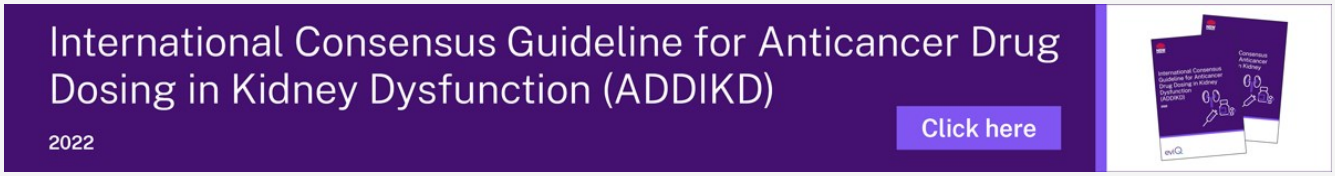
Bladder/Urothelial adjuvant or neoadjuvant ciSplatin and gemcitabine

ID: 4036 v.1 **Endorsed** Essential Medicine List

Some indications in this protocol are based on limited evidence; please refer to the individual evidence sections for more information.

Check for clinical trials in this patient group. Link to Australian Clinical Trials website

The anticancer drug(s) in this protocol may have been included in the ADDIKD guideline. Dose recommendations in kidney dysfunction have yet to be updated to align with the ADDIKD guideline. Recommendations will be updated once the individual protocol has been evaluated by the reference committee. For further information refer to the ADDIKD guideline. To assist with calculations, use the eviQ Estimated Glomerular Filtration Rate (eGFR) calculator.



Related pages:

- Bladder/Urothelial neoadjuvant ddMVAC (dose dense methotrexate vinBLASTine DOXOrubicin ciSplatin)
- Bladder/Urothelial neoadjuvant MVAC (methotrexate vinBLASTine DOXOrubicin ciSplatin) DISCONTINUED
- Bladder/Urothelial adjuvant ddMVAC (dose dense methotrexate vinBLASTine DOXOrubicin ciSplatin)
- Urothelial upper tract adjuvant cARBOplatin and gemcitabine

Treatment schedule - Overview

Cycle 1 to 4

Drug	Dose	Route	Day
Gemcitabine	1,000 mg/m^2	IV infusion	1 and 8
ciSplatin *^	70 mg/m^2	IV infusion	1

*For GFR <50 mL/min, consider substituting cisplatin with carboplatin.[1]

^Urothelial adjuvant indication- for GFR 50-70 mL/min, consider split dose cisplatin 35 mg/m^2 days 1 and 2.[1]

Frequency: 21 days

Cycles: 4

Notes:
Refer to Indications and patient population section for treatment considerations.

Drug status: All drugs in this protocol are on the PBS general schedule

Cost: ~ $260 per cycle

Treatment schedule - Detail

The supportive therapies (e.g. antiemetics, premedications, etc.), infusion times, diluents, volumes and routes of administration, if included, are listed as defaults. They may vary between institutions and can be substituted to reflect individual institutional policy.

*Antiemetics if included in the treatment schedule are based upon recommendations from national and international guidelines. These are **defaults only** and may be substituted to reflect individual institutional policy. Select here for recommended doses of alternative antiemetics.*

Cycle 1 to 4

Day 1		
Netupitant	300 mg (PO)	60 minutes before chemotherapy (fixed dose preparation with palonosetron)
Palonosetron	0.5 mg (PO)	60 minutes before chemotherapy (fixed dose preparation with netupitant)
Dexamethasone	12 mg (PO)	60 minutes before chemotherapy
Gemcitabine	1,000 mg/m^2 (IV infusion)	in 100 mL to 500 mL sodium chloride 0.9% over 30 minutes
ciSplatin	70 mg/m^2 (IV infusion)	in 1000 mL sodium chloride 0.9% over 60 minutes *^
Day 2 to 4		
Dexamethasone	8 mg (PO)	ONCE a day (or in divided doses) with or after food.
Day 8		
Metoclopramide	10 mg (PO)	one tablet when necessary (maximum of 30 mg/24 hours, up to 5 days)
Gemcitabine	1,000 mg/m^2 (IV infusion)	in 100 mL to 500 mL sodium chloride 0.9% over 30 minutes

*For GFR <50 mL/min, consider substituting cisplatin with carboplatin.[1]

^Urothelial adjuvant indication- for GFR 50-70 mL/min, consider split dose cisplatin 35 mg/m^2 days 1 and 2.[1]

Frequency: 21 days

Cycles: 4

Indications and patient population - Bladder/urothelial neoadjuvant

Indications:

- neoadjuvant transitional cell carcinoma (TCC) of the bladder
  - operable muscle invasive bladder cancer stage T2-T4a, eligible for radical cystectomy
  - ECOG performance status 0 to 1.

Cautions/Exclusions:

- pre existing neuropathies greater than or equal to Grade 2
- moderate/severe renal impairment (creatinine clearance less than 60 mL/min.)
- significant hearing impairment/tinnitus.

Notes:

- The evidence supporting bladder/urothelial neoadjuvant treatment used differing schedules and doses of gemcitabine-cisplatin. The 3-week schedule has been shown to have a better compliance profile and similar dose intensity to the 4-week schedule.[2] It is the consensus of the reference committee that a 3-week schedule is more appropriate for this patient population and best reflects clinical practice.
- Neoadjuvant cisplatin and gemcitabine is considered a reasonable alternative to dose dense MVAC based on equivalence to conventional MVAC in the setting of advanced disease.

Indications and patient population - Urothelial adjuvant

Indications:

- adjuvant treatment of predominant urothelial carcinoma histology of upper urinary tract (UTUC) following radical nephro-ureterectomy
  - either muscle invasive (pT2-pT4, Nx) or lymph node positive (pTx, N1-3) metastasis-free (M0) disease
  - ECOG performance status 0 to 1.

Cautions/Exclusions:

- pre existing neuropathies greater than or equal to Grade 2
- moderate/severe renal impairment (creatinine clearance less than 60 mL/min.)
- significant hearing impairment/tinnitus.

Notes:

- The cisplatin infusion duration in this protocol differs from the trial protocol duration of 4 hours.[1]

Clinical information

Venous access required	IV cannula (IVC) or central venous access device (CVAD) is required to administer this treatment. Read more about central venous access device line selection
Emetogenicity HIGH	Suggested default antiemetics have been added to the treatment schedule, and may be substituted to reflect institutional policy. Ensure that patients also have sufficient antiemetics for breakthrough emesis: Metoclopramide 10 mg three times a day when necessary (maximum of 30 mg/24 hours, up to 5 days) OR Prochlorperazine 10 mg PO every 6 hours when necessary. Read more about preventing anti-cancer therapy induced nausea and vomiting
Hydration	Hydration helps to prevent cisplatin-induced nephrotoxicity. The default regimen is appropriate for patients with normal electrolytes, kidney function, fluid status etc. and should be adjusted according to individual requirements. Read more about cisplatin hydration regimens
Peripheral neuropathy	Assess prior to each treatment. If a patient experiences grade 2 or greater peripheral neuropathy, a dose reduction, delay, or omission of treatment may be required; review by medical officer before commencing treatment. Read more about peripheral neuropathy Link to chemotherapy-induced peripheral neuropathy screening tool
Pulmonary toxicity	Dyspnoea developing within hours of the infusion has been reported in about 10% of patients treated with gemcitabine. Read more about pulmonary toxicity associated with anti-cancer drugs.
Ototoxicity	Ototoxicity may occur with platinum-based therapy; patients should be monitored for signs and symptoms. Platinum compounds should be used with caution in patients with pre-existing conditions or risk factors. Ototoxicity may become more severe in patients being treated with other drugs with nephrotoxic potential e.g. aminoglycosides. An audiometry test should be performed if symptoms develop. Read more about ototoxicity - tinnitus and hearing loss

Growth factor support	G-CSF (short or long-acting) is available on the PBS for chemotherapy induced neutropenia depending on clinical indication and/or febrile neutropenia risk. Access the PBS website
Blood tests	FBC, EUC, LFTs, calcium, magnesium and phosphate at baseline and prior to each treatment.
Hepatitis B screening and prophylaxis	Routine screening for HBsAg and anti-HBc is recommended prior to initiation of treatment. Prophylaxis should be determined according to individual institutional policy. Read more about hepatitis B screening and prophylaxis in cancer patients requiring cytotoxic and/or immunosuppressive therapy
Vaccinations	Live vaccines are contraindicated in cancer patients receiving immunosuppressive therapy and/or who have poorly controlled malignant disease. Refer to the recommended schedule of vaccination for immunocompromised patients, as outlined in the Australian Immunisation Handbook. Read more about COVID-19 vaccines and cancer.
Fertility, pregnancy and lactation	Cancer treatment can have harmful effects on fertility and this should be discussed with all patients of reproductive potential prior to commencing treatment. There is a risk of foetal harm in pregnant women. A pregnancy test should be considered prior to initiating treatment in females of reproductive potential if sexually active. It is important that all patients of reproductive potential use effective contraception whilst on therapy and after treatment finishes. Effective contraception methods and adequate contraception timeframe should be discussed with all patients of reproductive potential. Possibility of infant risk should be discussed with breastfeeding patients. Read more about the effect of cancer treatment on fertility

Dose modifications

Evidence for dose modifications is limited, and the recommendations made on eviQ are intended as a guide only. They are generally conservative with an emphasis on safety. Any dose modification should be based on clinical judgement, and the individual patient's situation including but not limited to treatment intent (curative vs palliative), the anti-cancer regimen (single versus combination therapy versus chemotherapy versus immunotherapy), biology of the cancer (site, size, mutations, metastases), other treatment related side effects, additional co-morbidities, performance status and patient preferences.Suggested dose modifications are based on clinical trial findings, product information, published guidelines and reference committee consensus . The dose reduction applies to each individual dose and not to the total number of days or duration of treatment cycle unless stated otherwise. Non-haematological gradings are based on Common Terminology Criteria for Adverse Events (CTCAE) unless otherwise specified. Renal and hepatic dose modifications have been standardised where possible. For more information see dosing considerations & disclaimer .

The dose recommendations in kidney dysfunction (i.e.renal impairment) displayed may not reflect those in the ADDIKD guideline and have been included for historical reference only. Recommendations will be updated once the individual protocol has been evaluated by the reference committee, with this version of the protocol then being archived. Clinicians are expected to refer to the ADDIKD guideline prior to prescribing in kidney dysfunction.
International Consensus Guideline for Anticancer Drug Dosing in Kidney Dysfunction (ADDIKD).

Note: All dose reductions are calculated as a percentage of the starting dose

Haematological toxicity	
ANC x 10^9/L (pre-treatment blood test)	
0.5 to less than 1.0	Delay treatment until recovery
less than 0.5	Delay treatment until recovery and reduce cisplatin and gemcitabine by 25% for subsequent cycles
Febrile neutropenia or previous delay for myelosuppression	Delay treatment until recovery and reduce cisplatin and gemcitabine by 25% for subsequent cycles

Haematological toxicity	
Prolonged recovery greater than two weeks delay or 3rd delay for myelosuppression	Delay treatment until recovery and reduce cisplatin and gemcitabine by 50% or cease
Platelets x 10^9/L (pre-treatment blood test)	
75 to less than 100	Refer to local institutional guidelines; it is the view of the expert clinicians that treatment should continue if patient is clinically well.
50 to less than 75	Delay treatment until recovery
less than 50	Delay treatment until recovery and reduce cisplatin and gemcitabine by 25% for subsequent cycles

If treatment cannot be delivered on Day 8, it should be omitted rather than delayed. Treatment for the next cycle should proceed on the date originally scheduled and should incorporate dose modifications as appropriate.

Renal impairment	
eGFR (CKI-EPI or MDRD) or eCrCl (Cockcroft Gault) (mL/min) *	
greater than or equal to 70	No dose modifications necessary
50 to less than 70	Reduce cisplatin by 25%
30 to less than 50	Reduce gemcitabine by 25% and cisplatin by 50% or consider substituting carboplatin for cisplatin
less than 30	Reduce gemcitabine by 50% and omit cisplatin or consider substituting carboplatin for cisplatin

** Each method has its limitations; refer to Nephrotoxicity associated with cisplatin for more information.*

Hepatic impairment	
Hepatic dysfunction	
Moderate	Reduce gemcitabine by 25%
Severe	No data for gemcitabine

Peripheral neuropathy	
Grade 2 which is present at the start of the next cycle	Reduce cisplatin by 25%; if persistent, reduce cisplatin by 50%
Grade 3 or Grade 4	Omit cisplatin

Mucositis and stomatitis	
Grade 2	Delay treatment until toxicity has resolved to Grade 1 or less and reduce doses for subsequent cycles as follows: 1st occurrence: No dose reduction 2nd occurrence: Reduce cisplatin and gemcitabine by 25% 3rd occurrence: Reduce cisplatin and gemcitabine by 50% 4th occurrence: Omit cisplatin and gemcitabine
Grade 3 or Grade 4	Delay treatment until toxicity has resolved to Grade 1 or less and reduce doses for subsequent cycles as follows: 1st occurrence: Reduce cisplatin and gemcitabine by 50% 2nd occurrence: Omit cisplatin and gemcitabine

Cease gemcitabine if either of the following develop:
Pulmonary toxicity Haemolytic uraemic syndrome (HUS)

Interactions

Drug interactions in eviQ protocols are under review and being updated to align with current literature. Further site-wide updates and changes will occur in due course. References & Disclaimer

The drug interactions shown below are not an exhaustive list. For a more comprehensive list and for detailed information on specific drug interactions and clinical management, please refer to the specific drug product information and the following key resources:

- *MIMS - interactions tab (includes link to a CYP-450 table) (login required)*
- *Australian Medicines Handbook (AMH) – interactions tab (login required)*
- *Micromedex Drug Interactions (login required)*
- *Cancer Drug Interactions*
- *Cytochrome P450 Drug Interactions*

Cisplatin		
	Interaction	**Clinical management**
Nephrotoxic drugs (e.g. aminoglycosides, amphotericin, contrast dye, frusemide, NSAIDs)	Additive nephrotoxicity	Avoid combination or monitor kidney function closely
Ototoxic drugs (e.g. aminoglycosides, frusemide, NSAIDs)	Additive ototoxicity	Avoid combination or perform regular audiometric testing
Neurotoxic drugs (e.g. vincristine, paclitaxel)	Additive neurotoxicity	Monitor closely for neuropathy if combination used
Paclitaxel	Administration schedule may influence the development of myelosuppression	Minimise toxicity by administering paclitaxel first in regimens using the combination
Carbamazepine, phenytoin, valproate	Decreased antiepileptic plasma levels	Monitor antiepileptic serum levels and seizure frequency for efficacy; adjust dosage as appropriate or select alternative antiepileptic (e.g. clonazepam, diazepam, lorazepam)

Gemcitabine		
	Interaction	**Clinical management**
Warfarin	Increased anticoagulant effect/increased bleeding risk due to decreased hepatic metabolism of warfarin and decreased synthesis of clotting factors	Monitor INR regularly and adjust warfarin dosage as appropriate

NK-1 antagonist e.g. aprepitant, fosaprepitant, netupitant		
	Interaction	**Clinical management**
Dexamethasone	Increased effects/toxicity of dexamethasone due to inhibition of its metabolism via CYP3A4	Reduce dose of **antiemetic dexamethasone** by approximately 50% when adding a NK-1 antagonist. For protocols that already recommend a NK-1 antagonist, the dose reduction of **antiemetic dexamethasone** has already been taken into account. If **dexamethasone is part of the chemotherapy protocol**, dose reduction as per the product information is not routinely recommended in clinical practice and no additional dexamethasone is required for antiemetic cover.
Warfarin	Reduced anticoagulant efficacy of warfarin due to increased clearance (aprepitant induces CYP2C9). *Note interaction only applicable to aprepitant/ fosaprepitant	INR should be monitored in the 2 week period, particularly at 7 to 10 days following the administration of aprepitant/ fosaprepitant
Combined oral contraceptive	Reduced contraceptive efficacy due to increased clearance. *Note interaction only applicable to aprepitant/ fosaprepitant	Alternative non-hormonal methods should be used during and for 1 month after stopping aprepitant/ fosaprepitant
CYP3A4 inducers (e.g. carbamazepine, phenytoin, phenobarbitone, rifampicin, St John's wort etc.)	Reduced efficacy of NK-1 antagonist possible due to increased clearance	Avoid combination or monitor for decreased antiemetic effect. Consider using an alternative antiemetic regimen
CYP3A4 inhibitors (e.g. azole antifungals, clarithromycin, erythromycin, grapefruit juice, ritonavir etc.)	Increased toxicity of NK-1 antagonist possible due to reduced clearance	Avoid combination or monitor for increased adverse effects of NK-1 antagonist (e.g. headache, hiccups, constipation)
Drugs metabolised by CYP3A4 (e.g. etoposide, imatinib, irinotecan, midazolam, paclitaxel, vinblastine, vincristine etc.)	Increased effects/toxicity of these drugs possible due to inhibition of CYP3A4 by NK-1 antagonist	Avoid combination or monitor for increased toxicity especially with orally administered drugs

General		
	Interaction	**Clinical management**
Warfarin	Anti-cancer drugs may alter the anticoagulant effect of warfarin.	Monitor INR regularly and adjust warfarin dosage as appropriate; consider alternative anticoagulant.
Direct oral anticoagulants (DOACs) e.g. apixaban, rivaroxaban, dabigatran	Interaction with both CYP3A4 and P-gp inhibitors /inducers. DOAC and anti-cancer drug levels may both be altered, possibly leading to loss of efficacy or toxicity (i.e. increased bleeding).	Apixaban: avoid concurrent use with strong CYP3A4 and P-gp inhibitors. If treating VTE, avoid use with strong CYP3A4 and P-gp inducers. Rivaroxaban: avoid concurrent use with strong CYP3A4 and P-gp inhibitors. Dabigatran: avoid combination with strong P-gp inducers and inhibitors. If concurrent use is unavoidable, monitor closely for efficacy/toxicity of both drugs.
Digoxin	Anti-cancer drugs can damage the lining of the intestine; affecting the absorption of digoxin.	Monitor digoxin serum levels; adjust digoxin dosage as appropriate.
Antiepileptics	Both altered antiepileptic and anti-cancer drug levels may occur, possibly leading to loss of efficacy or toxicity.	Where concurrent use of an enzyme-inducing antiepileptic cannot be avoided, monitor antiepileptic serum levels for toxicity, as well as seizure frequency for efficacy; adjust dosage as appropriate. Also monitor closely for efficacy of the anti-cancer therapy.
Antiplatelet agents and NSAIDs	Increased risk of bleeding due to treatment related thrombocytopenia.	Avoid or minimise combination. If combination deemed essential, (e.g. low dose aspirin for ischaemic heart disease) monitor for signs of bleeding.
Serotonergic drugs, including selective serotonin reuptake inhibitors (SSRIs e.g. paroxetine) and serotonin noradrenaline reuptake inhibitors (SNRIs e.g. venlafaxine)	Increased risk of serotonin syndrome with concurrent use of 5-HT3 receptor antagonists (e.g. palonosetron, ondansetron, granisetron, tropisetron, dolasetron, etc.)	Avoid combination. If combination is clinically warranted, monitor for signs and symptoms of serotonin syndrome (e.g. confusion, agitation, tachycardia, hyperreflexia). For more information link to TGA Medicines Safety Update
Vaccines	Diminished response to vaccines and increased risk of infection with live vaccines.	Live vaccines (e.g. BCG, MMR, zoster and varicella) are contraindicated in patients on immunosuppressive therapy. Use with caution in patients on non-immunosuppressive therapy. For more information; refer to the recommended schedule of vaccination for cancer patients, as outlined in the Australian Immunisation Handbook

Administration

eviQ provides safe and effective instructions on how to administer cancer treatments. However, eviQ does not provide every treatment delivery option, and is unable to provide a comprehensive list of cancer treatment agents and their required IV line giving set/filter. There may be alternative methods of treatment administration, and alternative supportive treatments that are also appropriate. Please refer to the individual

product information monographs via the TGA website for further information.

Day 1

Approximate treatment time: 5 hours

Safe handling and waste management

Safe administration

General patient assessment prior to each day of treatment.

Peripheral neuropathy assessment tool

Any toxicity grade 2 or greater may require dose reduction, delay or omission of treatment and review by medical officer before commencing treatment.

Prime IV line(s).

Insert IV cannula or access TIVAD or CVAD.

Pre treatment medication

Verify antiemetics taken or administer as prescribed.

Verify dexamethasone taken or administer as prescribed.

Chemotherapy - Time out

Gemcitabine

Administer gemcitabine (irritant):

- via IV infusion over 30 minutes
  - if pain develops along the vein, verify the drug has not extravasated
  - further dilution (using a second saline line), warmth or temporarily slowing the infusion may help
- flush with ~ 100 mL of sodium chloride 0.9%
- prolonged infusion times have been shown to increase toxicity.

Cisplatin

Commence prehydration for cisplatin:

- administer 10 mmol magnesium sulphate ($MgSO_4$) in 1000 mL sodium chloride 0.9% over 60 minutes
- followed by 200 mL of mannitol 20% over 15 minutes
  - mannitol should be administered via a controlled infusion
- mannitol 10% may be used as per institutional policy; there is much variation in the use of mannitol and although there is no conclusive evidence that mannitol should be used, many sites have used it routinely without renal toxicity. The routine use of frusemide to increase urine flow is not recommended. Refer to your institutional guidelines and medical orders.
- ensure patient has passed urine prior to cisplatin administration as per institutional policy.

Administer cisplatin (irritant):

- via IV infusion over 60 minutes
- flush with 100 mL of sodium chloride 0.9%.

Post hydration:

- 1000 mL sodium chloride 0.9% over 60 minutes.

Remove IV cannula and/or deaccess TIVAD or CVAD.

Continue safe handling precautions until 7 days after completion of drug(s)

Day 8

Approximate treatment time: 60 minutes

Safe handling and waste management

Safe administration

General patient assessment prior to each day of treatment.

Any toxicity grade 2 or greater may require dose reduction, delay or omission of treatment and review by medical officer before commencing treatment.

Prime IV line(s).

Insert IV cannula or access TIVAD or CVAD.

Pre treatment medication

Verify antiemetics taken or administer as prescribed.

Chemotherapy - Time out

Gemcitabine

Administer gemcitabine (irritant):

- via IV infusion over 30 minutes
  - if pain develops along the vein, verify the drug has not extravasated
  - further dilution (using a second saline line), warmth or temporarily slowing the infusion may help
- flush with ~ 100 mL of sodium chloride 0.9%
- prolonged infusion times have been shown to increase toxicity.

Remove IV cannula and/or deaccess TIVAD or CVAD.

Continue safe handling precautions until 7 days after completion of drug(s)

Discharge information

Antiemetics

- Antiemetics as prescribed.

Patient information

- Ensure patient receives patient information sheet.

Side effects

The side effects listed below are not a complete list of all possible side effects for this treatment. Side effects are categorised into the approximate onset of presentation and should only be used as a guide.

Immediate (onset hours to days)	
Nausea and vomiting	Read more about prevention of treatment induced nausea and vomiting
Taste and smell alteration	Read more about taste and smell changes
Flu-like symptoms	

Early (onset days to weeks)	
Neutropenia	Abnormally low levels of neutrophils in the blood. This increases the risk of infection. Any fever or suspicion of infection should be investigated immediately and managed aggressively. Read more about immediate management of neutropenic fever
Thrombocytopenia	A reduction in the normal levels of functional platelets, increasing the risk of abnormal bleeding. Read more about thrombocytopenia
Fatigue	Read more about fatigue
Diarrhoea	Read more about treatment induced diarrhoea
Oral mucositis	Erythematous and ulcerative lesions of the gastrointestinal tract (GIT). It commonly develops following chemotherapy, radiation therapy to the head, neck or oesophagus, and high dose chemotherapy followed by a blood and marrow transplant (BMT). Read more about oral mucositis
Skin rash	Anti-cancer drugs can cause a number of changes in the skin with maculo-papular rash the most common type of drug-induced skin reaction. Read more about skin rash
Fluid retention and oedema	An excess amount of fluid around the cells, tissues or serous cavities of the body, leading to swelling.
Peripheral neuropathy	Typically symmetrical sensory neuropathy, affecting the fingers and toes, sometimes progressing to the hands and feet. It is associated with several classes of anti-cancer drugs. These include taxanes, platinum-based compounds, vinca alkaloids and some drugs used to treat multiple myeloma. Read more about peripheral neuropathy
Hypomagnesaemia, hypokalaemia, hypocalcaemia	Abnormally low levels of magnesium, potassium and calcium in the blood.
Nephrotoxicity	Renal dysfunction resulting from damage to the glomeruli, tubules or renal vasculature.
Ototoxicity	Tinnitus and hearing loss may occur due to damage in the inner ear. Tinnitus is usually reversible, while hearing loss is generally irreversible. Hearing loss is dose-related, cumulative and may be worse in those with pre-existing hearing problems. Read more about ototoxicity - tinnitus and hearing loss

Late (onset weeks to months)	
Anaemia	Abnormally low levels of red blood cells (RBCs) or haemoglobin in the blood. Read more about anaemia
Alopecia - partial	Hair thinning and/or patchy hair loss. Patients can also experience mild to moderate discomfort of the hair follicles, and rarely pain as the hair is falling out. Read more about alopecia and scalp cooling
Pulmonary toxicity	Pulmonary toxicity may include damage to the lungs, airways, pleura and pulmonary circulation. Read more about pulmonary toxicity associated with anti-cancer drugs
Haemolytic uraemic syndrome (HUS)	A rare but serious acute syndrome characterised by haemolysis of red blood cells and renal failure. Read more about haemolytic uraemic syndrome (HUS)

Evidence - Bladder/urothelial neoadjuvant

The timing of chemotherapy when given as an adjunct to surgery has continued to provoke much debate over several years with proponents for neoadjuvant chemotherapy justifying their position on the basis of clinical trials such as SWOG 8710[3] and ABC meta analysis collaboration;[4, 5] whilst proponents for adjuvant chemotherapy criticise these trials (for slow and low accrual,

lack of use of cisplatin/gemcitabine regimens), and also have a meta-analysis in support and prefer to offer adjuvant chemotherapy to high-risk patients such as T3 and T4 and/or node positive tumours. A search of the literature did not find strong evidence to support the use of neoadjuvant gemcitabine and cisplatin (GC) in the treatment of muscle invasive bladder cancer. The expert reference panel supported publication of the protocol on the basis of the information summarised below.

A meta-analysis of neoadjuvant chemotherapy in the form of platinum-based combination treatment found that there was an absolute survival advantage of approximately 5% at 5 years in muscle invasive bladder cancer (HR 0.86, 95% CI 0.77-0.95, p=0.003). However, none of the trials reviewed used gemcitabine and cisplatin and the most common regimen was methotrexate, vinblastine, doxorubicin and cisplatin (MVAC).[6] GC has similar response rates, disease free survival (DFS) and overall survival (OS) in the metastatic setting when compared to MVAC with less grade 3/4 toxicity, especially non-haematological toxicities.[7] Therefore GC is being used in the neoadjuvant setting as it has been extrapolated that it is likely to be as efficacious as MVAC. There is stronger evidence for neoadjuvant MVAC however, this regimen may be preferred due to its better toxicity profile without the need for growth factor support. There are no phase III randomised controlled trials looking at GC in the neoadjuvant setting in muscle invasive bladder cancer. Most of these are retrospective cohort studies, which show that pathological down-staging to pT0 was seen in 25.6% of patients and to less than pT2 in 46.5%.[8] Pathological down-staging has been considered a surrogate marker for DFS and OS. As seen with neoadjuvant MVAC for muscle-invasive bladder cancer, of the patients who achieved pT0 at cystectomy the 5-year survival rate was 85%.[3]

Source	Study & Year Published	Supports Use	Is the dose and regimen consistent with the protocol?	Comments
Phase II trials	Herchenhorn et al 2007[9]	**Yes**	No	Cisplatin 75 mg/m^2 d1 and gemcitabine 1200 mg/m^2 d1,8 q21 days
Observational studies	Pal et al 2012[10]	**Yes**	Not specified	-
	Yeschina et al 2012[11]	**Yes**	Not specified	-
	Scosyrev et al 2012[12]	**Yes**	No	Uses split dose cisplatin (i.e. cisplatin 35 mg/m^2 d1,8 and gemcitabine 1000 mg/m^2 d1,8) q21 days
	Kaneko et al 2011[13]	**Yes**	No	Cisplatin 75 mg/m^2 d1 and gemcitabine 1200 mg/m^2 d1,8,15 q28 days
	Weight et al 2009[14]	**No**	No	Various regimens
	Dash et al 2008[15]	**Yes**	No	Uses split dose cisplatin (i.e. cisplatin 35 mg/m^2 d1,8 and gemcitabine 1000 mg/m^2 d1,8) q21 days
Guidelines	**Date published/revised**	**Supports Use**	**Is the dose and regimen consistent with the protocol?**	**Comments**
NCCN	-	**N/A**	-	-
BCCA	November 2012	**Yes**	No	Cisplatin 70 mg/m^2 d1 and gemcitabine 1250 mg/m^2 d1,8 q21 days
CCO	-	**Yes**	No	Cisplatin 70 mg/m^2 d1 and gemcitabine 1250 mg/m^2 d1,8 q21 days

Efficacy

A summary of the evidence supporting the effect of this protocol is below.

	Study	No. of patients	Control arm	Effect
Median overall survival	Pal et al[10]	24	MVAC n=22 Other regimen n=15	104.3 months
Median progression-free survival	Herchenhorn et al[9]	21	-	27 months
Overall response rate	Pal et al[10]	24	MVAC n=22 Other regimen n=15	25%
Down-staging to non-muscle invasive disease (<pT2)	Scosyrev et al[12]	25	135 no neoadjuvant chemotherapy	44%

Toxicity

A summary of the toxicities associated with this protocol are included in the table below. Only two studies reported on toxicities.

Grade 3/4 toxicity	Study	Incidence of event (%)
Neutropenia	Herchernhorn et al[9] (n=21)	33.33
Thrombocytopenia	Kaneko et al[13] (n=22)	21.4*
Febrile neutropenia	Kaneko et al[13] (n=22)	2.4*
Anaemia	Kaneko et al[13] (n=22)	2.4*
Nausea	Herchernhorn et al[9] (n=21)	28.6
Mucositis	Kaneko et al[13] (n=22)	0*
Rash	Herchernhorn et al[9] (n=21)	4.8

** Denominator represents number of cycles for Kaneko et al[13]*

Evidence - Urothelial adjuvant

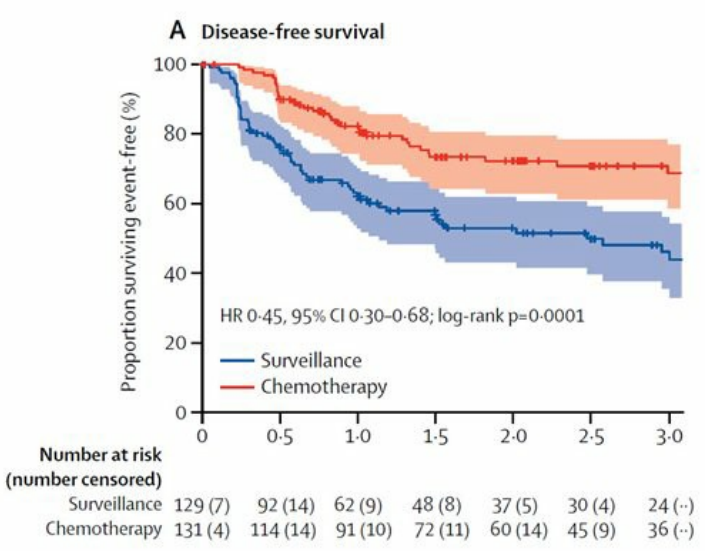
The evidence supporting this protocol is provided by POUT, a phase III multicentre open-label randomised trial.[1] Between June 2012 and November 2017, 261 patients with either muscle invasive or lymph node positive metastasis-free upper tract urothelial carcinoma (UTUC), following radical nephro-ureterectomy, were randomised to receive four cycles of adjuvant chemotherapy every 21 days (n=132) or surveillance (n=129). Chemotherapy involved cisplatin 70 mg/m^2 (or carboplatin AUC 4.5-5 if GFR 30-49 mL/min) on day 1 and gemcitabine 1000 mg/m^2 on day 1 and 8, commenced within 90 days following surgery. Of the group randomised to chemotherapy, 76 patients were planned to receive gemcitabine-cisplatin and 50 planned to receive gemcitabine-carboplatin. The majority of patients (91%) were nodal stage N0.

The primary endpoint was disease-free survival (DFS). Secondary endpoints included metastasis-free survival, overall survival (OS), treatment compliance, acute and late toxicity, and patient-reported quality of life.

Efficacy

After a median follow up of 30.3 months, the median DFS was 29.8 months in the surveillance group and was not reached in the chemotherapy group (HR=0.45; 95% CI 0.30-0.68; log-rank p=0.0001). There was no apparent heterogeneity of treatment effect and results were consistent across prespecified subgroups.[1]

Kaplan-Meier curve of disease-free survival[1]



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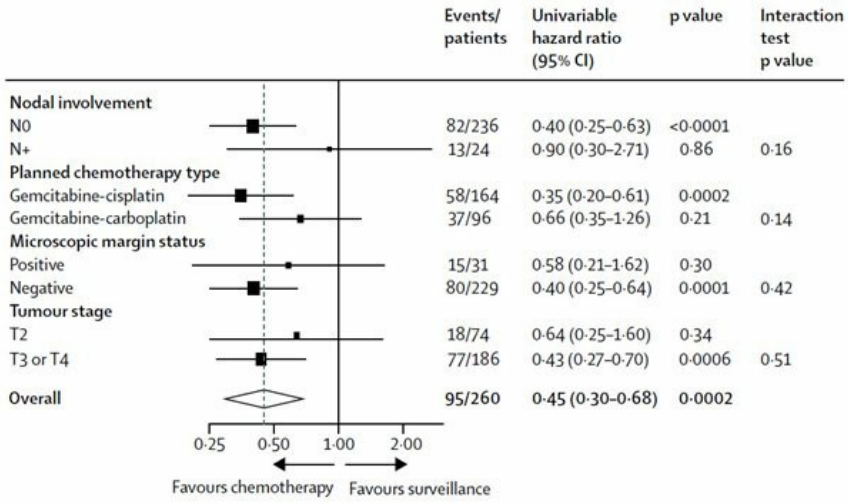
Subgroup analysis of disease-free survival[1]



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The risk of metastasis or death was lower in the chemotherapy group versus the surveillance group (HR=0.48; 95% CI 0.31-0.74; p=0.0007). 3-year event-free rates were 71% and 53% respectively, with an estimated absolute difference of 17% (95% CI 4-31). Data for OS is not yet mature.

Quality of life data showed the chemotherapy group had a lower mean overall global health status score during chemotherapy and immediately afterwards compared with the surveillance group, however this difference had resolved by 6 months.[1]

Toxicity

Consistent with known experience, grade ≥3 acute treatment-related adverse events were more common in the group that received chemotherapy (44%) compared with surveillance (4%). This included a higher incidence of febrile neutropenia, thrombocytopenia, nausea and vomiting. Early discontinuation of chemotherapy occurred in 31 patients due to clinician's decision (n=11), toxicity (n=10), patient's choice (n=8), or other unspecified reason (n=2). 16 (21%) of 76 participants intended for cisplatin switched to carboplatin due to a post-randomisation drop in GFR. There were no treatment related deaths.[1]

Adverse events[1]

Grade 3/4 adverse event	Surveillance		Cisplatin/gemcitabine		Carboplatin/gemcitabine	
	n	%	n	%	n	%
Nausea (n=253)	0	0	3	4	5	9
Vomiting (n=253)	0	0	2	3	5	9
Diarrhoea (n=255)	0	0	0	0	3	5

Grade 3/4 adverse event	Surveillance		Cisplatin/gemcitabine		Carboplatin/gemcitabine	
Neutropenia (n=251)	0	0	22	31	23	42
Febrile neutropenia (n=253)	0	0	4	6	4	7
Thrombocytopenia (n=252)	0	0	6	8	7	13
Anaemia (n=255)	0	0	3	4	3	5
ALT increased (n=249)	0	0	0	0	1	2
Tinnitus (n=252)	1	1	0	0	0	0
Alopecia (n=255)	0	0	0	0	1	2
Rash, eruptions and exanthenum (n=255)	0	0	1	1	1	2
Pulmonary thrombotic and embolic conditions (n=255)	0	0	4	6	2	4

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History

Version 1

Date	Summary of changes
22/10/2021	New protocol taken to Medical Oncology Reference Committee meeting.
11/11/2021	Protocol approved and published on eviQ. Next review in 1 year.
30/09/2022	Protocol reviewed electronically by Medical Oncology Reference Committee. No changes. Next review in 2 years.

As ID 4036 Bladder/Urothelial neoadjuvant/adjuvant replaces an existing approved protocol, the individual history section is included below for consistency in documentation.

ID 1437 Bladder/Urothelial neoadjuvant ciSplatin and gemcitabine version 4	
Date	**Summary of changes**
30/11/2012	New protocol taken to Medical Oncology Reference Committee meeting.
09/05/2014	Protocol discussed at Medical Oncology Reference Committee.
21/07/2014	Approved and published on eviQ. Review category 1.
23/03/2015	Reviewed electronically by Medical Oncology Reference Committee. No change. Review 2 years.
31/03/2017	Protocol discussed and decided to have a 5 year review period. Next due for review in 2020.
31/05/2017	Transferred to new eviQ website. Version number changed to V.2. Antiemetic change: Netupitant/palonosetron combination has replaced aprepitant and a $5HT_3$ receptor antagonist in combination with dexamethasone for all highly emetogenic regimens.
10/05/2018	Haematological dose modifications updated as per consensus of the expert clinician group. Version number changed to V.3.
08/10/2019	Clinical information updated with PBS expanded indications for GCSF.
30/06/2020	Protocol reviewed electronically by Medical Oncology Reference Committee. No changes. Review 5 years.

First approved: 11 November 2021
Last reviewed: 30 September 2022
Review due: 31 December 2024

The currency of this information is guaranteed only up until the date of printing, for any updates please check:
https://www.eviq.org.au/p/4036
19 Jun 2023

Patient information - Bladder/urinary tract cancer adjuvant or neoadjuvant - Cisplatin and gemcitabine

Patient's name:

Your treatment

This treatment may be used to treat different types and stages of cancer. Your doctor will advise you why you are receiving this treatment.

The treatment schedule below explains how the drugs for this treatment are given.

Cisplatin and gemcitabine			
This treatment cycle is repeated every 21 days. You will have 4 cycles.			
Day	**Treatment**	**How it is given**	**How long it takes**
1	**Gemcitabine** (*jem-sie-ta-been*) **Cisplatin** *(siss-PLAT-in)*	By a drip into a vein	About 5 hours
8	**Gemcitabine**	By a drip into a vein	About 1 hour

When to get help

Anticancer drugs (drugs used to treat cancer) can sometimes cause serious problems. It is important to get medical help immediately if you become unwell.

IMMEDIATELY go to your nearest hospital Emergency Department, or contact your doctor or nurse if you have any of the following at any time:	**Emergency contact details** Ask your doctor or nurse from your treating team who to contact if you have a problem
• a temperature of 38°C or higher • chills, sweats, shivers or shakes • shortness of breath • uncontrolled vomiting or diarrhoea • pain, tingling or discomfort in your chest or arms • you become unwell.	Daytime: Night/weekend: Other instructions:

During your treatment immediately tell the doctor or nurse looking after you if you get any of the following problems:

- leaking from the area where the drugs are being given
- pain, stinging, swelling or redness in the area where the drugs are being given or at any injection sites
- a skin rash, itching, feeling short of breath, wheezing, fever, shivers, or feeling dizzy or unwell in any way (allergic reaction).

Other information about your treatment

Changes to your dose or treatment delays

Sometimes a treatment may be started at a lower dose or the dose needs to be changed during treatment. There may also be times when your treatment is delayed. This can happen if your doctor thinks you are likely to have severe side effects, if you get severe side effects, if your blood counts are affected and causing delays in treatment, or if you are finding it hard to cope with the treatment. This is called a dose reduction, dose change or treatment delay. Your doctor will explain if you need any changes or delays to your treatment and the reason why.

Blood tests and monitoring

Anti-cancer drugs can reduce the number of blood cells in your body. You will need to have regular blood tests to check that your blood cell count has returned to normal. If your blood count is low, your treatment may be delayed until it has returned to normal. Your doctor or nurse will tell you when to have these blood tests.

Other medications given during this treatment

- **Anti-sickness (anti-nausea) medication:** you may be given some anti-sickness medication. Make sure you take this medication as your doctor or nurse tells you, even if you don't feel sick. This can help to prevent the sickness starting.

Side effects

Cancer treatments can cause damage to normal cells in your body, which can cause side effects. Everyone gets different side effects, and some people will have more problems than others.

The table below shows some of the side effects you may get with this treatment. You are unlikely to get all of those listed and you may also get some side effects that have not been listed.

Tell your doctor or nurse about any side effects that worry you. Follow the instructions below and those given to you by your doctor or nurse.

Immediate (onset hours to days)	
Nausea and vomiting	• You may feel sick (nausea) or be sick (vomit). • Take your anti-sickness medication as directed even if you don't feel sick. • Drink plenty of fluids (unless you are fluid restricted). • Eat small meals more frequently. • Try food that does not require much preparation. • Try bland foods like dry biscuits or toast. • Gentle exercise may help with nausea. • Ask your doctor or nurse for eviQ patient information - Nausea and vomiting during cancer treatment. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you have uncontrolled vomiting or feel dizzy or light-headed.**
Taste and smell changes	• You may find that food loses its taste or tastes different. • These changes are likely to go away with time. • Do your mouth care regularly. • Chew on sugar-free gum or eat sugar-free mints. • Add flavour to your food with sauces and herbs. • Ask your doctor or nurse for eviQ patient information - Taste and smell changes during cancer treatment.
Flu-like symptoms	• You may get: ◦ a fever ◦ chills or sweats ◦ muscle and joint pain ◦ a cough ◦ headaches. • The drug gemcitabine can cause a fever or flu-like illness within the first day or two of having the treatment. • You can take paracetamol to help settle these symptoms. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if the symptoms do not settle or you become unwell.**

Early (onset days to weeks)	
Infection risk (neutropenia)	• This treatment lowers the amount of white blood cells in your body. The type of white blood cells that help to fight infection are called neutrophils. Having low level of neutrophils is called neutropenia. If you have neutropenia, you are at greater risk of getting an infection. It also means that your body can't fight infections as well as usual. This is a serious side effect, and can be life threatening. • Wash your hands often. • Keep a thermometer at home and take your temperature regularly, and if you feel unwell. • Do your mouth care regularly. • Inspect your central line site (if you have one) daily for any redness, pus or swelling. • Limit contact with people who are sick. • Learn how to recognise the signs of infection. • Ask your doctor or nurse for eviQ patient information - Infection during cancer treatment. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you get any of the following signs or symptoms:** ◦ **a temperature of 38°C or higher** ◦ **chills, shivers, sweats or shakes** ◦ **a sore throat or cough** ◦ **uncontrolled diarrhoea** ◦ **shortness of breath** ◦ **a fast heartbeat** ◦ **become unwell even without a temperature.**

Low platelets (thrombocytopenia)	• This treatment lowers the amount of platelets in your blood. Platelets help your blood to clot. When they are low, you are at an increased risk of bleeding and bruising. • Try not to bruise or cut yourself. • Avoid contact sport or vigorous exercise. • Clear your nose by blowing gently. • Avoid constipation. • Brush your teeth with a soft toothbrush. • Don't take aspirin, ibuprofen or other similar anti-inflammatory medications unless your doctor tells you to. • Tell your doctor or nurse if you have any bruising or bleeding. • **Tell your doctor or nurse immediately, or go to your nearest hospital Emergency Department if you have any uncontrolled bleeding.**
Tiredness and lack of energy (fatigue)	• You may feel very tired, have no energy, sleep a lot, and not be able to do normal activities or things you enjoy. • Do not drive or operate machinery if you are feeling tired. • Nap for short periods (only 1 hour at a time) • Prioritise your tasks to ensure the best use of your energy. • Eat a well balanced diet and drink plenty of fluids (unless you are fluid restricted). • Try some gentle exercise daily. • Allow your friends and family to help. • **Tell your doctor or nurse if you get any of the symptoms listed above.**
Diarrhoea	• You may get bowel motions (stools, poo) that are more frequent or more liquid. • You may also get bloating, cramping or pain. • Take your antidiarrhoeal medication as directed by your doctor. • Drink plenty of fluids (unless you are fluid restricted). • Eat and drink small amounts more often. • Avoid spicy foods, dairy products, high fibre foods, and coffee. • Ask your doctor or nurse for eviQ patient information - Diarrhoea during cancer treatment. • **Tell your doctor or nurse immediately, or go to your nearest hospital Emergency Department if your diarrhoea is not controlled, you have 4 or more loose bowel motions per day, and if you feel dizzy or light-headed.**
Mouth pain and soreness (mucositis)	• You may have: ◦ bleeding gums ◦ mouth ulcers ◦ a white coating on your tongue ◦ pain in the mouth or throat ◦ difficulty eating or swallowing. • Avoid spicy, acidic or crunchy foods and very hot or cold food and drinks. • Try bland and soft foods. • Brush your teeth gently with a soft toothbrush after each meal and at bedtime. If you normally floss continue to do so. • Rinse your mouth after you eat and brush your teeth, using either: ◦ 1/4 teaspoon of salt in 1 cup of warm water, or ◦ 1/4 teaspoon of bicarbonate of soda in 1 cup of warm water • Ask your doctor or nurse for eviQ patient information - Mouth problems during cancer treatment. • **Tell your doctor or nurse if you get any of the symptoms listed above.**
Skin rash	• You may get a red, bumpy rash and dry, itchy skin. • Moisturise your skin with a gentle non-perfumed moisturising cream like sorbolene or aqueous cream. • Do not scratch your skin. • Protect your skin from the sun by wearing sun-protective clothing, a wide-brimmed hat, sunglasses and sunscreen of SPF 50 or higher. • **Talk to your doctor or nurse about other ways to manage your skin rash.**

Extra fluid in the body (fluid retention)	• You may gain weight over a short amount of time. • Your hands and feet may become swollen, appear red or feel hot and uncomfortable. • Wear loose clothing and shoes that are not too tight. • Try not to stand up or walk around too much at one time. • If your ankles or legs get swollen, try raising them. • Make sure that any cuts or areas of broken skin are treated as soon as possible. • **Tell your doctor or nurse as soon as possible if you get any of the symptoms listed above or gain 1 to 2 kg in a week.** • **Tell your doctor or nurse immediately or go to the nearest hospital Emergency Department if you become short of breath.**

Nerve damage (peripheral neuropathy)	• You may notice a change in the sensations in your hands and feet, including:
	  ◦ tingling or pins and needles
	  ◦ numbness or loss of feeling
	  ◦ pain.
	• You may find it difficult to do everyday activities, such as doing up buttons or picking up small objects.
	• Test water temperature with your elbow when bathing to avoid burns.
	• Use rubber gloves, pot holders and oven mitts in the kitchen.
	• Wear rubber shoes or boots when working in the garden or garage.
	• Keep rooms well lit and uncluttered.
	• Ask your doctor or nurse for eviQ patient information – Nerve problems during cancer treatment.
	• Tell your doctor or nurse if you get any of the symptoms listed above.

Low blood magnesium, potassium and calcium levels (hypomagnesaemia, hypokalaemia, hypocalcaemia)	• This may be found from your routine blood tests and treated by your doctor.
	• If it is severe you may get:
	  ◦ muscle cramps or twitches
	  ◦ numbness or tingling in your fingers, toes or around your mouth
	  ◦ constipation
	  ◦ an irregular heartbeat
	  ◦ sleepy, drowsy or confused
	• **Tell your doctor or nurse as soon as possible if you get any of the signs or symptoms listed above.**

Kidney damage	• This treatment can cause changes to how your kidneys work. • You will have blood tests to make sure your kidneys are working properly. • You may need to drink more fluids while you are having treatment. Your doctor or nurse will tell you if you need to do this. • **Tell your doctor or nurse as soon as possible if you notice that your urine changes colour or you don't need to empty your bladder as often.**
Hearing changes (ototoxicity)	• You may get ringing in your ears or loss of hearing. • You may have your hearing tested before and during your treatment. • **Tell your doctor or nurse as soon as possible if you notice any changes to your hearing.**

Late (onset weeks to months)	
Low red blood cells (anaemia)	• You may feel dizzy, light-headed, tired and appear more pale than usual. • Tell your doctor or nurse if you have any of these signs or symptoms. You might need a blood transfusion. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you have any chest pain, trouble breathing, or feel like your heart is racing.**
Hair thinning	• Your hair may become dry and may break easily. • You may lose some of your hair. • Use a gentle shampoo and a soft hairbrush. • Take care with hair products like hairspray, hair dye, bleaches and perms. • Protect your scalp from the cold with a hat or scarf. • Protect your scalp from the sun with a hat and sunscreen of SPF 50 or higher. • Ask your doctor or nurse about the Look Good Feel Better program (www.lgfb.org.au)
Lung problems	• Lung problems are rare, but can be serious. They may occur throughout treatment or after the completion of treatment. • You may get: ◦ shortness of breath ◦ fever ◦ dry cough ◦ wheezing ◦ fast heartbeat ◦ chest pain. • Your doctor will monitor how well your lungs are working during your treatment. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you have chest pain or become short of breath.**
Red blood cell and kidney damage (haemolytic uraemic syndrome)	• This side effect is rare, but can be very serious. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if it has been longer than 12 hours since you have emptied your bladder or if you have any of the following signs or symptoms:** ◦ **black, tarry bowel motions (stools, poo)** ◦ **blood in your urine or are not urinating as often** ◦ **pinpoint red spots on your skin** ◦ **major bruising** ◦ **a fever** ◦ **shortness of breath** ◦ **a severe headache** ◦ **confusion.**

General advice for people having cancer treatment

Chemotherapy safety

- Learn how to keep you and your family safe while you are having anticancer drugs.
- See our patient information sheet - Chemotherapy safety at home.

Blood clot risk

- Cancer and anticancer drugs can increase the risk of a blood clot (thrombosis).
- Tell your doctor if you have a family history of blood clots.
- A blood clot can cause pain, redness, swelling in your arms or legs, shortness of breath or chest pain.
- If you have any of these symptoms go to your nearest hospital Emergency Department.

Medications and vaccinations

- Before you start treatment, tell your doctor about any medications you are taking, including vitamins or herbal supplements.

- Don't stop or start any medications during treatment without talking to your doctor and pharmacist first.
- Paracetamol is safe to take if you have a headache or other mild aches and pains. It is recommended that you avoid taking aspirin, ibuprofen and other anti-inflammatory type medications for pain while you are having treatment. However, if these medications have been prescribed by your doctor, do not stop taking them without speaking with your doctor.
- Vaccinations such as flu and tetanus vaccines are safe to receive while having treatment. Do not have any live vaccines during your treatment or for 6 months after it finishes. If you are unsure, check with your doctor before you have any vaccinations.
- People you live with should be fully vaccinated, including having live vaccines according to the current vaccination schedule. Extra care needs to be taken with hand washing and careful disposal of soiled nappies for infants who have recently received the rotavirus vaccine.

Other medical and dental treatment

- If you go to hospital or any other medical appointment (including dental appointments), always tell the person treating you that you are receiving anticancer drugs.
- Before you have any dental treatment, talk to your doctor.

Diet

- While you are receiving this treatment it is important that you try to maintain a healthy diet.
- Speak to your doctor or nurse about whether drinking alcohol is safe with your treatment.
- If you have any concerns about recent weight loss or weight gain or questions about your diet, ask to speak to a dietitian.

Fertility

- Some cancer treatments can reduce your fertility. This can make it difficult or impossible to get pregnant or father a child.
- Talk to your doctor or nurse before you start any treatment. Depending on your situation there may be fertility sparing options available to you and/or your partner, discuss these with your doctor or nurse.

Pregnancy and breastfeeding

- Some cancer treatments can be dangerous to unborn babies. Talk to your doctor or nurse if you think there is any chance that you could be pregnant.
- Do not try to get pregnant or father a child during this treatment. Contraception should be used during treatment and after stopping treatment. Ask your doctor or nurse about what type of contraception you should use.
- If you are planning pregnancy/fatherhood after completing this treatment, talk to your doctor. Some doctors advise waiting between 6 months and 2 years after treatment.
- Do not breastfeed if you are on this treatment, as anti-cancer medications can also pass into breast milk.

Sex life and sexuality

- The desire to have sex may decrease as a result of this treatment or its side effects.
- Your emotions and the way you feel about yourself may also be affected by this treatment.
- It may help to discuss your concerns with your partner and doctor or nurse.

Risk of developing a second cancer

- Some anticancer treatments can increase your chance of developing a second cancer, this is rare. Your doctor will discuss with you the specific risks of your treatment.

Quitting smoking

- It is never too late to quit smoking. Quitting smoking is one of the best things you can do to help your treatment work better.
- There are many effective tools to improve your chances of quitting.
- Talk to your treating team for more information and referral to a smoking cessation support service.

Staying active

- Research shows that exercise, no matter how small, has many benefits for people during and after cancer treatment.
- Talk to your doctor before starting an exercise program. Your doctor can advise whether you need a modified exercise program.

For more information about cancer treatment, side effects and side effect management see our Patient and carers section.

Where to get more information

Telephone support

- Call Cancer Council on 13 11 20 for cancer information and support

Bladder and urinary tract cancer information

- Australian Government Bladder and Bowel – bladderbowel.gov.au
- Australian Government Department of Health & Ageing Stoma appliance scheme – health.gov.au/internet/main/publishing.nsf/Content/Stoma+Appliance+Scheme-1
- BEAT Bladder Cancer Australia Inc. – beatbladdercanceraustralia.org.au/
- Continence Foundation of Australia – continence.org.au
- National Continence Program – health.gov.au/initiatives-and-programs/national-continence-program-ncp
- National Public Toilet map – toiletmap.gov.au
- Recovering after Pelvic Radiation Therapy: A guide for women – Recovering after Pelvic Radiation Therapy: A guide for women

General cancer information and support

- Australian Rare Cancer (ARC) Portal – arcportal.org.au/
- Beyondblue – beyondblue.org.au
- Cancer Australia – canceraustralia.gov.au
- Cancer Council Australia – cancer.org.au
- Cancer Voices Australia – cancervoicesaustralia.org
- CanTeen – canteen.org.au
- Carers Australia – carersaustralia.com.au
- CHILL Cancer related hair loss - scalpcooling.org
- eviQ Cancer Treatments Online – eviq.org.au
- LGBTQI+ People and Cancer - cancercouncil.com.au/cancer-information/lgbtqi
- Look Good Feel Better – lgfb.org.au
- Patient Information – patients.cancer.nsw.gov.au
- Radiation Oncology Targeting Cancer – targetingcancer.com.au
- Redkite – redkite.org.au
- Return Unwanted Medicines – returnmed.com.au
- Staying active during cancer treatment – patients.cancer.nsw.gov.au/coping-with-cancer/physical-wellbeing/staying-active

Quit smoking information and support

Quitting smoking is helpful even after you have been diagnosed with cancer. The following resources provide useful information and support to help you quit smoking. Talk to your treating team about any other questions you may have.

- Call Quitline on 13 QUIT (13 78 48)
- iCanQuit – iCanQuit.com.au
- Patient Information – patients.cancer.nsw.gov.au/coping-with-cancer/physical-wellbeing/quitting-smoking
- Quitnow – quitnow.gov.au

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