Regimen Monograph

A - Regimen Name

GEMCNPAC(W) Regimen

Gemcitabine-Nab-Paclitaxel (ABRAXANE®)

Disease Site

Gastrointestinal
Pancreas

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

First-line treatment of locally advanced unresectable or metastatic adenocarcinoma of the pancreas, in patients with ECOG status of 0 to 2.

Note: GEMCNPAC will not be funded if a patient has previously progressed on FOLFIRINOX. See funding form for details.

Supplementary Public Funding

nab-PACLitaxel
New Drug Funding Program (Gemcitabine and Nab-Paclitaxel - Advanced Pancreatic Cancer) (NDFP Website)

back to top

B - Drug Regimen

nab-PACLitaxel	125 mg /m²	IV	Days 1, 8, 15
Do not substitute for or with other paclitaxel formulations.			
gemcitabine	1000 mg /m²	IV	Days 1, 8, 15

back to top

C - Cycle Frequency

REPEAT EVERY 28 DAYS

Until disease progression or unacceptable toxicity

back to top

D - Premedication and Supportive Measures

Antiemetic Regimen: Low

Other Supportive Care:

Also refer to CCO Antiemetic Summary

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

Nab-paclitaxel: No pre-medication to prevent hypersensitivity is required. Do not substitute for or with other paclitaxel formulations.

In the pivotal trial, patients were provided with a supply of antibiotic prophylaxis (ciprofloxacin or amoxicillin/clavulanate), to be used at first occurrence of fever ≥ 38.5C. The use of long-term antibiotic prophylaxis for recurrences in patients who had experienced a first febrile episode will be at the discretion of the treating physician.

G-CSF may be given according to institutional guidelines (also refer to dose modifications).

back to top

E - Dose Modifications

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

Dosage with toxicity

Dose levels

Dose Level	Nab-paclitaxel (mg/m^2)	Gemcitabine (mg/m^2)
Full dose	125	1000
-1	100	800
-2	75	600
Further reduction required	discontinue	discontinue

Start Day 1 when ANC ≥ 1.5 x 10^9/L, platelets ≥ 100 x 10^9/L and other toxicities ≤ grade 2 or as stated below. Do not escalate reduced doses.

Dose modifications at the start of cycle or during cycle

Worst Toxicity Experienced	Nab-paclitaxel Dose	Gemcitabine Dose
Grade 3 or 4 febrile neutropenia	Hold until afebrile and ANC ≥ 1.5 x 10^9/L, then ↓1 dose level	
Grade 2 or 3 skin toxicity	↓1 dose level and continue; discontinue if persists	↓1 dose level and continue; discontinue if persists
Grade 3 or 4 sensory neuropathy	Hold until ≤ grade 1, then ↓1 dose level OR consider discontinuing for Grade 4.	No change
Grade 3 other toxicity, including mucositis, diarrhea (except nausea/vomiting/alopecia)	Hold until ≤ grade 1, then ↓1 dose level	Hold until ≤ grade 1, then ↓1 dose level
Grade 4 other toxicity or any cystoid macular edema	Discontinue	Discontinue
Pneumonitis	Hold and investigate; discontinue if confirmed.	

Hematologic dose modifications during days 8 and 15 of cycle

Omitted doses during the cycle will not be made up. Note day 15 dose modifications depend on day 8 dosing.

Day 8 counts x 10^9/L	**Day 8** nab-paclitaxel and gemcitabine doses	**Day 15** counts x 10^9/L	**Day 15** nab-paclitaxel and gemcitabine doses
ANC ≥ 1 and platelets ≥ 75	DAY 1 DOSE	**If Day 8 dose unchanged from Day 1:**	
		ANC ≥ 1 and platelets ≥ 75	DAY 1 DOSE
		ANC 0.5-0.99 or platelets 50-74	DAY 1 DOSE, add G-CSF[1]
		ANC < 0.5 or platelets < 50	**OMIT**
ANC 0.5- 0.99 or platelets 50-74	↓ 1 DOSE LEVEL	**If Day 8 dose was REDUCED:**	
		ANC ≥ 1 and platelets ≥ 75	DAY 1 DOSE, add G-CSF[1]
		ANC 0.5-0.99 or platelets 50-74	DAY 8 DOSE, add G-CSF[1]
		ANC < 0.5 or platelets < 50	**OMIT**
Day 8 counts x 10^9/L	**Day 8** nab-paclitaxel and gemcitabine doses	**Day 15** counts x 10^9/L	**Day 15** nab-paclitaxel and gemcitabine doses
ANC < 0.5 or platelets < 50	OMIT FOR DAY 8	**If Day 8 dose was OMITTED:**	
		ANC ≥ 1 and platelets ≥ 75	DAY 1 DOSE, add G-CSF[1]
		ANC 0.5-0.99 or platelets 50-74	↓ 1 DOSE LEVEL, add G-CSF[1]
		ANC < 0.5 or platelets < 50	**OMIT**

[1]If G-CSF is not available, suggest reducing an additional dose level. G-CSF was optional for isolated thrombocytopenia.

Hepatic Impairment

Patients with hepatic impairment may be at increased risk of myelosuppression and should be closely monitored. Nab-paclitaxel is not recommended in patients with metastatic pancreatic cancer who have moderate to severe hepatic impairment.

Bilirubin		AST	Nab-paclitaxel* (% previous dose - suggested)	Gemcitabine* (% previous dose - suggested)
>1 to ≤ 1.5 x ULN	and	≤ 10 x ULN	100%	100%
>1.5 to ≤ 5 x ULN	and	≤ 10 x ULN	Insufficient data; discontinue	Consider ↓ to 75%
> 5 x ULN	or	> 10 x ULN	Discontinue	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.

Renal Impairment

Creatinine Clearance (mL/min)	Nab-paclitaxel* (% previous dose - suggested)	Gemcitabine* (% previous dose – suggested)
≥ 30 to < 90	100%	100%
< 30	Discontinue	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 75 years and older who received nab-paclitaxel in combination with gemcitabine for pancreatic cancer had a higher incidence of serious adverse reactions and no demonstrated survival benefit.

back to top

F - Adverse Effects

Refer to nab-PACLitaxel, gemcitabine 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 • Neuropathy (may be severe) • Increased LFTs (may be severe) • Nausea, vomiting	• Fatigue • Musculoskeletal pain • Flu-like symptoms • Proteinuria • Diarrhea • Myelosuppression +/- infection, bleeding (may be severe) • Rash (may be severe)	• Edema • Increased creatinine (may be severe) • Cough, dyspnea	• Injection site reaction • Hypersensitivity • Arterial/venous thromboembolism • Arrhythmia • Cardiotoxicity • Hemolytic uremic syndrome • GI obstruction/perforation • Vasculitis • PRES/RPLS • Pneumonitis, ARDS • Pancreatitis • Capillary leak syndrome • Keratitis, cystoid macular edema

back to top

G - Interactions

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

- Pharmacokinetic interactions between nab-paclitaxel and gemcitabine have not been evaluated in vivo. The drugs have different metabolic pathways.
- 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).
- Increased INR and risk of bleeding is possible with warfarin. Monitor INR closely and adjust warfarin dose as needed.

back to top

H - Drug Administration and Special Precautions

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

Administration

Nab-paclitaxel:

- 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.

Gemcitabine:

- May dilute reconstituted drug in normal saline for IV infusion, resulting in a minimum final concentration of at least 0.1 mg/mL.
- Infuse over 30 minutes through free-flowing IV. Infusion time beyond 60 minutes has been shown to increase toxicity.

Contraindications

- Patients who have a hypersensitivity to these drugs or any of their 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 (cases of serious pneumonitis were reported in those treated with combination nab-paclitaxel and gemcitabine)

Other Warnings / Precautions

- Patients with impaired hepatic function, including concurrent liver metastases or a previous history of hepatitis, alcoholism or liver cirrhosis
- 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 / Lactation

- This regimen is not recommended for use in pregnancy. Adequate contraception should be used by patients and their partners while on treatment and after the last treatment dose. Recommended methods and duration of contraception may differ depending on the treatment. Refer to the drug monograph(s) for more information.
- Breastfeeding is not recommended during this treatment and after the last treatment dose. Refer to the drug monograph(s) for recommendations after the last treatment dose (if available).
- Fertility effects: Probable

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

- CBC; baseline and at each visit
- ECG monitoring especially in patients who have cardiac risk factors; baseline and periodic
- Liver and renal function tests; baseline and regular
- Clinical toxicity assessment of neuropathy, infection and bleeding, hypersensitivity, musculoskeletal, GI, ophthalmic, pulmonary effects, thromboembolism, local reactions, 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
- INR for patient receiving warfarin; baseline and regular
- Urinalysis; baseline and regular

back to top

J - Administrative Information

Approximate Patient Visit	1.5 hours
Pharmacy Workload (average time per visit)	46.534 minutes
Nursing Workload (average time per visit)	38.333 minutes

back to top

K - References

Gemcitabine and nab-paclitaxel drug monographs, Cancer Care Ontario.

Von Hoff DD, Ervin T, Arena FP, et al. Increased survival in pancreatic cancer with nab-paclitaxel plus gemcitabine. N Engl J Med 2013;369(18):1691-703.

November 2023 Modified Pregnancy/breastfeeding section

back to top

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.

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