential, a condom is required along with another effective contraceptive method
- Niraparib/abiraterone acetate has moderate influence on the ability to drive or use machines. Patients who take niraparib/abiraterone acetate may experience asthenia, fatigue, dizziness or difficulties concentrating. Patients should use caution when driving or using machines
- Prophylactic anti-emetics should be considered for the first 2 weeks of treatment as clinically indicated **(Refer to local policy)**
- Patients who stop abiraterone may require a gradual withdrawal of the prednisolone

ADVERSE EFFECTS:

- Please refer to the relevant Summary of Product Characteristics (SmPC) for details.

DRUG INTERACTIONS:

- Current SmPC and drug interaction databases should be consulted for information.

REFERENCES:

1. Chi KN et al. MAGNITUDE Principal Investigators. Niraparib and Abiraterone Acetate for Metastatic Castration-Resistant Prostate Cancer. J Clin Oncol. 2023 Jun 20; 41(18):3339-3351.
2. Chi KN et al. Niraparib plus abiraterone acetate with prednisone in patients with metastatic castration-resistant prostate cancer and homologous recombination repair gene alterations: second interim analysis of the randomized phase III MAGNITUDE trial. Ann Oncol. 2023 Jul 1:S0923-7534(23)00757-3.
3. NCCP Classification Document for Systemic Anti-Cancer Therapy (SACT) Induced Nausea and Vomiting. V6 2025. 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
4. Niraparib and abiraterone acetate (Akeega®) SmPC EMA. Last updated 22/08/2024. Accessed November 2024. Available at: https://www.ema.europa.eu/en/documents/product-information/akeega-epar-product-information_en.pdf

Version	Date	Amendment	Approved By
1	01/11/2023		Dr Richard Bambury
2	05/03/2025	Regimen reviewed. Updated exclusions and cautions sections. Updated regimen in line with NCCP standardisation.	Dr Richard Bambury

Comments and feedback welcome at oncologydrugs@cancercontrol.ie