**Regimen Monograph**



## A - Regimen Name

# NPAC(W) Regimen

**Nab-Paclitaxel (weekly)**

| | |
|---|---|
| **Disease Site** | Genitourinary - Bladder / Urothelial |
| **Intent** | Palliative |
| **Regimen Category** | **Evidence-Informed :**<br>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 second-line treatment of locally advanced or metastatic urothelial bladder cancer after failure of a platinum-containing regimen. |

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## B - Drug Regimen

| | | | |
|---|---|---|---|
| **nab-PACLitaxel** | 100 to 150 mg /m² | IV | Days 1, 8, 15 |

**(This drug is not currently publicly funded for this regimen and intent)**

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## C - Cycle Frequency

**REPEAT EVERY 28 DAYS**

Until disease progression or unacceptable toxicity

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## D - Premedication and Supportive Measures

**Antiemetic Regimen:** Low (No premedication to prevent hypersensitivity is required)

**Other Supportive Care:**
Also refer to CCO Antiemetic Summary

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## E - Dose Modifications

Doses should be modified according to the protocol by which the patient is being treated. The following recommendations have been adapted from clinical trials or product monographs and could be considered.

**Dosage with toxicity**

| **Toxicity in previous cycle (x $10^9$/L)** | **nab-paclitaxel % of previous dose** |
|---|---|
| ANC < 0.5 ≥ 7 days or<br>febrile neutropenia or Grade 4 thrombocytopenia or bleeding | Hold*, then 80% |
| Grade 3 Sensory neuropathy or other related non-hematologic toxicity | Hold*, then 80% |
| Grade 4 sensory neuropathy or other related non-hematologic toxicity | Discontinue |
| Severe hypersensitivity or any occurence of cystoid macular edema | Discontinue |

*Do not retreat until ANC ≥ 1.5 x $10^9$/L, platelets ≥ 100 x $10^9$/L, other toxicity ≤ grade 2

## Hepatic Impairment

Patients with hepatic impairment may be at increased risk of myelosuppression and should be closely monitored.

| **Bilirubin** | | **AST** | **Nab-paclitaxel***<br><br>**(% previous dose - suggested)** |
|---|---|---|---|
| >1 to ≤ 1.5 x ULN | and | ≤ 10 x ULN | 100% |
| >1.5 to ≤ 5 x ULN | and | ≤ 10 x ULN | ↓ to 80%** |
| > 5 x ULN | or | > 10 x ULN | Discontinue |

*Based on clinical judgment – less conservative adjustments can be considered if hepatic changes are secondary to metastases rather than hepatic cirrhosis or hepatitis. Patients with elevated baseline bilirubin were excluded from clinical trials.
**Reduced dose may be escalated to 100% if treatment is tolerated for at least 2 cycles at the reduced dose.

## Renal Impairment

| **Creatinine Clearance (mL/min)** | **Nab-paclitaxel***<br><br>**(% previous dose - suggested)** |
|---|---|
| ≥ 30 to < 90 | 100% |
| < 30 | Discontinue |

* Based on clinical judgment. Patients with elevated baseline creatinine were excluded from clinical trials.

## Dosage in the Elderly

No dose adjustment is required. Patients age 65 years or older may have higher incidence of neutropenia in cycle 1. Patients aged 65 and older who received nab-paclitaxel monotherapy for metastatic breast cancer had a higher incidence of epistaxis, diarrhea, dehydration, fatigue and peripheral edema.

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## F - Adverse Effects

Refer to nab-PACLitaxel drug monograph(s) for additional details of adverse effects

| Very common (≥ 50%) | Common (25-49%) | Less common (10-24%) | Uncommon (< 10%), but may be severe or life-threatening |
|---|---|---|---|
| • Alopecia<br>• Sensory neuropathy (may be severe) | • Fatigue<br>• Musculoskeletal pain<br>• Increased LFTs (may be severe)<br>• Nausea, vomiting<br>• Diarrhea (may be severe) | • Edema<br>• Cough, dyspnea<br>• Constipation<br>• Myelosuppression +/- infection, bleeding (may be severe)<br>• Rash (may be severe)<br>• Increased creatinine (may be severe) | • Injection site reaction<br>• Hypersensitivity<br>• Cardiotoxicity<br>• Arrhythmia<br>• Autonomic neuropathy<br>• Arterial/venous thromboembolism<br>• Hemolytic uremic syndrome, TTP<br>• GI obstruction, perforation<br>• Pancreatitis<br>• Pneumonitis<br>• Keratitis, cystoid macular edema |

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## G - Interactions

Refer to nab-PACLitaxel drug monograph(s) for additional details

No drug interaction studies have been conducted with nab-paclitaxel, but are likely to be similar to those reported for paclitaxel (refer to the paclitaxel drug monograph).

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## H - Drug Administration and Special Precautions

Refer to nab-PACLitaxel drug monograph(s) for additional details

### Administration

- Refer to the product monograph for full instructions on reconstitution.
- The reconstituted suspension should be milky and homogenous without visible particulates.
- Avoid shaking drug suspension in order to minimize foaming.
- No further dilution is required after reconstitution. Transfer reconstituted drug to an empty, sterile IV PVC or non-PVC infusion bag.
- Infuse intravenously over 30 minutes. Slower infusion rates may increase the likelihood of infusion-related reactions.
- DEHP-free containers or administration sets may be used but are not required.
- Do not admix with other drugs.
- Use of syringes and IV bags containing silicone oil as lubricant may cause formation of proteinaceous strands. If strands are observed by visual inspection of IV bag, administer reconstituted suspension through filter of at least 15 µm pore size. If this is not possible, discard the product.

### Contraindications

- patients who have a hypersensitivity to this drug or any of its components (such as albumin) in the formulation or container
- patients with baseline ANC of < 1.5 x $10^9$/L or platelets < 100 x $10^9$/L on day 1 of each treatment cycle
- patients with a history of interstitial lung disease, multiple allergies, progressive dyspnea or unproductive cough

### Warnings/precautions

- the use of albumin-containing solutions is associated with a remote risk of viral transmission, including CJD
- radiation recall and pneumonitis have been reported in patients with concurrent radiotherapy
- caution is recommended prior to driving or operating machinery if fatigue or dizziness are present

### Pregnancy and lactation

- Nab-paclitaxel is not recommended for use in pregnancy. Adequate contraception should be used by both sexes during treatment and for at least 6 months after the last dose.
- Breastfeeding is not recommended.

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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.

Recommended Clinical Monitoring

- CBC; baseline and before each cycle
- Liver function tests; baseline and regular
- Clinical toxicity assessment of neuropathy, infection, hypersensitivity, musculoskeletal, GI, ophthalmic, thromboembolism, local reactions and pneumonitis; at each visit
- Grade toxicity using the current NCI-CTCAE (Common Terminology Criteria for Adverse Events) version

Suggested Clinical Monitoring

- ECG; as clinically indicated for patients at risk of arrhythmia

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## J - Administrative Information

| | |
|---|---|
| Approximate Patient Visit | 1 hour |
| Pharmacy Workload (average time per visit) | 32.929 minutes |
| Nursing Workload (average time per visit) | 35 minutes |

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## K - References

nab-paclitaxel drug monograph, Cancer Care Ontario.

Ko Y, Canil CM, Mukherjee SD, et al. Nanoparticle albumin-bound paclitaxel for second-line treatment of metastatic urothelial carcinoma: a single group, multicentre, phase 2 study. Lancet Oncol 2013; 14: 769–76.

Vaughn DJ, Broome CM, Hussain M, Gutheil JC, Markowitz AB. Phase II trial of weekly paclitaxel in patients with previously treated advanced urothelial cancer.
J Clin Oncol. 2002 Feb 15;20(4):937-40.

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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.*

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***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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