Regimen Monograph

A - Regimen Name

CABAPRED Regimen

Cabazitaxel-Prednisone

Disease Site

Genitourinary
Prostate

Intent

Palliative

Regimen Category

Evidence-Informed :

Regimen is considered appropriate as part of the standard care of patients; meaningfully improves outcomes (survival, quality of life), tolerability or costs compared to alternatives (recommended by the Disease Site Team and national consensus body e.g. pan-Canadian Oncology Drug Review, pCODR). Recommendation is based on an appropriately conducted phase III clinical trial relevant to the Canadian context OR (where phase III trials are not feasible) an appropriately sized phase II trial. Regimens where one or more drugs are not approved by Health Canada for any indication will be identified under Rationale and Use.

Rationale and Uses

For the treatment of metastatic castration resistant prostate cancer (mCRPC), in patients who have progressed on/after prior docetaxel-containing chemotherapy and an androgen-receptor-axis targeted agent (ARAT), regardless of the order of treatment or treatment settings. (Not funded for combination treatment with abiraterone, enzalutamide, or radium-233 for mCRPC)

(Refer to NDFP form for details.)

Supplementary Public Funding	**cabazitaxel** New Drug Funding Program (Cabazitaxel - Metastatic Castration Resistant Prostate Cancer) (NDFP Website) **prednisone** ODB - General Benefit (prednisone) (ODB Formulary)

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B - Drug Regimen

cabazitaxel*	20 to 25 mg /m²	IV	Day 1
prednisone	10 mg	PO	Daily

Patients who are receiving a GnRH agonist should continue to receive the GnRH agonist during cabazitaxel treatment.

* cabazitaxel 25 mg/m^2 may be used in select patients at the physician's discretion.

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C - Cycle Frequency

REPEAT EVERY 21 DAYS

Continue until disease progression or unacceptable toxicity

(de Bono et al. limited duration to 10 cycles because of the risk of cardiotoxicity in the mitoxantrone arm)

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D - Premedication and Supportive Measures

Antiemetic Regimen: Low

- Also refer to CCO Antiemetic Recommendations.

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

Pre-medications (prophylaxis for infusion reaction):

At least 30 minutes prior to each administration of cabazitaxel:

- A corticosteroid IV/PO (e.g. Dexamethasone 8 mg)
- An H1-receptor antagonist IV/PO (e.g. Diphenhydramine 25 mg)
- An H2- receptor antagonist IV/PO (e.g. Ranitidine 50 mg)

Other supportive care:

- Hemoglobin and hematocrit should be checked prior to treatment.
- The product monograph recommends that primary G-CSF prophylaxis be considered in patients at higher risk of complications from prolonged neutropenia (e.g. age > 65 years, poor performance or nutritional status, previous occurrence of febrile neutropenia, extensive prior radiation ports, or other serious comorbidities).
- Also refer to CCO GCSF recommendations.

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E - Dose Modifications

Doses should be modified according to the protocol by which the patient is being treated.

Patients on LHRH agonists should continue on the agents.

Use with caution in patents with hemoglobin < 10 g/dL. Hemoglobin and hematocrit should be checked prior to treatment.

Dosage with toxicity

Do not treat until ANC > 1.5 x 10^9/L and platelets are ≥ 100 x 10^9/L.

	Dose (mg/m^2)	Dose (mg/m^2)
Starting dose	25	20
First reduction	20	15
Second reduction	15	Discontinue

Adverse reactions / Counts (x 10^9/L)	Action	Dose for Next Cycle*
Neutropenia grade ≥3 for ≥ 7 days (despite supportive care)	Hold until ANC >1.5 and platelets ≥ 100, then	↓ 1 dose level
Febrile neutropenia or thrombocytopenic bleeding	Hold until ANC >1.5 and platelets ≥ 100, then	↓ 1 dose level
Diarrhea grade 2 persisting despite adequate supportive care	Hold until recovery to grade ≤1	↓ 1 dose level
Diarrhea or other organ/ non-hematologic toxicity grade 3	Hold until recovery to ≤ grade 2	↓ 1 dose level
Grade 3 peripheral neuropathy	Hold until recovery to ≤ grade 2	↓ 1 dose level
Grade 3 GI perforation/hemorrhage	Hold or Discontinue	↓ 1 dose level or Not applicable
Grade 4 organ, other non-hematologic toxicity	Discontinue	Not applicable
≥ grade 3 renal failure	Discontinue	Not applicable
New or worsening respiratory symptoms	Hold and investigate	Discontinue if confirmed pneumonitis/ILD or ARDS
Signs & symptoms suggesting cystitis	Hold and investigate	Consider discontinuing if confirmed cystitis
*Do not retreat until neutrophils > 1.5 x 10^9/L, platelets ≥ 100 x 10^9/L and other toxicity ≤ grade 2 (grade 1 for persistent diarrhea) **Discontinue if toxicity continues at reduced dose		

Management of Infusion Reactions

Also refer to the CCO guideline for detailed description of Management of Cancer Medication-Related Infusion Reactions.

Grade	Management	Re-Challenge
1 or 2	• Stop or slow the infusion rate. • Manage the symptoms. **Restart:** • After symptom resolution, restart with pre-medications ± reduced infusion rate.	• Consider re-challenge with pre-medications and at a reduced infusion rate. • After 2 subsequent IRs, replace with a different taxane. Give intensified pre-medications and reduce the infusion rate. • May consider adding oral montelukast ± oral acetylsalicylic acid.
3 or 4	• Stop treatment • Aggressively manage symptoms.	• Re-challenge is discouraged, especially if vital symptoms have been affected. • Consider desensitization if therapy is necessary. • There is insufficient evidence to recommend substitution with another taxane at re-challenge • High cross-reactivity rates have been reported.

Hepatic Impairment

Total Bilirubin		AST/ALT	Dose (mg/m^2)
< ULN	and	<1.5 x ULN	No change
>1 to ≤ 1.5 x ULN	or	>1.5 x ULN	20 (monitor carefully)
>1.5 to ≤ 3 x ULN	and	any	Maximum 15 (unknown efficacy; monitor carefully)
>3 x ULN	and	any	Contraindicated

Renal Impairment

No dosage adjustment is needed in patients with renal impairment not requiring hemodialysis.

Creatinine Clearance (ml/min)	Dosage modification
50 - 80	No adjustment.
15 - 50	No adjustment.
<15; end stage renal disease	Limited clinical data. Treat with caution and monitor patient carefully.

Dosage in the Elderly

No specific dose adjustment recommended in elderly patients, but they are more at risk for severe toxicity, including myelosuppression, infection and cardiac effects.

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F - Adverse Effects

Refer to cabazitaxel, prednisone product or drug monograph(s) for additional details of adverse effects.

Common (25-49%)	Less common (10-24%)	Uncommon (< 10%), but may be severe or life-threatening
• Myelosuppression +/- infection, bleeding, anemia (may be severe) • Diarrhea (may be severe) • Fatigue • Nausea, vomiting	• Constipation • Anorexia • Musculoskeletal pain • Steroid effects (weight gain, myopathy, hyperglycemia, GI irritation)	• Arrhythmia/QT prolongation, atrial fibrillation • Venous thromboembolism • Nephrotoxicity • Hypersensitivity • Peripheral neuropathy • Cardiotoxicity • GI obstruction, perforation, hemorrhage

		• Pneumonitis/ILD/ARDS • Increased LFTs • Hypotension • Radiation cystitis (with previous pelvic radiation and docetaxel)

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G - Interactions

Refer to cabazitaxel, prednisone drug or product monograph(s) for additional details.

- Drug interactions with therapeutic doses of cabazitaxel and co-administration of CYP3A4 substrates are not expected.
- CYP3A4 inducers may increase cabazitaxel metabolism; avoid strong inducers.
- CYP3A4 inhibitors may reduce cabazitaxel metabolism; avoid strong inhibitors, including grapefruit juice and related products.
- Cabazitaxel may inhibit OATP1B1 at clinically relevant doses. Avoid or separate cabazitaxel and OATP1B1 substrate administration.

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H - Drug Administration and Special Precautions

Refer to cabazitaxel, prednisone drug or product monograph(s) for additional details.

Administration: Cabazitaxel

- Use non-PVC equipment for preparation and administration, as cabazitaxel contains polysorbate 80 that increases the rate of di-(2-ethylhexyl) phtalate extraction (DEHP) from polyvinyl chloride (PVC). Also do not use polyurethane equipment.
- Use a 0.22 micron in-line filter.
- Cabazitaxel products have different dilution instructions; refer to the respective product monograph to ensure that the appropriate instructions are followed.
- The concentrate-diluent solution should be further diluted immediately with either 5% dextrose or 0.9% sodium chloride solution.
- The final concentration of the infusion solution should be 0.1mg/mL-0.26mg/mL. Infuse IV over 1 hour at room temperature.
- Gently rotate the IV bag prior to rotating to ensure proper mixing
- Do not mix with other drugs. Crystallized infusion solutions should not be used.

- Store the unopened vials at room temperature (15°C- 30°C). Do not refrigerate.

Also refer to the CCO guideline for detailed description of Management of Cancer Medication-Related Infusion Reactions.

Administration: Prednisone

- Take with food in the morning at about the same time each day
- If a dose is missed, skip that dose and continue with regular dosing the following day

Contraindications

- Patients who have hypersensitivities to this drug or any of its components, including other drugs formulated with polysorbate 80
- Patients with neutrophil counts of ≤1.5 x 10^9/L
- Patients with severe hepatic impairment (total bilirubin > 3 x ULN)
- Concomitant use of yellow fever vaccines

Other Warnings/Precautions

- Avoid use of live vaccines in patients receiving cabazitaxel. Inactivated vaccines may be administered; however, response may be diminished.
- Exercise caution in patients with anemia and those most at risk of developing gastrointestinal complications: patients with neutropenia, with a prior history of pelvic radiotherapy, GI disease (e.g. ulceration, bleeding), the elderly, concomitant use of NSAIDs, anti-platelet therapy or anti-coagulants.
- Patients should exercise caution when driving or operating a vehicle or potentially dangerous machinery as fatigue and dizziness have been reported.

Pregnancy/Lactation

- Cabazitaxel may cause harm to a developing fetus or lead to loss of pregnancy. Adequate contraception should be used by both sexes during treatment and for **6 months** after the last dose.
- Fertility effects: Probable (cabazitaxel)

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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

- CBC; Baseline, weekly during cycle 1, before each cycle, and as clinically indicated (also in patients with symptoms of anemia)
- Liver and renal function tests; Baseline and before each cycle
- Clinical toxicity assessment for infusion reactions, GI effects, infection, hypersensitivity, bleeding, anemia, respiratory effects, peripheral neuropathy, thromboembolism; At each visit
- Grade toxicity using the current NCI-CTCAE (Common Terminology Criteria for Adverse Events) version

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J - Administrative Information

Approximate Patient Visit	2 hours
Pharmacy Workload (average time per visit)	27.184 minutes
Nursing Workload (average time per visit)	38.083 minutes

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K - References

Cabazitaxel drug monograph, Ontario Health (Cancer Care Ontario).

de Bono J.S, Oudard S, Ozguroglu M et al. Prednisone plus cabazitaxel or mitoxantrone for metastatic castration-resistant prostate cancer progressing after docetaxel treatment: a randomised open-label trial. Lancet. 2010; 376: 1147–54.

Eisenberger M, Hardy-Bessard AC, Kim CS, et al. Phase III study comparing a reduced dose of cabazitaxel (20 mg/m^2) and the currently approved dose (25 mg/m2) in post-docetaxel patients with metastatic castration-resistant prostate cancer-PROSELICA. J Clin Oncol 2017;35(28):3198-206.

PEBC Advice Documents or Guidelines

- Systemic Therapy in Men with Metastatic Castration-Resistant Prostate Cancer

February 2023 Updated Dosage with hepatic impairment, Dosage with renal impairment, Adverse effects, and Special precautions sections

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M - Disclaimer

Regimen Abstracts

A Regimen Abstract is an abbreviated version of a Regimen Monograph and contains only top level information on usage, dosing, schedule, cycle length and special notes (if available). It is intended for healthcare providers and is to be used for informational purposes only. It is not intended to constitute or be a substitute for medical advice, and all uses of the Regimen Abstract are subject to clinical judgment. 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, and Cancer Care Ontario disclaims all liability for the use of this information, and for any claims, actions, demands or suits that arise from such use.

Information in regimen abstracts is accurate to the extent of the ST-QBP regimen master listings, and has not undergone the full review process of a regimen monograph. Full regimen monographs will be published for each ST-QBP regimen as they are developed.

Regimen Monographs

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

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