Drug Monograph

A - Drug Name

niraparib / abiraterone

COMMON TRADE NAME(S): Akeega™

back to top

B - Mechanism of Action and Pharmacokinetics

Niraparib is an inhibitor of poly (ADP-ribose) polymerase (PARP) enzymes, PARP-1 and PARP-2, and acts to increase formation of PARP-DNA complexes resulting in DNA damage, apoptosis and cell death. Increased cytotoxicity has been observed in tumor cell lines, regardless of BRCA1/2 deficiencies.

Abiraterone acetate is converted in vivo to abiraterone, which acts as an androgen biosynthesis inhibitor. Abiraterone inhibits the enzyme 17α-hydroxylase/C17,20-lyase (CYP17) which is required for androgen biosynthesis in testicular, adrenal, and prostatic tumour tissues, including the formation of testosterone precursors, dehydroepiandrosterone (DHEA), and androstenedione.

The combination of niraparib and abiraterone acetate targets two oncogenic dependencies in patients with metastatic castration-resistant prostate cancer (mCRPC) and homologous recombination repair (HRR) gene alterations.

Absorption	Bioavailability	~73% (niraparib)
	Effects with food	Administration with food ↑ exposure of abiraterone acetate by up to 10-fold and C_{max} by up to 17-fold, depending on the fat content of the meal.
	Peak plasma levels	~3 hours (niraparib), ~1.5 hours (abiraterone)

Distribution	PPB	83% (niraparib) > 99% (abiraterone)
Metabolism	Niraparib is metabolized by carboxylesterases and UDP-glucuronosyltransferases *in vivo*. Abiraterone acetate is hydrolyzed to abiraterone by a CYP independent pathway. Abiraterone then undergoes sulphation, hydroxylation, and oxidation catalyzed by CYP3A4 and SULT2A1.	
	Active metabolites	Yes
	Inactive metabolites	Yes
Elimination	Half-life	~62 hours (niraparib, when given in combination with abiraterone) ~20 hours (abiraterone, when given in combination with niraparib)
	Urine	48%, 11% unchanged (niraparib) 5% (abiraterone acetate)
	Feces	39%, 19% unchanged (niraparib) 88%, 55% unchanged (abiraterone acetate)

back to top

C - Indications and Status

Health Canada Approvals:

- Prostate cancer

Refer to the product monograph for a full list and details of approved indications

back to top

D - Adverse Effects

Emetogenic Potential: Moderate – Consider prophylaxis daily

The following table lists adverse effects that occurred in > 2% of mCRPC patients treated with niraparib and abiraterone acetate plus prednisone versus abiraterone acetate plus prednisone (AAP) alone in a phase III study. It also includes severe, life-threatening adverse effects effects from other sources or post-marketing.

ORGAN SITE	SIDE EFFECT* (%)	ONSET**
Cardiovascular	Arrhythmia (13%) (3% severe)	E
	Cardiotoxicity (5%)	E D
	Hypertension (34%) (17% severe)	E
	QT interval prolonged (<1%)	E
	Venous thromboembolism (7%) (5% severe)	E
Dermatological	Photosensitivity (<1%)	E
Gastrointestinal	Abdominal pain (5%)	E
	Anorexia, weight loss (16%)	E
	Constipation (34%)	E
	Diarrhea (9%)	E
	Dyspepsia (7%)	E
	Nausea, vomiting (25%) (1% severe)	E
General	Fall / fractures (reported with abiraterone) (6%)	E
	Fatigue (31%)	E
	Fluid retention (17%)	E
Hematological	Myelosuppression (52%) (31% severe) (including anemia)	E D L

Hepatobiliary	↑ Bilirubin (3%)	E
	Hepatotoxicity (2%)	E
Hypersensitivity	Hypersensitivity (rare; reported with abiraterone)	E
Metabolic / Endocrine	Adrenal insufficiency (<2%) (reported with abiraterone)	E D
	↑ ALP (12%) (6% severe)	E
	Hyperglycemia (13%) (4% severe)	E
	↓ K (16%) (6% severe)	E
Musculoskeletal	Musculoskeletal pain (18%)	E
	Other - Myopathy (rare; reported with abiraterone)	E
	Rhabdomyolysis (rare; reported with abiraterone)	E
Neoplastic	MDS /AML (rare; reported with niraparib)	E D L
Nervous System	Dizziness (13%) (<1% severe)	E
	Insomnia (11%)	E
	Posterior reversible encephalopathy syndrome (PRES) (rare; reported with niraparib)	E
Renal	Creatinine increased (10%)	E
Respiratory	Cough, dyspnea (21%) (2% severe)	E
	Pneumonitis (2%)	E

* "*Incidence*" may refer to an absolute value or the higher value from a reported range.
"*Rare*" may refer to events with < 1% incidence, reported in post-marketing, phase 1 studies, isolated data or anecdotal reports.

** I = *immediate* (onset in hours to days) E = *early* (days to weeks)
D = *delayed* (weeks to months) L = *late* (months to years)

The most common side effects for niraparib / abiraterone include myelosuppression, constipation, hypertension, fatigue, nausea/vomiting, cough/dyspnea, musculoskeletal pain, fluid retention, hypokalemia, and anorexia/weight loss.

Hematological toxicities (anemia, thrombocytopenia, and neutropenia) are the most frequent adverse reactions associated with niraparib, and generally occur within the first 3 months of treatment.

Myelodysplastic Syndrome/Acute Myeloid Leukemia (MDS/AML) have been reported rarely with niraparib use. Patients should be referred to a hematologist for suspected MDS/AML or prolonged hematological toxicities that have not resolved with treatment interruption or dose reduction.

Hypertension is an adverse reaction for both niraparib and abiraterone acetate. Median time of onset of hypertension was ~2 months.

Mineralocorticoid effects, which include hypertension, fluid retention, and hypokalemia resulting from CYP17 inhibition, are commonly reported. Corticosteroid co-administration suppresses the adrenocorticotropic hormone (ACTH) drive, reducing the incidence and severity of these effects. Patients on prednisone may require an increased dose of a corticosteroid before, during, and after stressful conditions, such as surgery, trauma or severe infections.

Hepatotoxicity is a significant risk associated with abiraterone acetate. Median time to onset of hepatotoxicity was ~1.5 months.

back to top

E - Dosing

Refer to protocol by which the patient is being treated.

Screen for hepatitis B virus in all cancer patients starting systemic treatment. Refer to the hepatitis B virus screening and management guideline.

A validated test to confirm BRCA tumour status is required before starting treatment.

Hypertension should be controlled before initiating treatment

Hypokalemia should be corrected prior to starting treatment before treatment. Consider maintaining the patient's potassium level at ≥ 4 mM in patients who develop hypokalemia.

Patients should be counselled to avoid sun exposure when possible while on treatment.

Adults:

Oral*: niraparib 200 mg / abiraterone acetate 1000 mg Daily
*Administered as 2 tablets, each containing 100 mg of niraparib and 500 mg of abiraterone acetate.

- Administer with 10 mg prednisone daily.
- Patients should continue with a gonadotropin releasing hormone (GnRH) agonist, unless the patient has had prior bilateral orchiectomy.

Dosage with Toxicity:

Note: Niraparib/abiraterone tablets are available in two strengths. Use correct tablet strength for respective dose modifications.

Table 1 - Dose Levels:

Dose Level	Niraparib/abiraterone Dose (mg Daily) (for Hematologic Toxicity)	Niraparib/abiraterone Dose (mg Daily) (for Hepatotoxicity)
0	200/1000 (2 tablets of 100/500 each)	200/1000 (2 tablets of 100/500 each)
-1	100/1000 (2 tablets of 50/500 each)	100/500 (1 tablet of 100/500)
-2	Discontinue	Discontinue

Table 2 - Dose Modifications for Anemia:

Toxicity	Action
Hgb 100 g/L to LLN	Consider monitoring blood counts weekly.
Hgb 80 to <100 g/L	Monitor blood counts at least weekly for 28 days if Hgb ≥ 100 g/L at baseline.
Hgb < 80 g/L; transfusion indicated	First occurrence: • Hold* combination niraparib / abiraterone. • Switch to abiraterone acetate plus prednisone (AAP) until recovery. Monitor blood counts at least weekly. • After recovery, resume combination niraparib / abiraterone at same dose, or consider 1 dose level ↓ (if anemia persists), as clinically indicated. Monitor blood counts weekly for 28 days after restart.
	Second occurrence: • Hold* combination niraparib / abiraterone. • Switch to AAP until recovery. Monitor blood counts at least weekly. • After recovery, resume combination niraparib / abiraterone at 1 dose level ↓. Monitor blood counts weekly for 28 days after restart. • If dose was previously reduced, consider discontinuing.
	Third occurrence: • Consider discontinuing.

*Do not restart until Hgb ≥ 80 g/L, platelets ≥ 75 x 10^9/L, ANC ≥ 1.5 x 10^9/L, and recovery of non-hematologic toxicity (see table 4).

Table 3 - Dose Modifications for Thrombocytopenia or Neutropenia:

Toxicity		Toxicity	Action
Platelets 75 x 10^9/L to <LLN	and	ANC 1.5 x 10^9/L to <LLN	Consider monitoring blood counts weekly.
Platelets 50 to <75 x 10^9/L	or	ANC 1 to <1.5 x 10^9/L	Monitor blood counts at least weekly. Consider holding* combination niraparib / abiraterone and switching to AAP until recovery. After recovery, resume combination niraparib / abiraterone at same dose. Monitor blood counts at least weekly for 28 days after restart.
Platelets <50 x 10^9/L	or	ANC <1 x 10^9/L	<u>First occurrence:</u> • Hold* combination niraparib / abiraterone. • Switch to AAP until recovery. Monitor blood counts at least weekly. • After recovery, resume combination niraparib / abiraterone at same dose or consider 1 dose level ↓ if clinically indicated**. Monitor blood counts weekly for 28 days after restart.
			<u>Second occurrence:</u> • Hold* combination niraparib / abiraterone. • Switch to AAP until recovery. Monitor blood counts at least weekly. • After recovery, resume combination niraparib / abiraterone at 1 dose level ↓. Monitor blood counts weekly for 28 days after restart. • If dose was previously reduced, consider discontinuing
			<u>Third occurrence:</u> • Discontinue and switch to AAP.

*Do not restart until Hgb ≥ 80 g/L, platelets ≥ 75 x 10^9/L, ANC ≥ 1.5 x 10^9/L, and recovery of non-hematologic toxicity (see table 4).

**If platelet transfusion or G-CSF required, restart at 1 dose level ↓ after recovery.

Table 4 - Dose Modification for Non-Hematologic Toxicities:

Toxicity	Grade/ Severity	Action*
Hepatotoxicity	ALT or AST > 5 x ULN OR Total bilirubin > 3 x ULN	Hold combination niraparib / abiraterone and closely monitor LFTs . Resume at 1 dose level ↓ if LFTs return to baseline. Monitor LFTs at a minimum of every two weeks for three months and monthly thereafter. Recurrence: Discontinue.
	ALT or AST > 20 x ULN	Discontinue.
	ALT > 3 x ULN and total bilirubin > 2 x ULN in the absence of biliary obstruction or other causes responsible for the concurrent elevation	
PRES, MDS/AML, or Hypertensive Crisis	Any	Discontinue.
Other	Grade ≥ 3	Hold combination niraparib / abiraterone if toxicity cannot be definitively attributed to either niraparib or abiraterone acetate alone. Initiate AAP after recovery to Grade 1 or baseline; then switch to combination niraparib / abiraterone acetate ≥ 7 days of starting AAP (if recovery is maintained). If dose was previously reduced, discontinue if no resolution > 28 days.

*Do not restart until Hgb ≥ 80 g/L, platelets ≥ 75 x 10^9/L, ANC ≥ 1.5 x 10^9/L, and recovery of non-hematologic toxicity.

Dosage with Hepatic Impairment:

The pivotal trial excluded patients with moderate and severe hepatic impairment, baseline hepatitis or significant abnormalities of liver function tests.

Hepatic Impairment	Niraparib / Abiraterone Acetate Dose
Mild	No dose adjustment required
Moderate or Severe	Do not use

Dosage with Renal Impairment:

Creatinine Clearance (mL/min)	Niraparib / Abiraterone Dose
≥ 30	No dose adjustment required
< 30	No data

Dosage in the elderly:

No dose adjustment is necessary for elderly patients aged ≥ 65 years. No overall differences in safety and efficacy of niraparib and abiraterone acetate combination therapy were observed between these patients and younger patients. Higher exposure (~25%) of niraparib and abiraterone acetate has been observed in patients aged 75-90 years compared to patients aged 45-65 years. Consider close monitoring of individuals aged ≥ 75 years.

Dosage based on gender:

Niraparib/abiraterone is only indicated in patients with prostate cancer.

Dosage based on ethnicity:

Ethnicity does not have a clinically significant effect on the exposure to niraparib or abiraterone.

Children:

No data available in pediatric patients < 18 years of age.

back to top

F - Administration Guidelines

- Administer each dose on an empty stomach, at least 1 hour before or 2 hours after food.
- Tablets should be swallowed whole with water. Do not break, crush, or chew tablets.
- If a dose is missed, the missed dose should be taken as soon as possible on the same day. Then, administer the next dose at the usual time on the next day. Do not give extra tablets to make up for the missed dose.
- Store at room temperature (15-30°C) in original container.

back to top

G - Special Precautions

Contraindications:

- Patients who have a hypersensitivity to this drug or any of its components

Other Warnings/Precautions:

- Niraparib / abiraterone acetate contains lactose and should not be used in patients with hereditary galactose intolerance, severe lactase deficiency or glucose-galactose malabsorption.
- The pivotal trial excluded patients with certain medical conditions including uncontrolled hypertension, clinically significant heart disease (e.g., myocardial infarction, thrombotic events within the past 6 months, severe or unstable angina, LVEF < 50%), or a history of adrenal dysfunction.

- Use with caution in patients with a history of cardiovascular disease. Cardiac function should be optimized before and during treatment of patients with a significant risk for congestive heart failure (e.g., a history of cardiac failure, or cardiac events such as ischemic heart disease).
- Niraparib / abiraterone acetate can cause hypokalemia and fluid retention due to mineralocorticoid excess from CYP17 inhibition. Use with caution in patients whose underlying medical conditions (e.g. QT prolongation) may be affected by these effects.
- Use with caution in patients concomitantly treated with medications known to reduce platelet counts due to the risk of thrombocytopenia.
- Caution is advised if patients need to be withdrawn from prednisone. Monitoring for adrenal insufficiency should occur.
- Adrenal insufficiency has been reported in patients taking abiraterone and prednisone. Increased corticosteroid dosage may be required before, during and after a stressful situation.
- Severe infections, including fatal outcomes, occurred more frequently in patients treated with niraparib / abiraterone. Severe infections may occur with or without neutropenia and/or leukopenia.
- Caution with driving or using machinery as dizziness may occur with treatment.

Other Drug Properties:

- Carcinogenicity:
  MDS/AML have been reported in patients treated with niraparib in ovarian, fallopian tube or primary peritoneal cancer trials.
- Phototoxicity: Yes

Pregnancy and Lactation:

- Mutagenicity: No
- Clastogenicity: Yes
- Genotoxicity: Probable
- Embryotoxicity: Documented in animals
- Fetotoxicity: Documented in animals
- Pregnancy:
  Niraparib / abiraterone acetate **is only indicated in patients with prostate cancer**. Adequate contraception should be used by patients and their partners during treatment, and for **3 months** after the last dose.
- Breastfeeding:
  Niraparib / abiraterone acetate **is only indicated in patients with prostate cancer.** There are no data on the presence of niraparib/abiraterone metabolites in human milk, or on the effects of the breastfed child or milk production.
- Fertility effects: Probable
  Documented in animals; may be reversible

back to top

H - Interactions

Niraparib is metabolized by carboxylesterases and UDP-glucuronosyltransferases in vivo.

In vitro, niraparib is a:

- weak inducer of CYP1A2
- weak inhibitor of BCRP, P-gp and OCT1
- inhibitor of MATE-1 and -2
- substrate of P-gp and BCRP

Caution is recommended when niraparib is combined with active substances with CYP3A4- and CYP1A2-dependent metabolism, that undergo uptake transport by OCT1 or with known inhibitors or inducers of carboxylesterases and conjugation (UGT) pathways.

Abiraterone is mainly metabolized by CYP3A4 and SULT2A1. Abiraterone is an inhibitor of CYP2C8 and CYP2D6. *In vitro*, abiraterone moderately inhibits CYP2C9, CYP2C19 and CYP3A4/5 (clinical significance unknown). Abiraterone and its major metabolites also inhibit the hepatic uptake transporter OATP1B1 (*in vitro* data only).

Also refer to abiraterone and niraparib drug monographs for details on drug interactions.

AGENT	EFFECT	MECHANISM	MANAGEMENT
Strong CYP3A4 inducers (i.e. phenytoin, carbamazepine, rifampicin, rifabutin, rifapentine, phenobarbital, St. John's wort)	↓ abiraterone concentration and/or efficacy	↑ metabolism of abiraterone	Avoid concomitant use.
Spironolactone	May stimulate disease progression	Spironolactone may bind and activate the wild-type androgen receptor.	Avoid use with abiraterone.
Radium-223 dichloride	↑ risk of fractures and mortality	Unknown	Avoid use with abiraterone.
CYP2D6 substrates (e.g. metoprolol, propranolol, desipramine, venlafaxine, haloperidol,	↑ CYP2D6 substrates concentration and/or toxicity	Abiraterone is a strong CYP2D6 inhibitor.	Caution with concomitant use, particularly CYP2D6 substrates with narrow therapeutic index. Consider ↓ dose of CYP2D6 substrates.

risperidone, propafenone, flecainide, codeine, oxycodone and tramadol)			
CYP2C8 substrates (i.e. paclitaxel, sorafenib, amiodarone, enzalutamide)	↑ CYP 2C8 substrates concentration and/or toxicity	Abiraterone inhibits CYP2C8.	Caution with concomitant use. Monitor for signs of toxicity related to CYP2C8 substrates with a narrow therapeutic index.
CYP2C8 substrates (pioglitazone, repaglinide)	Hypoglycemia reported in patients with pre-existing diabetes taking pioglitazone or repaglinide with abiraterone and prednisone	Abiraterone inhibits CYP2C8	Monitor blood glucose closely in applicable patients.
MATE-1 and MATE-2 substrates (e.g. metformin)	↑ MATE-1 and -2 substrates concentration and/or toxicity	Niraparib inhibits MATE-1 and -2.	Caution with concomitant use. Monitor for adverse reactions related to MATE-1 and -2 substrates with a narrow therapeutic index.
Drugs that increase risk of myopathy (e.g. statins)	↑ risk of myopathy/rhabdomyolysis	May be additive with abiraterone	Caution and monitor for myopathy/rhabdomyolysis.

back to top

I - Recommended Clinical Monitoring

Treating physicians may decide to monitor more or less frequently for individual patients but should always consider recommendations from the product monograph.

Refer to the hepatitis B virus screening and management guideline for monitoring during and after treatment.

Recommended Clinical Monitoring

Monitor Type	Monitor Frequency
CBC	Baseline, weekly for the first month, then bi-weekly for 2 months, then monthly for the first year, then every other month thereafter. (Weekly monitoring for the second month may be warranted based on individual laboratory values)
Liver function tests	Baseline, every 2 weeks for 3 months, then monthly for the first year, then every other month thereafter
Serum potassium	Baseline, monthly for the first year, then every other month thereafter
Blood pressure and heart rate	Baseline, at least weekly for 2 months, then monthly for the first year, then every other month thereafter (More frequent monitoring may be required in patients with cardiovascular disorders, especially coronary insufficiency, cardiac arrhythmias, and hypertension)
Fluid retention (weight gain, peripheral edema)	Baseline, every 2 weeks for 3 months, then monthly thereafter
Adrenal insufficiency	As clinically indicated when prednisone is withdrawn, or during periods of infection/stress
Mineralocorticoid excess	As clinically indicated if patient continues on abiraterone after stopping prednisone
Blood glucose levels	Baseline and as clinically indicated (especially in patients with diabetes)

Clinical toxicity assessment for anemia, bleeding, infection, fatigue, hypersensitivity, secondary malignancy, venous thromboembolism, GI, cardiac, musculoskeletal, neurologic, or respiratory effects	At each visit

Grade toxicity using the current NCI-CTCAE (Common Terminology Criteria for Adverse Events) version

Suggested Clinical Monitoring

Monitor Type	Monitor Frequency
Symptoms of congestive heart failure (patients with a history of cardiovascular disease)	Baseline, every 2 weeks for 3 months, then monthly thereafter

back to top

J - Supplementary Public Funding

Exceptional Access Program (EAP Website)

- niraparib / abiraterone - For the treatment of metastatic castration resistant prostate cancer in patients with a BRCA mutation

back to top

K - References

Abiraterone drug monograph. Ontario Health (Cancer Care Ontario).

CADTH reimbursement recommendation. Niraparib-abiraterone (Akeega). February 2024.

Chi KN, Rathkopf D, Smith MR, et al. Niraparib and Abiraterone Acetate for Metastatic Castration-Resistant Prostate Cancer. J Clin Oncol. 2023 Jun 20;41(18):3339-3351. doi: 10.1200/JCO.22.01649.

Niraparib drug monograph. Ontario Health (Cancer Care Ontario).

Prescribing Information: Akeega™ (niraparib and abiraterone acetate). Janssen Biotech, Inc. August 11, 2023.

Product Monograph: Akeega™ (niraparib and abiraterone acetate). Janssen Inc. March 12, 2023.

June 2025 New drug monograph

back to top

L - Disclaimer

Refer to the New Drug Funding Program or Ontario Public Drug Programs websites for the most up-to-date public funding information.

The information set out in the drug monographs, regimen monographs, appendices and symptom management information (for health professionals) contained in the Drug Formulary (the "Formulary") is intended for healthcare providers and is to be used for informational purposes only. The information is not intended to cover all possible uses, directions, precautions, drug interactions or adverse effects of a particular drug, nor should it be construed to indicate that use of a particular drug is safe, appropriate or effective for a given condition. The information in the Formulary is not intended to constitute or be a substitute for medical advice and should not be relied upon in any such regard. All uses of the Formulary are subject to clinical judgment and actual prescribing patterns may not follow the information provided in the Formulary.

The format and content of the drug monographs, regimen monographs, appendices and symptom management information contained in the Formulary will change as they are reviewed and revised on a periodic basis. The date of last revision will be visible on each page of the monograph and regimen. Since standards of usage are constantly evolving, it is advised that the Formulary not be used as the sole source of information. It is strongly recommended that original references or product monograph be consulted prior to using a chemotherapy regimen for the first time.

Some Formulary documents, such as the medication information sheets, regimen information sheets and symptom management information (for patients), are intended for patients. Patients should always consult with their healthcare provider if they have questions regarding any information set out in the Formulary documents.

While care has been taken in the preparation of the information contained in the Formulary, such information is provided on an “as-is” basis, without any representation, warranty, or condition, whether express, or implied, statutory or otherwise, as to the information’s quality, accuracy, currency, completeness, or reliability.

CCO and the Formulary’s content providers shall have no liability, whether direct, indirect, consequential, contingent, special, or incidental, related to or arising from the information in the Formulary or its use thereof, whether based on breach of contract or tort (including negligence), and even if advised of the possibility thereof. Anyone using the information in the Formulary does so at his or her own risk, and by using such information, agrees to indemnify CCO and its content providers from any and all liability, loss, damages, costs and expenses (including legal fees and expenses) arising from such person’s use of the information in the Formulary.

back to top