

Bladder/Urothelial neoadjuvant ddMVAC (dose dense methotrexate vinBLASTine DOXOrubicin ciSplatin)

ID: 1616 v.8 Endorsed Essential Medicine List

This protocol is based on limited evidence; refer to the evidence section of this protocol 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](#).

International Consensus Guideline for Anticancer Drug Dosing in Kidney Dysfunction (ADDIKD)

2022

[Click here](#)



Related pages:

- [Bladder/Urothelial neoadjuvant MVAC \(methotrexate vinBLASTine DOXOrubicin ciSplatin\) DISCONTINUED](#)
- [Bladder/Urothelial adjuvant or neoadjuvant ciSplatin and gemcitabine](#)
- [Bladder/Urothelial metastatic MVAC \(methotrexate vinBLASTine DOXOrubicin ciSplatin\)](#)

Treatment schedule - Overview

Cycle 1 to 3

Drug	Dose	Route	Day
Methotrexate	30 mg/m ²	IV bolus	1
DOXOrubicin	30 mg/m ²	IV	2
vinBLASTine	3 mg/m ²	IV	2
ciSplatin	70 mg/m ²	IV infusion	2
Pegfilgrastim *	6 mg	Subcut	4

*if filgrastim 5 micrograms/kg/day is used, administer ONCE daily (at least 24 hours post chemotherapy) on days 3 to 10

An alternative schedule is to give 3 cycles with all chemotherapy drugs administered on day 1¹

Frequency: 14 days

Cycles: 3 to 6 pre cystectomy

Drug status: All drugs (except G-CSF) in this protocol are on the [PBS schedule](#) **Pegfilgrastim** is [PBS authority](#)

Cost: ~ \$190 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 3

Day 1		
Methotrexate	30 mg/m ² (IV bolus)	over 3 to 5 minutes
Day 2		
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
DOXOrubicin	30 mg/m ² (IV)	over 5 to 15 minutes
vinBLASTine	3 mg/m ² (IV)	in 50 mL sodium chloride 0.9% over 5 to 10 minutes
ciSplatIn	70 mg/m ² (IV infusion)	in 1000 mL sodium chloride 0.9% over 60 minutes
Day 3		
Dexamethasone	8 mg (PO)	ONCE a day (or in divided doses) with or after food.
Day 4		
Dexamethasone	8 mg (PO)	ONCE a day (or in divided doses) with or after food.
Pegfilgrastim	6 mg (Subcut)	inject subcutaneously on day 4*
Day 5		
Dexamethasone	8 mg (PO)	ONCE a day (or in divided doses) with or after food.

*if filgrastim 5 micrograms/kg/day is used, administer ONCE daily (at least 24 hours post chemotherapy) on days 3 to 10

An alternative schedule is to give 3 cycles with all chemotherapy drugs administered on day 1¹

Frequency: 14 days

Cycles: 3 to 6 pre cystectomy

Indications and patient population

Indications:

- neoadjuvant transitional cell carcinoma (TCC) of the bladder
 - operable muscle invasive bladder cancer stage T2-T4a, eligible for radical cystectomy

Cautions / Exclusions:

- ECOG performance status 2 or greater
- pre existing neuropathies [Grade 2](#) or greater
- moderate/severe renal impairment (creatinine clearance less than 60 mL/min.).
- significant hearing impairment/tinnitus.
- left ventricular ejection fraction less than 50%.

Clinical information

Venous access required	<p>IV cannula (IVC) or central venous access device (CVAD) is required to administer this treatment.</p> <p>Read more about central venous access device line selection</p>
Emetogenicity HIGH	<p>Suggested default antiemetics have been added to the treatment schedule, and may be substituted to reflect institutional policy.</p> <p>Ensure that patients also have sufficient antiemetics for breakthrough emesis:</p> <p>Metoclopramide 10 mg three times a day when necessary (maximum of 30 mg/24 hours, up to 5 days) OR</p> <p>Prochlorperazine 10 mg PO every 6 hours when necessary.</p> <p>Read more about preventing anti-cancer therapy induced nausea and vomiting</p>
Cumulative lifetime dose of anthracyclines	<p>Cumulative doses should take into account all previous anthracyclines received during a patient's lifetime (i.e. daunorubicin, doxorubicin, epirubicin, idarubicin and mitoxantrone).</p> <p>Criteria for reducing the total anthracycline cumulative lifetime dose include:</p> <ul style="list-style-type: none"> • patient is elderly • prior mediastinal radiation • hypertensive cardiomegaly • concurrent therapy with high dose cyclophosphamide and some other cytotoxic drugs (e.g. bleomycin, dacarbazine, dactinomycin, etoposide, melphalan, mitomycin and vincristine). <p>Baseline clinical assessments include echocardiogram (ECHO) or gated heart pool scan (GHPS) and electrocardiogram (ECG) evaluation.</p> <p>Patients with normal baseline cardiac function (left ventricular ejection fraction (LVEF) > 50%) and low risk patients require LVEF monitoring when greater than 70% of the anthracycline threshold is reached or if the patient displays symptoms of cardiac impairment. Post-treatment cardiac monitoring is recommended for patients who have received high levels of total cumulative doses of anthracyclines at the clinician's discretion.</p> <p>Read more about cardiac toxicity associated with anthracyclines</p>
Hydration	<p>Hydration helps to prevent cisplatin-induced nephrotoxicity.</p> <p>The default regimen is appropriate for patients with normal electrolytes, kidney function, fluid status etc. and should be adjusted according to individual requirements.</p> <p>Read more about cisplatin hydration regimens</p>
Constipation	<p>Prescribe prophylactic laxatives to prevent constipation related to the use of vinca alkaloids.</p>
Pleural effusion or ascites	<p>Methotrexate should be used with caution in patients with pleural effusions or ascites, as methotrexate may accumulate in third space fluid compartments.</p>
Ototoxicity	<p>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.</p> <p>Ototoxicity may become more severe in patients being treated with other drugs with nephrotoxic potential e.g. aminoglycosides.</p> <p>An audiometry test should be performed if symptoms develop.</p> <p>Read more about ototoxicity - tinnitus and hearing loss</p>
Peripheral neuropathy	<p>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.</p> <p>Read more about peripheral neuropathy</p> <p>Link to chemotherapy-induced peripheral neuropathy screening tool</p>
Biosimilar drug	<p>Read more about biosimilar drugs on the Biosimilar Awareness Initiative page</p>
Growth factor support	<p>G-CSF (short or long-acting) is available on the PBS for chemotherapy induced neutropenia depending on clinical indication and/or febrile neutropenia risk.</p> <p>Access the PBS website</p>
Blood tests	<p>FBC, EUC, LFTs, calcium and magnesium at baseline and prior to each cycle.</p>

Hepatitis B screening and prophylaxis	<p>Routine screening for HBsAg and anti-HBc is recommended prior to initiation of treatment. Prophylaxis should be determined according to individual institutional policy.</p> <p>Read more about hepatitis B screening and prophylaxis in cancer patients requiring cytotoxic and/or immunosuppressive therapy</p>
Vaccinations	<p>Live vaccines are contraindicated in cancer patients receiving immunosuppressive therapy and/or who have poorly controlled malignant disease.</p> <p>Refer to the recommended schedule of vaccination for immunocompromised patients, as outlined in the Australian Immunisation Handbook.</p> <p>Read more about COVID-19 vaccines and cancer.</p>
Fertility, pregnancy and lactation	<p>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.</p> <p>Read more about the effect of cancer treatment on fertility</p>

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 methotrexate, vinblastine, doxorubicin and cisplatin by 25% for subsequent cycles
Febrile neutropenia	Delay treatment until recovery and reduce methotrexate, vinblastine, doxorubicin and cisplatin by 25% for subsequent cycles
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

Haematological toxicity	
less than 50	Delay treatment until recovery and reduce methotrexate, vinblastine, doxorubicin and cisplatin by 25% for subsequent cycles

Renal impairment	
eGFR (CKI-EPI or MDRD) or eCrCl (Cockcroft Gault) (mL/min) *	
greater than or equal to 55	No dose modifications necessary ²
50 to less than 55	Reduce cisplatin by 25%
30 to less than 50	Reduce methotrexate and cisplatin by 50%, consider proceeding directly to definitive management with radiation therapy or surgery
less than 30	Omit methotrexate and cisplatin and consider proceeding directly to definitive management with radiation therapy or surgery

* Each method has its limitations; refer to [Nephrotoxicity associated with cisplatin](#) for more information.

Hepatic impairment	
Hepatic dysfunction	
Mild	Reduce vinblastine and doxorubicin by 25%
Moderate	Reduce vinblastine and doxorubicin by 50%
Severe	Omit vinblastine and doxorubicin

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

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

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)

Doxorubicin		
	Interaction	Clinical management
Cardiotoxic drugs (eg. bevacizumab, calcium channel blockers, propranolol, trastuzumab)	Increased risk of doxorubicin-induced cardiotoxicity	Avoid combination or monitor closely for cardiotoxicity
Cyclophosphamide	Sensitises the heart to the cardiotoxic effects of doxorubicin; also, doxorubicin may exacerbate cyclophosphamide induced cystitis	Monitor closely for cardiotoxicity and ensure adequate prophylaxis for haemorrhagic cystitis when combination is used
Glucosamine	Reduced efficacy of doxorubicin (due to induction of glucose-regulated stress proteins resulting in decreased expression of topoisomerase II <i>in vitro</i>)	The clinical effect of glucosamine taken orally is unknown. Avoid combination or monitor for decreased clinical response to doxorubicin
CYP2D6 inhibitors (e.g. SSRIs (esp. paroxetine), perhexiline, cinacalcet, doxepin, flecainide, quinine, terbinafine)	Increased toxicity of doxorubicin possible due to reduced clearance	Monitor for doxorubicin toxicity
CYP3A4 inhibitors (e.g. aprepitant, azole antifungals, clarithromycin, erythromycin, grapefruit juice, ritonavir etc.)	Increased toxicity of doxorubicin possible due to reduced clearance	Monitor for doxorubicin toxicity
CYP3A4 inducers (e.g. carbamazepine, phenytoin, phenobarbitone, rifampicin, St John's wort etc.)	Reduced efficacy of doxorubicin possible due to increased clearance	Monitor for decreased clinical response to doxorubicin

Methotrexate		
	Interaction	Clinical management
Ciprofloxacin NSAIDs Probenecid Proton pump inhibitors (e.g. esomeprazole, omeprazole, pantoprazole)	Increased toxicity of methotrexate possible due to reduced clearance	Avoid combination or monitor for methotrexate toxicity Important note: with high-dose methotrexate therapy, many of these drug combinations are <i>contraindicated</i>
Sulphonamides and penicillins (e.g. sulfamethoxazole (in Bactrim[®], Septrin[®]), piperacillin (in Tazocin[®]) etc.)	Increased toxicity of methotrexate possible due to displacement from serum protein binding	Avoid combination or monitor for methotrexate toxicity
Trimethoprim	Increased toxicity of methotrexate possible due to additive antifolate activity	Avoid combination or monitor for methotrexate toxicity
Mercaptopurine	Increased toxicity of mercaptopurine possible due to reduced clearance	Avoid combination or monitor for mercaptopurine toxicity
Nephrotoxic drugs (e.g. aminoglycosides, amphotericin, contrast dye, frusemide, NSAIDs)	Additive nephrotoxicity	Avoid combination or monitor kidney function closely
Hepatotoxic drugs (e.g. azathioprine, leflunomide, retinoids, sulfasalazine)	Additive hepatotoxicity	Avoid combination or monitor liver function closely
Folic acid (e.g. as in multivitamins) Asparaginase (administered immediately prior or concurrently)	Reduced efficacy of methotrexate possible due to antagonism of its action	Avoid combination or monitor for decreased clinical response to methotrexate Note: asparaginase administered shortly after methotrexate can enhance its efficacy and reduce its toxicity

Vinblastine		
	Interaction	Clinical management
CYP3A4 and P-gp inhibitors (e.g. amiodarone, aprepitant, azole-antifungals, ritonavir, lapatinib, nilotinib, sorafenib, macrolides, ciclosporin, grapefruit juice etc.)	Increased toxicity of vinblastine possible due to reduced clearance	Monitor for vinblastine toxicity (esp. neurotoxicity, adynamic ileus)
CYP3A4 inducers (e.g. carbamazepine, phenytoin, phenobarbitone, rifampicin, St John's wort etc.)	Reduced efficacy of vinblastine possible due to increased clearance	Monitor for decreased clinical response to vinblastine
Drugs undergoing P-gp-mediated elimination (e.g. dabigatran, loperamide, phenytoin etc.)	Reduced efficacy of these drugs possible due to induction of P-gp by vinblastine resulting in increased clearance	Avoid combination or monitor for decreased clinical response to interacting drugs
Mitomycin	Increased risk of pulmonary toxicity when vinblastine administered following or concomitantly with mitomycin	Avoid combination or monitor closely for pulmonary toxicity (i.e. interstitial infiltrates, pleural effusion resulting in respiratory distress and cough)
Ototoxic drugs (e.g. cisplatin, aminoglycosides, frusemide, NSAIDs)	Additive ototoxicity (as reported with other vinca alkaloids)	Avoid combination or perform regular audiometric testing

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	<p>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.</p> <p>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.</p>
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	<p>Interaction with both CYP3A4 and P-gp inhibitors /inducers.</p> <p>DOAC and anti-cancer drug levels may both be altered, possibly leading to loss of efficacy or toxicity (i.e. increased bleeding).</p>	<p>Apixaban: avoid concurrent use with strong CYP3A4 and P-gp inhibitors. If treating VTE, avoid use with strong CYP3A4 and P-gp inducers.</p> <p>Rivaroxaban: avoid concurrent use with strong CYP3A4 and P-gp inhibitors.</p> <p>Dabigatran: avoid combination with strong P-gp inducers and inhibitors.</p> <p>If concurrent use is unavoidable, monitor closely for efficacy/toxicity of both drugs.</p>
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-HT ₃ receptor antagonists (e.g. palonosetron, ondansetron, granisetron, tropisetron, dolasetron, etc.)	<p>Avoid combination.</p> <p>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</p>
Vaccines	Diminished response to vaccines and increased risk of infection with live vaccines.	<p>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.</p> <p>For more information; refer to the recommended schedule of vaccination for cancer patients, as outlined in the Australian Immunisation Handbook</p>

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

Day 1

Approximate treatment time: 30 minutes

[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.

Chemotherapy - Time out

Methotrexate

- over 3 to 5 minutes
 - by IV bolus via a side port of a freely flowing IV infusion **OR**
- over 5 to 15 minutes
 - via a minibag
- flush with ~50 mL of sodium chloride 0.9%

Remove IV cannula and/or deaccess [TIVAD](#) or [CVAD](#).

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

Day 2

Approximate treatment time: 4 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

Doxorubicin

Administer doxorubicin (vesicant):

- over 5 to 15 minutes
 - via a minibag **OR**
 - by IV bolus via a side port of a freely flowing IV infusion
- ensure vein is patent and monitor for signs of extravasation throughout administration
- flush with ~150 mL of sodium chloride 0.9%
- potential for flare reaction during administration of doxorubicin (facial flushing and red streaking along the vein) stop infusion and exclude extravasation before continuing at a slower rate of infusion.

Although rare, cardiac arrhythmias may occur during or immediately after doxorubicin administration. If sudden onset of dyspnoea, palpitations or irregular pulse occurs, stop administration immediately and obtain urgent medical officer review.

Vinblastine

Administer vinblastine (vesicant):

- via a minibag over 5 to 10 minutes
- ensure vein is patent and monitor for signs of extravasation throughout administration
- flush with ~150 mL of sodium chloride 0.9%.

Cisplatin

Commence prehydration for cisplatin:

- administer 10 mmol magnesium sulphate (MgSO₄) 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)

Discharge information

Antiemetics

- Antiemetics as prescribed.

Growth factor support

- Arrangements for administration if prescribed.

Laxatives

- Ensure patient has prophylactic laxatives.

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
Extravasation, tissue or vein injury	The unintentional instillation or leakage of a drug or substance out of a blood vessel into surrounding tissue. This has the potential to cause damage to affected tissue. Read more about extravasation management
Bone pain	Bone pain, usually in the lower back or pelvis, associated with G-CSF.
Taste and smell alteration	Read more about taste and smell changes
Flare reaction	Anthracycline flare reaction is caused by a localised allergic reaction. It is characterised by erythematous vein streaking, urticaria and pruritus which may occur during drug administration and is often associated with too rapid an infusion. Extravasation must be ruled out if flare occurs.
Red-orange discolouration of urine	Pink/red/orange discolouration of the urine. This can last for up to 48 hours after some anthracycline drugs.
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
Constipation	
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
Fatigue	Read more about fatigue
Oesophagitis	Inflammation of the mucosal lining of the oesophagus. It can progress to ulceration, haemorrhage, secondary infection and pain.
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
Photosensitivity	Increased sensitivity to ultraviolet (UV) light resulting in an exaggerated sunburn-like reaction accompanied by stinging sensations and urticaria.
Radiation recall	Erythematous or inflammatory skin reaction resembling severe sunburn at sites previously treated with radiation therapy can occur with certain anti-cancer drugs. Symptoms include vesiculation, desquamation and ulceration of the skin. Read more about radiation recall
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	Hair loss may occur from all parts of the body. 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
Nail changes	Hyperpigmentation, paronychia, onycholysis, splinter haemorrhage, pyogenic granuloma formation, subungal haematoma and subungal hyperkeratosis are some of the nail changes associated with anti-cancer drugs. Read more about nail toxicities
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

Delayed (onset months to years)	
Cardiotoxicity	Anthracyclines are the most frequently implicated anti-cancer drugs associated with cardiotoxicity, which typically manifests as a reduction in left ventricular ejection fraction (LVEF), cardiomyopathy, or symptomatic CHF. Anthracycline induced cardiotoxicity has been categorised into acute, early-onset chronic progressive and late-onset chronic progressive and is usually not reversible. The risk of clinical cardiotoxicity increases with a number of risk factors including higher total cumulative doses. Read more about cardiac toxicity associated with anthracyclines

Evidence

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 8710³ and meta-analysis results as published by the ABC meta analysis collaboration,⁴ whilst proponents for adjuvant chemotherapy criticise these trials for slow accrual, low patient numbers and lack of use of cisplatin/gemcitabine regimens. Proponents for adjuvant chemotherapy may prefer to offer adjuvant chemotherapy to high-risk patients such as T3 and T4 and/or node positive tumours. Meta-analyses have also demonstrated survival advantage when adjuvant chemotherapy is used.

A search of the literature did not find strong evidence to support the use of ddMVAC (dose dense methotrexate/vinblastine/adriamycin/cisplatin) for the neoadjuvant treatment of muscle invasive bladder cancer. The expert reference panel supported publication of the protocol on the basis of the information summarised below. The committee was most strongly influenced by the results from the meta-analysis demonstrating an improvement in overall survival for classical MVAC and other platinum-based neoadjuvant chemotherapy in comparison to definitive treatment alone.⁴

A similar protocol ("classical" MVAC, 4 week cycles) has been used extensively for the treatment of advanced bladder cancer and may also be utilised in the neoadjuvant setting.³ ddMVAC is used in preference to classical MVAC due to its better side effect profile and trend to improved efficacy in advanced disease.^{5, 6}

Source	Study & Year Published	Supports Use	Is the dose and regimen consistent with the protocol?	Comments
Phase III trials	Pfister et al 2022 ⁷	Yes	Yes	6 cycles ddMVAC
	Grossman et al 2003 ³	Yes	No	3 cycles classical MVAC regimen
Phase II trials	Plimack et al 2012 ¹	Yes	Yes	3 cycles ddMVAC (dose regimen from Sternberg et al ⁵)
	Choueiri et al 2014 ⁸	Yes	Yes	4 cycles ddMVAC (dose regimen from Sternberg et al ⁵)

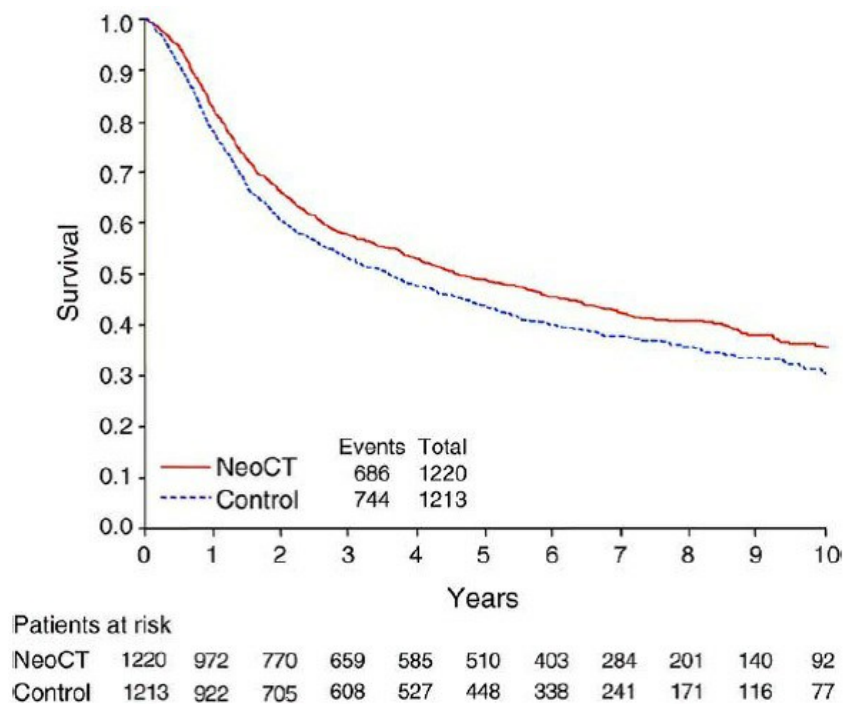
Source	Study & Year Published	Supports Use	Is the dose and regimen consistent with the protocol?	Comments
Observational studies	Blick et al 2012 ²	Yes	Yes	3-4 cycles ddMVAC (dose regimen from Sternberg et al ⁵)
Case series	-	-	-	-
Meta-analyses	ABC Meta-analysis Collaboration 2005 ⁴	Yes	N/A	Improved overall survival with use of neoadjuvant chemotherapy
	Tjokrowidjaja et al 2013 ⁹	Yes	N/A	Improved overall survival with use of neoadjuvant chemotherapy
Guidelines	Date published/revised	Supports Use	Is the dose and regimen consistent with the protocol?	Comments
NCCN	v.1 2014	Yes	Yes	3-4 cycles ddMVAC (dose regimen from Sternberg et al ⁵)
BCCA	April 2008	Yes	-	Recommend neoadjuvant chemotherapy (no regimen specified) for T2b-T4 not T2a
CCO	Feb 2013	Yes	Yes	-

Efficacy

Initial studies of neoadjuvant classical MVAC showed a 23% absolute complete response improvement over cystectomy alone, however whilst there was a trend towards improved overall survival, this was not significant.³ A subsequent 2005 meta-analysis of platinum-based neoadjuvant chemotherapy did demonstrate a statistically significant improvement in overall survival (see Kaplan-Meier curves below).⁴ There has been further confirmation of this in a 2013 meta-analysis of chemotherapy in muscle invasive bladder cancer, which revealed an improvement in overall and disease free survival for both neoadjuvant and adjuvant treatment in separate analyses.⁹ There has been no head-to-head trial of neoadjuvant and adjuvant chemotherapy.

Cisplatin-gemcitabine and ddMVAC regimens have been compared to classical MVAC in head-to-head trials in the advanced bladder cancer setting. Cisplatin-gemcitabine¹⁰ and ddMVAC^{5, 6} were associated with no detriment in efficacy but much improved side effect profile. Similar trials in the neoadjuvant setting are lacking. The advantages that ddMVAC provide over classical MVAC include improved tolerability of the regimen and shorter duration of treatment, allowing quicker progression to cystectomy.

Kaplan-Meier curves for overall survival⁴

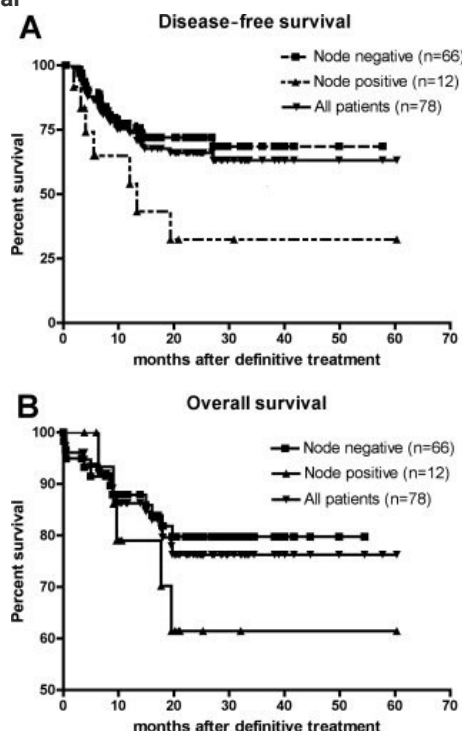


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Blick et al retrospectively reviewed the records of 80 consecutive patients receiving a planned 3 or 4 cycles of ddMVAC neoadjuvantly for muscle invasive bladder cancer. Those eligible had T2-T4a disease, any nodal status, and no distant metastases. 75% of patients had cystectomy as definitive management; the remaining 25% underwent radical radiation therapy treatment.²

Complete (T0) pathological response was seen in 43% of those who underwent cystectomy. 2 year overall survival was 77% and 2 year disease free survival was 65%. Those who were node positive did considerably poorer than those who were node negative.

(A) Disease-free survival (B) Overall survival²



Plimack et al conducted a phase 2 trial comparing the effects of ddMVAC with classical MVAC in the neoadjuvant setting utilising historical controls. 44 patients with T2-T4 (and either N0 or N1, but M0) bladder cancer with ECOG 0 or 1 were planned for 3 cycles of neoadjuvant ddMVAC which was completed 3 to 8 weeks prior to cystectomy. The primary outcome was pathological response, with secondary outcomes including safety parameters, side effect profile and survival.¹

Complete (T0) pathological response was seen in 35% of evaluable patients (those who underwent cystectomy) compared to 38% seen in the Grossman et al trial using classical MVAC. Median follow up was too short to have meaningful survival results. The side effect profile was much more favourable; in particular 11% had a grade 3/4 neutropaenia compared with 54% in the standard MVAC

Toxicity

A summary of the toxicities associated with this protocol are included in the table below. The most clinically significant toxicities for this treatment are neutropenia and neuropathy.

Toxicity ²	Grade 1/2 (%)	Grade 3/4 (%)
Neutropenia	11	11
Neuropathy	9	0
Infection	6	0
Nausea/vomiting	59	6
Diarrhoea	9	3
Stomatitis	47	6
Fatigue	65	6
Dyspnoea	3	0
Reflux symptoms	3	0
Constipation	3	0

There have also been reports of grade 3 or 4 anaemia, thrombocytopenia, lymphopenia, hyponatraemia, hypokalemia and mucositis with this regimen. Toxicity data was only available for 34 of the 80 enrolled patients in the largest neoadjuvant accelerated MVAC study; however this data was consistent with toxicity data published in larger trials using this regimen in the advanced bladder setting.

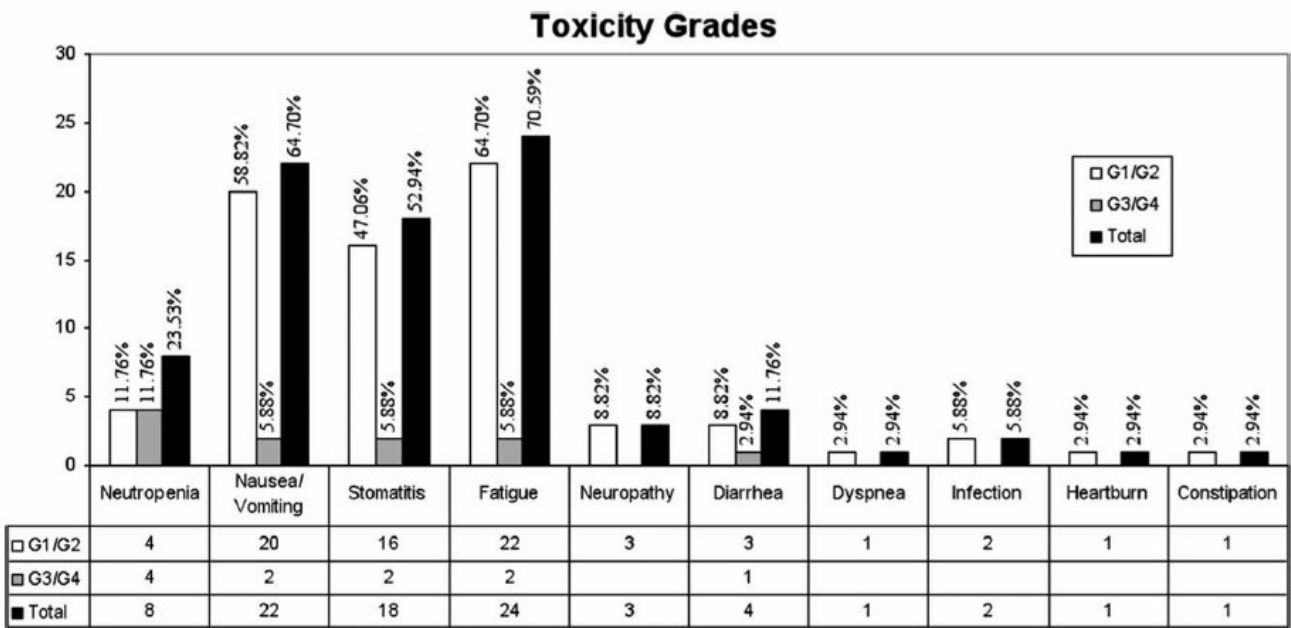


Figure 2. Toxicity of accelerated methotrexate, vinblastine, doxorubicin, and cisplatin neoadjuvant chemotherapy. Full toxicity data are available from 34 of 80 patients. Data are tabulated as numbers of patients experiencing grades 1 or 2 (G1/G2) and grades 3 or 4 (G3/G4) toxicity, in one or more cycles. Percentages of the 34 patients experiencing G1/G2 or G3/G4 toxicity are shown above the histograms.

© Cancer 2012

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History

Version 8

Date	Summary of changes
21/10/2022	Treatment schedule cycle changed to '3 to 6 pre cystectomy'. Patient information updated to include 'You will have 3 to 6 cycles'. Evidence updated to include Pfister et al 2022. Version number changed to V.8.

Version 7

Date	Summary of changes
04/09/2020	Biosimilar drug added to clinical information. Version number changed to V.7.
11/11/2021	ID 4036 Bladder/Urothelial adjuvant or neoadjuvant ciSPlatin and gemcitabine added as a related page.

Version 6

Date	Summary of changes
04/05/2020	Treatment schedule cycle title changed to 'cycle 1 to 3'. Patient information updated to include 'You will have 3 to 4 cycles'. Day 2 approximate treatment time changed to 4 hours. Version number changed to V.6.

Version 5

Date	Summary of changes
08/10/2019	Clinical information updated with PBS expanded indications for GCSF. Drug status updated.

Version 4

Date	Summary of changes
09/05/2014	New protocol taken to Medical Oncology Reference Committee meeting.
22/06/2014	Protocol approved and published on eviQ.
27/03/2015	Reviewed electronically by Medical Oncology Reference Committee. No change. Review 2 years.
15/05/2015	Skin rash (Dryness, Erythema and Pruritus) side effect removed.
19/09/2016	Updated/added volume to vinblastine (50 mL sodium chloride 0.9%) in treatment schedule.
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.
25/06/2019	Protocol reviewed at Medical Oncology Reference Committee meeting on 15/03/2019. Treatment schedule note added regarding alternative dosing option. Filgrastim changed to pegfilgrastim in treatment schedule and patient information. Version number changed to V.4. Next review in 5 years.

The information contained in this protocol is based on the highest level of available evidence and consensus of the eviQ reference committee regarding their views of currently accepted approaches to treatment. Any clinician (medical oncologist, haematologist, radiation oncologist, medical physicist, radiation therapist, pharmacist or nurse) seeking to apply or consult this protocol is expected to use independent clinical judgement in the context of individual clinical circumstances to determine any patient's care or treatment. While eviQ endeavours to link to reliable sources that provide accurate information, eviQ and the Cancer Institute NSW do not endorse or accept responsibility for the accuracy, currency, reliability or correctness of the content of linked external information sources. Use is subject to eviQ's disclaimer available at www.eviQ.org.au

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Review due: 30 June 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/1616>

10 Jul 2023

Patient information - Bladder/urinary tract cancer neoadjuvant - ddMVAC (dose dense methotrexate, vinblastine, doxorubicin, cisplatin)

Patient's name:

Your treatment

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


ddMVAC (dose dense methotrexate, vinblastine, doxorubicin, cisplatin)

This treatment cycle is repeated every 14 days. You will have 3 to 6 cycles. Your doctor will advise you of the number of treatments you will have.

Day	Treatment	How it is given	How long it takes
1	Methotrexate (Meth-o-TREX-ate)	By a drip into a vein	About 30 minutes
2	Vinblastine (vin-BLAS-teen) Doxorubicin (dox-oh-roo-bi-sin) Cisplatin (siss-PLAT-in)	By a drip into a vein	About 4 hours
4	Pegfilgrastim (peg-fil-GRA-stim)	By injection under the skin	About 5 minutes

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
<ul style="list-style-type: none">• 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.
- **Laxatives:** you may be given some medication to prevent or treat constipation. Your doctor or nurse will tell you how and when to take the laxatives.
- **G-CSF:** you will be given injection(s) of a drug called G-CSF (also called filgrastim, lipegfilgrastim or pegfilgrastim) under your skin. This helps to boost your white blood cell count. Your white blood cells help to fight infection. Lipegfilgrastim and pegfilgrastim are given once. Filgrastim is given for several days until your white blood cells recover.

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	<ul style="list-style-type: none"> 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.
Pain or swelling at injection site (extravasation)	<ul style="list-style-type: none"> This treatment can cause serious injury if it leaks from the area where it is going into the vein. This can cause pain, stinging, swelling or redness at or near the site where the drug enters the vein. If not treated correctly, you may get blistering and ulceration. Tell your doctor or nurse immediately if you get any of the symptoms listed above during or after treatment.
Bone pain after G-CSF injection	<ul style="list-style-type: none"> You may have discomfort or a dull ache in your pelvis, back, arms or legs. To reduce the pain, take paracetamol before each injection. Tell your doctor or nurse as soon as possible if your pain is not controlled.
Taste and smell changes	<ul style="list-style-type: none"> 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.
Redness and itching along vein	<ul style="list-style-type: none"> You may get redness and itching along the vein where your chemotherapy is being infused. This will usually go away within 30 minutes of stopping the injection. Tell your doctor or nurse as soon as possible if you get any of the symptoms listed above. Your nurse will check to make sure the drug has not leaked out of the vein.
Urine turning orange or red	<ul style="list-style-type: none"> Your urine will turn an orange or red colour. This is not harmful and should only last for up to 48 hours after treatment.

Early (onset days to weeks)

Infection risk (neutropenia)	<ul style="list-style-type: none"> • 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: <ul style="list-style-type: none"> ◦ 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)	<ul style="list-style-type: none"> • 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.
Constipation	<ul style="list-style-type: none"> • You may have bowel motions (stools, poo) that are less frequent, harder, smaller, painful or difficult to pass. • You may also get: <ul style="list-style-type: none"> ◦ bloating, cramping or pain ◦ a loss of appetite ◦ nausea or vomiting. • Drink plenty of fluids (unless you are fluid restricted). • Eat plenty of fibre-containing foods such as fruit, vegetables and bran. • Take laxatives as directed by your doctor. • Try some gentle exercise daily. • Tell your doctor or nurse if you have not opened your bowels for more than 3 days.

Mouth pain and soreness (mucositis)	<ul style="list-style-type: none"> You may have: <ul style="list-style-type: none"> 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: <ul style="list-style-type: none"> 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.
Tiredness and lack of energy (fatigue)	<ul style="list-style-type: none"> 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.
Oesophagus inflammation (oesophagitis)	<ul style="list-style-type: none"> You may get heartburn or have difficult or painful swallowing. Eat small meals that are high in protein and calories. Avoid eating acidic, hot, salty or spicy foods, and drinking alcohol. Sit upright when eating. Ask to speak with a dietitian if you are having trouble eating. Tell your doctor or nurse as soon as possible if you have the any of the symptoms listed above and they are suddenly getting worse.
Nerve damage (peripheral neuropathy)	<ul style="list-style-type: none"> You may notice a change in the sensations in your hands and feet, including: <ul style="list-style-type: none"> 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.
Skin that is more sensitive to the sun (photosensitivity)	<ul style="list-style-type: none"> After being out in the sun you may develop a rash like a bad sunburn. Your skin may become red, swollen and blistered. Avoid direct sunlight. Protect your skin from the sun by wearing sun-protective clothing, a wide-brimmed hat, sunglasses and a sunscreen of SPF 50 or higher. Tell your doctor or nurse if you get any of the symptoms listed above.

Skin reaction in an area previously treated with radiation therapy (radiation recall)	<ul style="list-style-type: none"> • In the area that was treated with radiation therapy, your skin may become: <ul style="list-style-type: none"> ◦ dry, red and itchy ◦ tender and swollen • It may also: <ul style="list-style-type: none"> ◦ peel or blister ◦ form ulcers • This usually happens weeks or months after chemotherapy treatment. • Avoid wearing tight clothing. • Avoid direct sunlight and very hot or cold temperatures. • Protect your skin from the sun by wearing sun-protective clothing, a wide-brimmed hat, sunglasses and a sunscreen of SPF 50 or higher. • Tell your doctor or nurse if you get any of the symptoms listed above.
Low blood magnesium, potassium and calcium levels (hypomagnesaemia, hypokalaemia, hypocalcaemia)	<ul style="list-style-type: none"> • This may be found from your routine blood tests and treated by your doctor. • If it is severe you may get: <ul style="list-style-type: none"> ◦ 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	<ul style="list-style-type: none"> • 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)	<ul style="list-style-type: none"> • 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)	<ul style="list-style-type: none"> 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 loss (alopecia)	<ul style="list-style-type: none"> Your hair may start to fall out from your head and body. Hair loss usually starts 2 to 3 weeks after your first treatment. You may become completely bald and your scalp might feel tender. Use a gentle shampoo and a soft brush. Take care with hair products like hairspray, hair dye, bleaches and perms. Protect your scalp from the cold with a hat, scarf or wig. Protect your scalp from the sun with a hat or sunscreen of SPF 50 or higher. Moisturise your scalp to prevent itching. Ask your doctor or nurse about the Look Good Feel Better program
Nail changes	<ul style="list-style-type: none"> Your nails may: <ul style="list-style-type: none"> grow more slowly become darker develop ridges or white lines become brittle and flaky In some cases, you may lose your nails completely. Keep your nails clean and short. Avoid things like biting your fingernails, getting a manicure, pedicure or false nails. Wear gloves when you wash the dishes, work in the garden, or clean the house.
Lung problems	<ul style="list-style-type: none"> Lung problems are rare, but can be serious. They may occur throughout treatment or after the completion of treatment. You may get: <ul style="list-style-type: none"> 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.

Delayed (onset months to years)	
Heart problems	<ul style="list-style-type: none"> You may get: <ul style="list-style-type: none"> chest pain or tightness shortness of breath swelling of your ankles an abnormal heartbeat. Heart problems can occur months to years after treatment. Tell your doctor if you have a history of heart problems or high blood pressure. Before or during treatment, you may be asked to have a test to see how well your heart is working. Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you get any of the symptoms listed above.

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.
- Grapefruit and grapefruit juice can interact with your medication and should be avoided while you are on this treatment.
- 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

Additional notes:

This document is a guide only and cannot cover every possible situation. The health professionals caring for you should always consider your individual situation when making decisions about your care. Contact your cancer clinic staff or doctor if you have any questions or concerns about your treatment, or you are having problems coping with side effects. While eviQ endeavours to link to reliable sources that provide accurate information, eviQ and the Cancer Institute NSW do not endorse or accept responsibility for the accuracy, currency, reliability or correctness of the content of linked external information sources. Use of this document is subject to eviQ's disclaimer available at www.eviQ.org.au

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