

Gemcitabine (1000mg/m²), CARBOplatin (AUC 4) and Bevacizumab 15mg/kg Therapy- 21 day

INDICATIONS FOR USE:

INDICATION	ICD10	Regimen Code	Reimbursement status
Treatment of adult patients with first recurrence of platinum-sensitive epithelial ovarian, fallopian tube or primary peritoneal cancer who have not received prior therapy with bevacizumab or other VEGF inhibitors or VEGF receptor-targeted agents	C56 C57 C48	00499a	Hospital

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 patient's individual clinical circumstances.

Bevacizumab is administered once every **3 weeks** as an intravenous infusion in combination with CARBOplatin (Day 1) and gemcitabine (Day 1 and 8) for 6 cycles (and up to 10 cycles) followed by continued use of bevacizumab as single agent until disease progression or unacceptable toxicity develops.

Facilities to treat anaphylaxis MUST be present when the chemotherapy is administered.

Admin. Order	Day	Drug	Dose	Route	Diluent & Rate	Cycle
1	1	Bevacizumab	15mg/kg	IV infusion	100ml NaCl 0.9% over 90mins*	Every 21 days
2	1 and 8	Gemcitabine	1000mg/m ²	IV infusion	250ml NaCl 0.9% over 30mins	Every 21 days
3	1	CARBOplatin	AUC4	IV infusion	500ml glucose 5% over 60 min	Every 21 days

Flush line with NaCl 0.9% pre and post bevacizumab dose as it should not be mixed with glucose solutions.

*The initial dose of bevacizumab should be delivered over 90 minutes as an intravenous infusion. If the first infusion is well tolerated, the second infusion may be administered over 60 minutes. If the 60-minute infusion is well tolerated, all subsequent infusions may be administered over 30 minutes.

It should not be administered as an intravenous push or bolus.

NCCP Regimen: Gemcitabine (1000mg/m ²) CARBOplatin (AUC 4) and Bevacizumab-21 day	Published: 13/08/2018 Review: 30/07/2025	Version number: 5
Tumour Group: Gynaecology NCCP Regimen Code: 00499	ISMO Contributor: Prof Maccon Keane	Page 1 of 9
<p>The information contained in this document is a statement of consensus of NCCP and ISMO or IHS professionals regarding their views of currently accepted approaches to treatment. Any clinician seeking to apply or consult these documents is expected to use independent medical judgement in the context of individual clinical circumstances to determine any patient's care or treatment. Use of these documents is the responsibility of the prescribing clinician and is subject to HSE's terms of use available at http://www.hse.ie/eng/Disclaimer</p> <p><i>This information is valid only on the day of printing, for any updates please check www.hse.ie/NCCPchemoregimens</i></p>		

CARBOplatin dose:

The dose in mg of CARBOplatin to be administered is calculated as follows:

$$\text{Dose (mg)} = \text{target AUC (mg/ml x min)} \times (\text{GFR ml/min} + 25)$$

- **Measured GFR** (e.g. nuclear renogram) is preferred whenever feasible

Estimation of GFR (eGFR) can be done by using the Wright formula or using the Cockcroft and Gault formula to measure creatinine clearance

- The GFR used to calculate the AUC dosing should not exceed 125ml/min.
- For obese and anorexic patients the formulae may not give accurate results and measured GFR is recommended. Where obesity or overweight is likely to lead to an overestimate of GFR and isotope GFR is not available the use of the adjusted ideal body weight for Cockcroft and Gault may be considered (3).

WRIGHT FORMULA

There are two versions of the formula depending on how serum creatinine values are obtained, by the kinetic Jaffe method or the enzymatic method. The formula can be further adapted if covariant creatine kinase (CK) values are available (not shown).

1. *SCr measured using enzymatic assay.*

$$\text{GFR (ml/min)} = \frac{(6230 - 32.8 \times \text{Age}) \times \text{BSA} \times (1 - 0.23 \times \text{Sex})}{\text{SCr (micromol/min)}}$$

2. *SCr measured using Jaffe assay*

$$\text{GFR (ml/min)} = \frac{(6580 - 38.8 \times \text{Age}) \times \text{BSA} \times (1 - 0.168 \times \text{Sex})}{\text{SCr (micromol/min)}}$$

Key: Sex = 1 if female, 0 if male; Age in years; BSA= DuBois BSA

COCKCROFT-GAULT FORMULA

$$\text{GFR (ml/min)} = \frac{S \times (140 - \text{age in years}) \times \text{wt (kg)}}{\text{serum creatinine (micromol/L)}}$$

S = 1.04 for females and 1.23 for males

NCCP Regimen: Gemcitabine (1000mg/m ²) CARBOplatin (AUC 4) and Bevacizumab-21 day	Published: 13/08/2018 Review: 30/07/2025	Version number: 5
Tumour Group: Gynaecology NCCP Regimen Code: 00499	ISMO Contributor: Prof Maccon Keane	Page 2 of 9
<p>The information contained in this document is a statement of consensus of NCCP and ISMO or IHS professionals regarding their views of currently accepted approaches to treatment. Any clinician seeking to apply or consult these documents is expected to use independent medical judgement in the context of individual clinical circumstances to determine any patient's care or treatment. Use of these documents is the responsibility of the prescribing clinician and is subject to HSE's terms of use available at http://www.hse.ie/eng/Disclaimer</p> <p><i>This information is valid only on the day of printing, for any updates please check www.hse.ie/NCCPchemoregimens</i></p>		

ELIGIBILITY:

- Indications as above
- ECOG 0-1

EXCLUSIONS:

- Hypersensitivity to bevacizumab, gemcitabine, CARBOplatin* or any of the excipients
- Hypersensitivity to Chinese Hamster Ovary (CHO) cell products or other recombinant human or humanised antibodies
- Pregnancy or Breast Feeding

*If it is felt that the patient may have a major clinical benefit from CARBOplatin, it may in exceptional circumstances be feasible to rechallenge a patient with a prior mild hypersensitivity reaction e.g. using a desensitisation protocol, but only with immunology advice, premedication as advised, and a desensitisation protocol under carefully controlled conditions with resuscitation facilities available and medical and/or ITU/ HDU supervision (2).

USE WITH CAUTION:

Use bevacizumab with caution in patients with

- Previous pelvic radiotherapy
- Pre-existing uncontrolled hypertension
- Clinically significant cardiovascular disease
- Renal disease including proteinuria
- Bleeding/Clotting disorders
- Previous anthracycline exposure
- History of significant venous thromboembolism
- Recent (less than 6 months) arterial thromboembolic events
- Prior radiation to the chest wall or other serious medical illness

PRESCRIPTIVE AUTHORITY:

The treatment plan must be initiated by a Consultant Medical Oncologist

TESTS:

Baseline tests:

- FBC, renal and liver profile
- Audiometry and creatinine clearance as clinically indicated
- Dipstick urinalysis for protein
- Blood pressure measurement, cardiac assessment including history and physical exam
- ECHO should be considered in patients who have had chest wall radiation or prior treatment with an anthracycline
- INR if clinically indicated*
- Audiometry and creatinine clearance as clinically indicated (CARBOplatin)

Regular tests:

- Day 1: FBC, renal and liver profile, dipstick urinalysis for protein
- Blood pressure prior to each cycle and post treatment.
- Day 8: FBC, renal profile
- INR if clinically indicated*

*(For patients on warfarin, weekly INR until stable warfarin dose established, then INR prior to each cycle.)

NCCP Regimen: Gemcitabine (1000mg/m ²) CARBOplatin (AUC 4) and Bevacizumab-21 day	Published: 13/08/2018 Review: 30/07/2025	Version number: 5
Tumour Group: Gynaecology NCCP Regimen Code: 00499	ISMO Contributor: Prof Maccon Keane	Page 3 of 9
<p>The information contained in this document is a statement of consensus of NCCP and ISMO or IHS professionals regarding their views of currently accepted approaches to treatment. Any clinician seeking to apply or consult these documents is expected to use independent medical judgement in the context of individual clinical circumstances to determine any patient's care or treatment. Use of these documents is the responsibility of the prescribing clinician and is subject to HSE's terms of use available at http://www.hse.ie/eng/Disclaimer</p> <p><i>This information is valid only on the day of printing, for any updates please check www.hse.ie/NCCPchemoregimens</i></p>		

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.
- Bevacizumab dose reduction for adverse events is not recommended (SmPC). If indicated, bevacizumab therapy should either be permanently discontinued or temporarily suspended until toxicity resolves (Table 5 and Table 6).

Haematological:

Prior to commencing a new treatment cycle (i.e **day 1**), ANC must be $> 1.5 \times 10^9/L$ and platelets $> 100 \times 10^9/L$

Dose modifications for **gemcitabine within a cycle (i.e. day 8)**

Table 1: Dose modifications for gemcitabine within a cycle (i.e Day 8)

ANC ($\times 10^9 /L$)		Platelet count ($\times 10^9 /L$)		Other toxicity	Recommended dose of Gemcitabine
>1	and	>100			100%
0.5-1	or	50-100			75%
<0.5	or	<50			Omit*

*Treatment omitted will not be re-instated within a cycle. Treatment will start on day 1 of next cycle once the ANC $\geq 1.5 \times 10^9/L$ and platelets reach $\geq 100 \times 10^9/L$.

Table 2: Dose modifications due to haematological toxicity in subsequent cycles

ANC ($\times 10^9 /L$)		Platelet count ($\times 10^9 /L$)		Other toxicity	Recommended dose of Gemcitabine
ANC < 0.5 for > 5 days or ANC < 0.1 for > 3 days or Any incidence of febrile neutropenia	or	< 25	or	cycle delay of >1 week due to any toxicity	Reduce dose to 75% of the original cycle initiation dose for all subsequent cycles.

NCCP Regimen: Gemcitabine ($1000\text{mg}/\text{m}^2$) CARBOplatin (AUC 4) and Bevacizumab-21 day	Published: 13/08/2018 Review: 30/07/2025	Version number: 5
Tumour Group: Gynaecology NCCP Regimen Code: 00499	ISMO Contributor: Prof Maccon Keane	Page 4 of 9
<p>The information contained in this document is a statement of consensus of NCCP and ISMO or IHS professionals regarding their views of currently accepted approaches to treatment. Any clinician seeking to apply or consult these documents is expected to use independent medical judgement in the context of individual clinical circumstances to determine any patient's care or treatment. Use of these documents is the responsibility of the prescribing clinician and is subject to HSE's terms of use available at http://www.hse.ie/eng/Disclaimer</p> <p><i>This information is valid only on the day of printing, for any updates please check www.hse.ie/NCCPchemoregimens</i></p>		

Renal and Hepatic Impairment:

Table 3: Dose modifications in renal and hepatic impairment

Drug	Renal Impairment	Hepatic Impairment
Bevacizumab	No studies have been performed in patients with renal impairment.	No studies have been performed in patients with hepatic impairment
CARBOplatin	<ul style="list-style-type: none"> Patients with creatinine clearance values of < 60ml/min are at greater risk to develop myelosuppression. In case of GFR ≤ 20ml/min CARBOplatin should not be administered at all. If Cockcroft & Gault or Wright formula are used, the dose should be adjusted per cycle based on a serum creatinine obtained within 48 hrs of drug administration. If isotope GFR is used, the dose should remain the same provided the serum creatinine is ≤110% of its value at the time of the isotope measurement. If the serum creatinine is higher than this, consideration should be given to remeasuring the GFR or to recalculating using Cockcroft & Gault or Wright formulae taking care this does result in a dose reduction 	Probably no dose modification required
Gemcitabine	CrCl (ml/min)	Dose
	>30	100%
	<30	Consider dose reduction, clinical decision.
		AST elevations do not seem to cause dose limiting toxicities. If bilirubin > 27 micromol/L, initiate treatment with dose of 800 mg/m ² .

Management of adverse events:

Table 4: Dose modification schedule of gemcitabine and CARBOplatin for adverse events

Adverse reactions	Recommended dose modification
Grade ≥ 3 Non-haematological toxicity (except nausea/vomiting)	Therapy with gemcitabine and CARBOplatin should be withheld (until toxicity has resolved to grade ≤ 1) and may be resumed with dose reduction at discretion of prescribing consultant.

Proteinuria:

Table 5: Dose modifications of bevacizumab for proteinuria

≥2+ proteinuria (dipstick)	24 hour urine collection for total protein
≥2+ proteinuria (dipstick) and 24 hour proteinuria ≤ 2g	Continue with normal dose.
≥2+ proteinuria (dipstick) and 24 hour proteinuria > 2g	Withhold treatment until proteinuria < 2g at discretion of prescribing consultant. Re-check 24 hour urine protein every 2-4 weeks or as clinically indicated.
Nephrotic syndrome	Discontinue bevacizumab.

NCCP Regimen: Gemcitabine (1000mg/m ²) CARBOplatin (AUC 4) and Bevacizumab-21 day	Published: 13/08/2018 Review: 30/07/2025	Version number: 5
Tumour Group: Gynaecology NCCP Regimen Code: 00499	ISMO Contributor: Prof Maccon Keane	Page 5 of 9
<p>The information contained in this document is a statement of consensus of NCCP and ISMO or IHS professionals regarding their views of currently accepted approaches to treatment. Any clinician seeking to apply or consult these documents is expected to use independent medical judgement in the context of individual clinical circumstances to determine any patient's care or treatment. Use of these documents is the responsibility of the prescribing clinician and is subject to HSE's terms of use available at http://www.hse.ie/eng/Disclaimer <i>This information is valid only on the day of printing, for any updates please check www.hse.ie/NCCPchemoregimens</i></p>		

Table 6: Dose modifications of bevacizumab for adverse events

Adverse reactions	Discontinue	Recommended dose modification
Hypertension Uncontrolled or symptomatic hypertension on Day 1	Discontinue bevacizumab	Withhold bevacizumab treatment, start antihypertensive therapy or adjust pre-existing medication
Grade 4 hypertension or persisting grade 3 hypertension		
Grade 4 Proteinuria	Discontinue bevacizumab	
Tracheoesophageal (TE) fistula or any Grade 4 fistula	Discontinue bevacizumab	
Grade 4 Thromboembolic events	Discontinue bevacizumab	
Haemorrhagic event ≥ Grade 3	Discontinue bevacizumab	
Gastrointestinal Perforation	Discontinue bevacizumab	

SUPPORTIVE CARE:

EMETOGENIC POTENTIAL:

Bevacizumab: Minimal (**Refer to local policy**)
 Gemcitabine: Low (**Refer to local policy**)
 CARBOplatin: High (**Refer to local policy**).

PREMEDICATIONS: None usually required

OTHER SUPPORTIVE CARE: No specific recommendations

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS

The adverse effects listed are not exhaustive. Please refer to the relevant Summary of Product Characteristics for full details.

- **Neutropenia:** Fever or other evidence of infection must be assessed promptly and treated appropriately.

Bevacizumab

- **Gastrointestinal perforations:** Patients may be at an increased risk for the development of gastrointestinal perforation and gall bladder perforation when treated with bevacizumab. Intra-abdominal inflammatory process may be a risk factor for gastrointestinal perforations in patients with metastatic carcinoma of the colon or rectum, therefore, caution should be exercised when treating these patients. Therapy should be permanently discontinued in patients who develop gastrointestinal perforation.
- **Wound healing complications:** Bevacizumab may adversely affect the wound healing process. Therapy should not be initiated for at least 28 days following major surgery or until the surgical wound is fully healed. In patients who experienced wound healing complications during therapy, treatment should be

NCCP Regimen: Gemcitabine (1000mg/m ²) CARBOplatin (AUC 4) and Bevacizumab-21 day	Published: 13/08/2018 Review: 30/07/2025	Version number: 5
Tumour Group: Gynaecology NCCP Regimen Code: 00499	ISMO Contributor: Prof Maccon Keane	Page 6 of 9
<p>The information contained in this document is a statement of consensus of NCCP and ISMO or IHS professionals regarding their views of currently accepted approaches to treatment. Any clinician seeking to apply or consult these documents is expected to use independent medical judgement in the context of individual clinical circumstances to determine any patient's care or treatment. Use of these documents is the responsibility of the prescribing clinician and is subject to HSE's terms of use available at http://www.hse.ie/eng/Disclaimer</p> <p><i>This information is valid only on the day of printing, for any updates please check www.hse.ie/NCCPchemoregimens</i></p>		

withheld until the wound is fully healed. Therapy should be withheld for major elective surgery for 28 days and for 7 days for minor surgery or as directed by the prescribing Consultant. Necrotising fasciitis, including fatal cases, has rarely been reported in patients treated with bevacizumab. This condition is usually secondary to wound healing complications, gastrointestinal perforation or fistula formation. Bevacizumab therapy should be discontinued in patients who develop necrotising fasciitis, and appropriate treatment should be promptly initiated.

- **Hypertension:** An increased incidence of hypertension has been observed in patients treated with bevacizumab. Clinical safety data suggest that the incidence of hypertension is likely to be dose-dependent.
- Pre-existing hypertension should be adequately controlled before starting bevacizumab treatment. Bevacizumab may be continued in conjunction with standard anti-hypertensive therapy at physician's discretion.
 - Patients should have their blood pressure measured before each dose or more frequently if hypertension develops/worsens.
 - Any patient who develops hypertension (>150/100 mmHg) should be treated with anti-hypertensive medications, or have their pre-existing medications adjusted. Patients developing severe hypertension (>200/110 mm Hg) that is not controlled with medication should have bevacizumab discontinued.
 - It should be permanently discontinued if the patient develops hypertensive crisis or hypertensive encephalopathy.
- **Posterior Reversible Encephalopathy Syndrome (PRES):** There have been rare reports of bevacizumab-treated patients developing signs and symptoms that are consistent with PRES, a rare neurologic disorder, which can present with the following signs and symptoms among others: seizures, headache, altered mental status, visual disturbance, or cortical blindness, with or without associated hypertension. A diagnosis of PRES requires confirmation by brain imaging, preferably magnetic resonance imaging (MRI). In patients developing PRES, treatment of specific symptoms including control of hypertension is recommended along with discontinuation of bevacizumab. The safety of reinitiating therapy in patients previously experiencing PRES is not known.
- **Proteinuria:** Patients with a history of hypertension may be at increased risk for the development of proteinuria.
- **Thromboembolism:** Patients receiving bevacizumab plus chemotherapy, with a history of arterial thromboembolism or age > 65 years have an increased risk of developing arterial thromboembolic reactions during therapy. Caution should be taken when treating these patients. Therapy should be permanently discontinued in patients who develop arterial thromboembolic reactions.
- Patients may be at risk of developing venous thromboembolic reactions, including pulmonary embolism under bevacizumab treatment. Bevacizumab should be discontinued in patients with life-threatening (Grade 4) thromboembolic reactions, including pulmonary embolism. Patients with thromboembolic reactions ≤ Grade 3 need to be closely monitored.
- **Haemorrhage:** Patients treated with bevacizumab have an increased risk of haemorrhage, especially tumour associated haemorrhage and minor mucocutaneous haemorrhage. Bevacizumab should be used with caution in patients at risk of bleeding.

Gemcitabine

- **Renal Toxicity:** Irreversible renal failure associated with hemolytic uremic syndrome may occur (rare) with gemcitabine. Use caution with pre-existing renal dysfunction.
- **Pulmonary Toxicity:** Acute shortness of breath may occur with gemcitabine. Discontinue treatment with

NCCP Regimen: Gemcitabine (1000mg/m ²) CARBOplatin (AUC 4) and Bevacizumab-21 day	Published: 13/08/2018 Review: 30/07/2025	Version number: 5
Tumour Group: Gynaecology NCCP Regimen Code: 00499	ISMO Contributor: Prof Maccon Keane	Page 7 of 9
<p>The information contained in this document is a statement of consensus of NCCP and ISMO or IHS professionals regarding their views of currently accepted approaches to treatment. Any clinician seeking to apply or consult these documents is expected to use independent medical judgement in the context of individual clinical circumstances to determine any patient's care or treatment. Use of these documents is the responsibility of the prescribing clinician and is subject to HSE's terms of use available at http://www.hse.ie/eng/Disclaimer</p> <p><i>This information is valid only on the day of printing, for any updates please check www.hse.ie/NCCPchemoregimens</i></p>		

gemcitabine if drug-induced pneumonitis is suspected.

- **Cardiovascular:** Due to the risk of cardiac and/or vascular disorders with gemcitabine, particular caution must be exercised with patients presenting a history of cardiovascular events.

CARBOplatin

- **Hypersensitivity:** Reactions to CARBOplatin may develop in patients who have been previously exposed to platinum therapy. However allergic reactions have been observed upon initial exposure to CARBOplatin.
- **Neurotoxicity and ototoxicity:** Neurological evaluation and an assessment of hearing should be performed on a regular basis, especially in patients receiving high dose CARBOplatin. Neurotoxicity, such as parasthesia, decreased deep tendon reflexes, and ototoxicity are more likely seen in patients previously treated with CISplatin, other platinum treatments and other ototoxic agents. Frequency of neurologic toxicity is also increased in patients older than 65 years.

DRUG INTERACTIONS:

- The safety and efficacy of concomitant administration of radiotherapy and bevacizumab has not been established.
- CARBOplatin may potentiate the nephrotoxic and ototoxic effects of loop diuretics and aminoglycosides so concurrent use should be avoided.
- Current drug interaction databases should be consulted for more information.

REFERENCES:

1. Aghajanian C, Blank, SV et al. OCEANS: A Randomized, Double-Blind, Placebo-Controlled Phase III Trial of Chemotherapy With or Without Bevacizumab in Patients With Platinum-Sensitive Recurrent Epithelial Ovarian, Primary Peritoneal, or Fallopian Tube Cancer. *J Clin Oncol.* 2012;30 (17) 2039-2045.
2. NCCN Guidelines Version3.2017 Epithelial Ovarian Cancer/Fallopian Tube Cancer/Primary Peritoneal Cancer
3. Ekhart C, Rodenhuis S et al. Carboplatin dosing in overweight and obese patients with normal renal function, does weight matter? *Cancer Chemother Pharmacol* 2009; 64:115-122.
4. Appropriate chemotherapy dosing for obese adult patients with cancer: American Society of Clinical Oncology Clinical Practice Guideline. *J Clin Oncol* 2012; 30 (13) 1553-1561.
5. Dosage Adjustment for Cytotoxics in Renal Impairment January 2009; North London Cancer Network.
6. Dosage Adjustment for Cytotoxics in Hepatic Impairment January 2009; North London Cancer Network.
7. Avastin® 25mg/ml Concentrate for solution for infusion Summary of Product Characteristics accessed July 2020. Available at <https://www.medicines.ie/medicines/avastin-25mg-ml-concentrate-for-solution-for-infusion-31375/smpc>
8. Gemcitabine 40 mg/ml Concentrate for Solution for Infusion Summary of Product Characteristics Accessed July 2020. Available at http://www.hpra.ie/img/uploaded/swedocuments/Licence_PA2315-092-004_25062020164320.pdf
9. CARBOplatin Summary of Product Characteristics. Accessed July 2020. Available at http://www.hpra.ie/img/uploaded/swedocuments/Licence_PA2315-080-001_25022019105713.pdf
10. NCCP Classification Document for Systemic Anti-Cancer Therapy (SACT) Induced Nausea and Vomiting.

NCCP Regimen: Gemcitabine (1000mg/m ²) CARBOplatin (AUC 4) and Bevacizumab-21 day	Published: 13/08/2018 Review: 30/07/2025	Version number: 5
Tumour Group: Gynaecology NCCP Regimen Code: 00499	ISMO Contributor: Prof Maccon Keane	Page 8 of 9
<p>The information contained in this document is a statement of consensus of NCCP and ISMO or IHS professionals regarding their views of currently accepted approaches to treatment. Any clinician seeking to apply or consult these documents is expected to use independent medical judgement in the context of individual clinical circumstances to determine any patient's care or treatment. Use of these documents is the responsibility of the prescribing clinician and is subject to HSE's terms of use available at http://www.hse.ie/eng/Disclaimer</p> <p><i>This information is valid only on the day of printing, for any updates please check www.hse.ie/NCCPchemoregimens</i></p>		

V2 2019. 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>

Version	Date	Amendment	Approved By
1	13/08/2018		Prof Maccon Keane
2	22/11/2018	Update of dose modifications of bevacizumab for proteinuria	Prof Maccon Keane
3	12/02/2020	Clarification of dose modifications of bevacizumab for proteinuria	Prof Maccon Keane
4	30/07/2020	Updated emetogenic potential	Prof Maccon Keane
5	23/03/2021	Updated dose modifications of gemcitabine for haematological toxicity.	Prof Maccon Keane

Comments and feedback welcome at oncologydrugs@cancercontrol.ie.

NCCP Regimen: Gemcitabine (1000mg/m ²) CARBOplatin (AUC 4) and Bevacizumab-21 day	Published: 13/08/2018 Review: 30/07/2025	Version number: 5
Tumour Group: Gynaecology NCCP Regimen Code: 00499	ISMO Contributor: Prof Maccon Keane	Page 9 of 9
<p>The information contained in this document is a statement of consensus of NCCP and ISMO or IHS professionals regarding their views of currently accepted approaches to treatment. Any clinician seeking to apply or consult these documents is expected to use independent medical judgement in the context of individual clinical circumstances to determine any patient's care or treatment. Use of these documents is the responsibility of the prescribing clinician and is subject to HSE's terms of use available at http://www.hse.ie/eng/Disclaimer</p> <p><i>This information is valid only on the day of printing, for any updates please check www.hse.ie/NCCPchemoregimens</i></p>		