Gastric adjuvant ciSplatin and capecitabine chemoradiation



ID: 1994 v.3 Endorsed Essential Medicine List

A Fluoropyrimidine overdose or overexposure:

Fluoropyrimidine overdose or overexposure may result in severe or life-threatening toxicity. An antidote is available and is highly effective if given within 96 hours. Read more about fluoropyrimidine overdose or overexposure.

This protocol is not exportable and does not have a calculator.

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

The anticancer drug(s) in this protocol <u>may</u> 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 <u>eviQ Estimated Glomerular Filtration Rate (eGFR) calculator</u>.

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

Click here



Related pages:

2022

• Adjuvant CAPOX (XELOX) (capecitabine and oxaliplatin)

Treatment schedule - Overview

Cycles 1 to 4

Drug	Dose	Route	Day
ciSplatin	60 mg/m ²	IV infusion	1
Capecitabine	1,000 mg/m ² TWICE a day	PO	1 to 14

Frequency: 21 days

Cycles: 4 (2 cycles are given prior to radiation therapy and 2 cycles are given post radiation therapy)

During radiation therapy

Drug	Dose	Route	Day
Capecitabine	825 mg/m ² TWICE a day on radiation therapy days ONLY	РО	1 to 5

Cycles: with concurrent radiation therapy (usually 5 weeks)

Drug status:	All drugs are on the PBS general schedule	
	Capecitabine is available as 150 mg and 500 mg tablets	
Cost:	~ \$150 per cycle (capecitabine and cisplatin)	

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**.

Cycles 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
ciSplatin	60 mg/m ² (IV infusion)	in 1000 mL sodium chloride 0.9% over 60 minutes
Capecitabine	1,000 mg/m ² (PO)	TWICE a day within 30 minutes after the end of a meal.
Day 2 to 4		
Capecitabine	1,000 mg/m ² (PO)	TWICE a day within 30 minutes after the end of a meal.
Dexamethasone	8 mg (PO)	ONCE a day (or in divided doses) with or after food
Day 5 to 14		
Capecitabine	1,000 mg/m ² (PO)	TWICE a day within 30 minutes after the end of a meal.

Frequency: 21 days

Cycles: 4 (2 cycles are given prior to radiotherapy and 2 cycles are given post radiotherapy)

During radiotherapy

Day 1 to 5		
Capecitabine	825 mg/m ² (PO)	TWICE a day within 30 minutes after the end of a meal on radiotherapy days ONLY
Cycles: concurrent	with radiotherapy (usually 5 weeks)	

Treatment schema	
Week 1	Cycle 1 chemotherapy begins
Week 4	Cycle 2 chemotherapy begins
Week 7	Chemotherapy with radiation therapy begins
	Capecitabine only
Week 12	Cycle 3 chemotherapy begins
Week 15	Cycle 4 chemotherapy begins

Indications and patient population

Indications:

 adjuvant treatment of stage IB to IV (M0) adenocarcinoma of stomach following curative resection, where adjuvant chemoradiation therapy has been recommended, as an alternative to perioperative chemotherapy or adjuvant chemotherapy.

Cautions/Exclusions:

- pre existing neuropathies Grade 2 or greater
- moderate/severe renal impairment (creatinine clearance less than 60 mL/min)
- significant dysphagia or nausea
- patients who are unlikely to be able to absorb capecitabine.
- significant hearing impairment/tinnitus.

Note:

- This is a multimodality treatment, it requires multidisciplinary discussion before commencement of treatment
- The evidence supporting this protocol is limited and benefit of chemoradiation therapy may be limited to patients with lymphnode positive gastric cancer (see Evidence section)

Clinical information	
Safety alert fluoropyrimidines	Fluoropyrimidines can be administered by different routes and schedules with each method having associated increased risk of certain side effects. Fluoropyrimidine overdose or overexposure is a rare but potentially life threatening side effect of this drug class and can occur by any route of administration. An antidote is available and highly effective if given within 96 hours. Read more about the medication safety alert for infusional fluorouracil and fluoropyrimidine overdose or overexposure
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
Caution with oral anti-cancer drugs	Select links for information on the safe prescribing, dispensing and administration of orally administered anti-cancer drugs. Read more about the COSA guidelines and oral anti-cancer therapy
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
Cardiac toxicity	Angina-like chest pain, tachycardia, arrhythmias, heart failure, myocardial infarction and cardiac arrest may occur with capecitabine especially in patients with a prior history of coronary artery disease. Cardiac symptoms may require cessation of capecitabine and referral to a cardiologist for symptomatic treatment. Re-challenge is controversial and generally not recommended. Read more about cardiac toxicity associated with anti-cancer drugs
Diarrhoea	Antidiarrhoeals (e.g. loperamide) are usually prescribed with this treatment. Read more about treatment induced diarrhoea
Dihydropyrimidine dehydrogenase (DPD) enzyme deficiency	Rare, life-threatening toxicities such as mucositis, neutropenia, neurotoxicity and diarrhoea have been reported following administration of fluoropyrimidines (e.g. fluorouracil and capecitabine). Severe unexplained toxicities require investigation prior to continuing with treatment. Testing for DPD enzyme deficiency is available in Australia but not currently reimbursed. Read more about dihydropyrimidine dehydrogenase (DPD) enzyme deficiency

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
Hyperbilirubinaemia	Capecitabine can induce hyperbilirubinaemia which may require an interruption in treatment (see dose modifications).
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
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
Nutrition risk HIGH	Consider a dietitian review in week 1, with weekly reviews as necessary.
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 and magnesium at baseline and prior to each cycle and as clinically indicated. INR as clinically indicated.
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 consider reducing cisplatin and capecitabine by 25% for subsequent cycles
Febrile neutropenia	Delay treatment until recovery and consider reducing cisplatin and capecitabine by 25% for subsequent cycles
Platelets x10 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 consider reducing cisplatin and capecitabine by 25% for subsequent cycles

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 capecitabine by 25% and cisplatin by 50%
less than 30	Withhold chemotherapy

* each method has its limitations. Refer to Nephrotoxicity associated with cisplatin for more information.

Hepatic impairment	Hepatic impairment	
Hepatic dysfunction		
Mild	No dose modifications necessary	
Moderate	Reduce capecitabine by 25%	
Severe	Reduce capecitabine by 50%	
Treatment related Grade 3 or 4 Hyperbilirubinaemia	Delay treatment until toxicity resolves to Grade 2 or less	

Peripheral neuropathy	
Grade 2, 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 the dose for

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

<u>Diarrhoea</u>	
Grade 2	Delay treatment until toxicity has resolved to Grade 1 or less and reduce the dose for subsequent cycles as follows: 1 st occurrence: No dose reduction 2 nd occurrence: Reduce capecitabine 25% 3 rd occurrence: Reduce capecitabine by 50% 4 th occurrence: Omit capecitabine
Grade 3 or Grade 4	Delay treatment until toxicity has resolved to Grade 1 or less and reduce the dose for subsequent cycles as follows: 1 st occurrence: Reduce capecitabine by 50% 2 nd occurrence: Omit capecitabine

Hand and foot syndron	<u>ne (Palmar-plantar erythrodysesthesia syndrome)</u>
Grade 2	Delay treatment until toxicity has resolved to Grade 1 or less and reduce the dose for subsequent cycles as follows: 1 st occurrence: No dose reduction 2 nd occurrence: Reduce capecitabine 25% 3 rd occurrence: Reduce capecitabine by 50% 4 th occurrence: Omit capecitabine
Grade 3	Delay treatment until toxicity has resolved to Grade 1 or less and reduce the dose for subsequent cycles as follows: 1 st occurrence: Reduce capecitabine by 50% 2 nd occurrence: Omit capecitabine

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

	Interaction	Clinical management
Sorivudine* and analogues (e.g. brivudine*)	Potentially fatal increased toxicity of fluorouracil, the active metabolite of capecitabine, due to reduced clearance	Combination contraindicated and at least 4 weeks must elapse between the end of treatment with sorivudine (or analogues, such as brivudine) and the start of capecitabine therapy
Warfarin and other drugs metabolised by CYP2C9 (e.g. phenytoin etc.)	Increased effects/toxicity of these drugs possible due to inhibition of CYP2C9 by capecitabine and/or its metabolites resulting in reduced clearance	Avoid combination or monitor for increased effect/toxicity (e.g. INR can be increased by 91% in patients on warfarin)
Allopurinol	Reduced efficacy of capecitabine possible due to reduced conversion to the active metabolites	Avoid combination or monitor for reduced capecitabine efficacy

* currently not marketed in Australia

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)

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

Cycle 1, 2 day 1

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.

O Chemotherapy - Time out

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.

Capecitabine

- administer orally TWICE a day on days 1 to 14
- to be swallowed whole with a glass of water; do not break, crush or chew
- to be taken morning and night (approximately 12 hours apart) within thirty minutes after the end of a meal
- tablets may also be dispersed in water if patient has swallowing difficulties:
 - place the required number of tablets in a disposable cup and fill with approximately 200mL of water, leave the tablets to dissolve (approximately 15 minutes) and swallow immediately
 - o mix any residues in the cup with water and swallow
 - avoid direct contact of the tablets or solution with the skin or mucous membrane. If such contact occurs, wash thoroughly.

Note: missed doses should not be replaced; if a dose is forgotten or vomited, normal dosing should be resumed at the next scheduled dose.

Remove IV cannula and/or deaccess TIVAD or CVAD.

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

During radiation therapy

This is an oral treatment

Safe handling and waste management

Safe administration

General patient assessment prior to each treatment.

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

Pre treatment medication

Administer antiemetics if required

O Chemotherapy - Time out

Capecitabine

- administer orally TWICE a day concurrently with the radiation therapy treatment (on days of radiation therapy only)
- to be swallowed whole with a glass of water; do not break, crush or chew
- to be taken morning and night (approximately 12 hours apart) within thirty minutes after the end of a meal
- the first dose of capecitabine should ideally be taken at least 1 to 2 hours before the first fraction of radiation therapy with subsequent doses taken in the morning after breakfast and in the evening after the evening meal including on the last day of treatment
- tablets may also be dispersed in water if patient has swallowing difficulties:
 - place the required number of tablets in a disposable cup and fill with approximately 200 mL of water, leave the tablets to dissolve (approximately 15 minutes) and swallow immediately
 - mix any residues in the cup with water and swallow
 - avoid direct contact of the tablets or solution with the skin or mucous membrane. If such contact occurs, wash thoroughly.

Note: missed doses should not be replaced; if a dose is forgotten or vomited, normal dosing should be resumed at the next scheduled dose.

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

Cycle 3, 4 day 1

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.

O Chemotherapy - Time out

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.

Capecitabine

- administer orally TWICE a day on days 1 to 14
- to be swallowed whole with a glass of water; do not break, crush or chew
- to be taken morning and night (approximately 12 hours apart) within thirty minutes after the end of a meal
- tablets may also be dispersed in water if patient has swallowing difficulties:
 - place the required number of tablets in a disposable cup and fill with approximately 200mL of water, leave the tablets to dissolve (approximately 15 minutes) and swallow immediately
 - mix any residues in the cup with water and swallow
 - avoid direct contact of the tablets or solution with the skin or mucous membrane. If such contact occurs, wash thoroughly.

Note: missed doses should not be replaced; if a dose is forgotten or vomited, normal dosing should be resumed at the next scheduled dose.

Remove IV cannula and/or deaccess TIVAD or CVAD.

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

Discharge information

Capecitabine tablets

• Capecitabine tablets with written instructions on how to take them.

Antiemetics

Antiemetics as prescribed.

Antidiarrhoeals

• Antidiarrhoeals 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				
Cardiotoxicity	Coronary artery spasm is a temporary, sudden narrowing of one of the coronary arteries that may present at any time during treatment with fluoropyrimidines. It most commonly manifests as angina.				

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
Abdominal pain	Dull ache, cramping or sharp pains are common with some anti-cancer drugs. These are caused by either increased or decreased gastrointestinal motility and can be associated with diarrhoea or constipation.
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
Ocular changes	Symptoms may include eye pain, blurred vision, blepharitis, uveitis, optic neuritis, tear duct stenosis, conjunctivitis, hyperlacrimation, watery or dry eyes and photophobia.
Oesophagitis	Inflammation of the mucosal lining of the oesophagus. It can progress to ulceration, haemorrhage, secondary infection and pain.
Fatigue	Read more about fatigue
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
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
Actinic keratoses flare	Pre-existing actinic keratoses (AKs) can become more inflamed and scaly as a result of
Actinic keratoses nare	immunosuppression. Read more about actinic keratoses flare
Photosensitivity	Increased sensitivity to ultraviolet (UV) light resulting in an exaggerated sunburn-like reaction accompanied by stinging sensations and urticaria.
Nephrotoxicity	Renal dysfunction resulting from damage to the glomeruli, tubules or renal vasculature.
Hypomagnesaemia, hypokalaemia, hypocalcaemia	Abnormally low levels of magnesium, potassium and calcium in the blood.
Palmar-plantar erythrodysaesthesia (PPE) - hand-foot syndrome (HFS)	Bilateral erythema, tenderness, pain, swelling, tingling, numbness, pruritus, dry rash, or moist desquamation and ulceration of the palms and soles. It is also known as hand-foot syndrome (HFS). Symptoms appear to be dose dependent and palms are affected more than soles. Read more about hand-foot syndrome associated with chemotherapy
Anorexia	Loss of appetite accompanied by decreased food intake. Read more about anorexia
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

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				
Hyperbilirubinaemia	An abnormal increase in the amount of bilirubin circulating in the blood which may result in jaundice.				

Evidence

The evidence supporting this protocol is provided by the ARTIST trial, a phase III randomised controlled trial which was designed to compare postoperative treatment with capecitabine with cisplatin versus capecitabine with cisplatin plus radiation therapy with capecitabine.¹ Evidence for this protocol is limited by multiple factors, including the trial design that compared two non standard regimens, was not powered for overall survival, did not have a statistically significant result for the primary outcome, required D2 gastrectomy, and was performed in a Korean population. Nevertheless, the eviQ Reference Committee endorsed this protocol on the basis of reduced toxicity and extremely favourable outcomes in both treatment arms, as well as concerns regarding toxicity of the eviQ protocol Gastric Adjuvant MacDonald (Modified) (fluorouracil and radiation therapy).²

Between November 2004 and April 2008, 228 patients were randomised to capecitabine and cisplatin arm (6 cycles of cisplatin/capecitabine, capecitabine 2000 mg/m2 per day on days 1 to 14 and cisplatin 60 mg/m2 on day 1, repeated every 3 weeks) and 230 patients to capecitabine plus cisplatin with concurrent capecitabine radiation therapy arm (2 cycles of cisplatin/capecitabine followed by 45 Gy chemoradiation, capecitabine 1650 mg/m2 per day for 5 weeks, followed by 2 cycles of cisplatin/capecitabine).¹

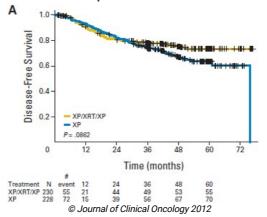
The primary end point was disease free survival (DFS) and secondary end points were overall survival (OS), recurrence rate and toxicity.

Efficacy

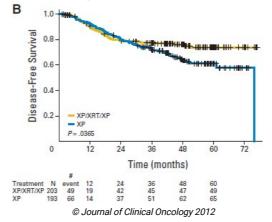
Three year DFS rates were 78.2% vs 74.2% in the chemoradiation therapy arm and chemotherapy arm respectively (P=0.0862).¹ DFS remained similar between both arms after 7 years of follow up (HR 0.74, 95% Cl, 0.52 to 1.05, P =0.922). After a median follow up of 7 years, 5 year OS was 73% in the chemoradiation therapy arm and 75% in the chemotherapy arm (HR 1.130, 95% Cl, 0.775 to 1.647, P = 0.5272).³ In a subset analysis of 396 patients with lymph nodes involvement, DFS rates were 76% vs 72% in the chemoradiation therapy arm respectively (P=0.04).³ Treatment was completed as planned by 75.4% of patients (172/228) in chemotherapy arm and 81.7% (188/230) in chemoradiation therapy arm.

The ARTIST trial only included patients who underwent a D2 resection for pathologically staged 1B to IV (M0) gastric cancer. Although there was no difference in the primary end point of three year DFS between both arms, there was some indication of benefit for patients with lymph-node positive gastric cancer in the chemoradiation therapy arm. Locoregional relapse occurred more frequently in the chemotherapy arm than chemoradiation therapy arm (13% vs 7%, P =0.0033) but no significant difference in rates of distant metastasis (27% vs 24%, P =0.5568).³ A subsequent trial (ARTIST-II) is ongoing in patients with lymph node positive gastric cancer after D2 resection.

(A) Kaplan-Meier analysis for Disease Free Survival in all patients in the ARTIST trial:¹



(B) Kaplan Meier analysis for Disease-free Survival in lymph node positive patients in the ARTIST trial:¹



Toxicity

The most common non-haematologic grade 3 to 4 adverse events were vomiting, stomatitis, HFS and diarrhoea.¹ Grade 4 neutropenia occurred in 5.7% of patients in the chemotherapy arm vs 4.8% of patients in the chemoradiation therapy arm. Two treatment related deaths occurred during the study. One patient died of neutropenic septic shock in the chemotherapy arm and one patient died of non-neutropenic pneumonia in the chemoradiation therapy arm. Adverse events that led to treatment modifications (delays or dose reductions) occurred in 52% of patients in the chemotherapy arm and 35% of patients in the chemoradiation therapy arm. The most frequent adverse event that led to treatment modifications was neutropenia (58 patients in chemotherapy arm vs 41 patients in chemoradiation therapy arm).

Toxicity (all grades):1

				XP Arm (I	n = 226	<u> </u>		Ξ.	22		XP/X	RT/XP Ar	m (n = 2	227)		8
	Gra	de 1	Gra	ade 2	Gra	ade 3	Gra	de 4	Gra	de 1	Gra	ade 2	Gra	ide 3	Gra	ade 4
Toxicity	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Nausea	114	50.4	63	27.9	28	12.4	0	0.0	132	58.1	43	18.9	28	12.3	0	0.0
Vomiting	57	25.2	19	8.4	8	3.5	0	0.0	75	33.0	11	4.8	7	3.1	0	0.0
Diarrhea	83	36.7	16	7.1	4	1.8	1	0.4	86	37.9	14	6.1	2	0.9	0	0.0
Stomatitis	60	26.5	11	4.9	3	1.3	0	0.0	50	22.0	3	1.3	4	1.8	0	0.0
Constipation	85	37.6	7	3.1	2	0.9	0	0.0	94	41.4	6	2.6	2	0.9	0	0.0
HFS	94	41.6	26	11.5	5	2.2	_	_	88	38.7	17	7.4	7	3.1	-	_
Anemia	124	54.9	64	28.3	3	1.3	1	0.4	109	48.0	80	35.2	1	0.4	0	0.0
Neutropenia	28	12.4	78	34.5	79	35.0	13	5.7	21	9.3	76	33.5	99	43.6	11	4.8
Thrombocytopenia	30	13.3	4	1.8	0	0.0	0	0.0	49	21.6	24	10.6	2	0.9	0	0.0

Abbreviations: HFS, hand-foot syndrome; XP, capecitabine plus cisplatin; XRT, radiotherapy with capecitabine © Journal of Clinical Oncology 2012

References

- 1 Lee, J., D. H. Lim, S. Kim, et al. 2012. "Phase III trial comparing capecitabine plus cisplatin versus capecitabine plus cisplatin with concurrent capecitabine radiotherapy in completely resected gastric cancer with D2 lymph node dissection: the ARTIST trial." J Clin Oncol 30(3):268-273.
- 2 Macdonald, J. S., S. R. Smalley, J. Benedetti, et al. 2001. "Chemoradiotherapy after surgery compared with surgery alone for adenocarcinoma of the stomach or gastroesophageal junction." N.Engl.J.Med. 345(10):725-730.
- 3 Park, S. H., T. S. Sohn, J. Lee, et al. 2015. "Phase III Trial to Compare Adjuvant Chemotherapy With Capecitabine and Cisplatin Versus Concurrent Chemoradiotherapy in Gastric Cancer: Final Report of the Adjuvant Chemoradiotherapy in Stomach Tumors Trial, Including Survival and Subset Analyses." J Clin Oncol 33(28):3130-3136.

History

Version 3

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

Version 2

Date	Summary of changes	
21/10/2016	New protocol taken to Medical Oncology Reference Committee meeting.	
11/12/2017	Approved and published on eviQ	
16/02/2018	Fluoropyrimidine overdose or overexposure warning added.	
10/05/2018	Haematological dose modifications updated as per consensus of the expert clinician group. DPD enzyme deficiency wording in clinical information updated. Fluoropyrimidine safety alert in clinical information added. Version changed to number V.2.	
20/05/2019	Protocol reviewed electronically by the Medical Oncology Reference Committee. No changes. Review 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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Patient's name:

Your treatment

The treatment schedule below explains how the drugs for this treatment are given. This treatment uses both chemotherapy and radiation therapy. At times you will just have the chemotherapy, at other times it may be combined with the radiation therapy. Your doctor will discuss this with you.

Cisplatin and capecitabine with radiation therapy Before radiation therapy cycle 1 and 2			
			Day
1	Cisplatin (siss-PLAT-in)	By drip into a vein	About 4 hours
1 to 14	Capecitabine (<i>KAP-e-SYE-ta-been</i>)	Take orally TWICE a day with a glass of water within 30 minutes of finishing a meal (just after breakfast and then again after evening meal). Do not break, crush or chew tablets. If you are unable to swallow the tablets whole they may be dissolved in water and the solution swallowed (see directions in <i>Other information about your</i> <i>treatment</i>). If you forget to take a tablet or vomit a tablet, take your normal dose the next time it is due. Do not take an extra dose.	
15-21	Do not take capecitabine tablets from day 15 to 21.		

During radiation therapy			
Day	Treatment	How it is given	How long it takes
Only on the days you are having radiation therapy	Capecitabine	 Take orally TWICE a day with a glass of water within 30 minutes of finishing a meal (just after breakfast and then again after evening meal). Do not break, crush or chew tablets. If you are unable to swallow the tablets whole they may be dissolved in water and the solution swallowed (see directions in <i>Other information about your treatment</i>). If you forget to take a tablet or vomit a tablet, take your normal dose the next time it is due. Do not take an extra dose. 	

After radia	After radiation therapy cycle 3 and 4		
Day	Treatment	How it is given	How long it takes
1	Cisplatin (siss-PLAT-in)	By drip into a vein	About 4 hours
1 to 14	Capecitabine (<i>KAP-e-SYE-ta-been</i>)	Take orally TWICE a day with a glass of water within 30 minutes of finishing a meal (just after breakfast and then again after evening meal).	

	Do not break, crush or chew tablets. If you are unable to swallow the tablets whole they may be dissolved in water and the solution swallowed (see directions in <i>Other information about your</i> <i>treatment</i>). If you forget to take a tablet or vomit a tablet, take your normal dose the next time it is due. Do not take an extra dose.
15 to 21	Do not take capecitabine tablets from day 15 to 21.

Capecitabine tablets are available in two tablet strengths, 150 mg and 500 mg. It is important that you take the correct tablets and understand how to take them. Ask your doctor, nurse or pharmacist to complete the table below with the correct number of tablets for you.

Capecitabine	Morning	Evening
Number of 150 mg tablets		
Number of 500 mg tablets		

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.

Stop taking capecitabine and contact your doctor if you have any of the following side effects:

- diarrhoea passing an extra 4 to 6 bowel motions per day, or passing bowel motions through the night
- vomiting 2 to 5 episodes of vomiting in a 24 hour period
- · a sore mouth which is making it difficult to eat
- pain and redness on the palms of your hands and the soles of your feet.

IMMEDIATELY go to your nearest hospit Emergency Department, or contact your nurse if you have any of the following at time:	doctor or Ask your doctor or purse from your treating team who to
 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).

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. Tell your doctor if you are on an anticoagulant (medication used to treat or prevent blood clots) e.g. warfarin. You may need to have additional 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.
- Antidiarrhoeals: you may be given some medication to treat diarrhoea. Your doctor or nurse will tell you how and when to take your antidiarrhoeal medication.

Instructions for dissolving capecitabine tablets:

- Capecitabine tablets should never be crushed, cut or broken.
- You (or whoever is dissolving the tablets) should wear disposable gloves and try to minimise touching the tablets.
- Put the tablet(s) needed for the dose into a disposable cup with a lid, if possible. If using a non-disposable cup, ensure the cup is kept only for this purpose.
- Fill the cup with approximately 200 mL of water and cover with lid if available.
- Leave the tablets in the water to dissolve, this may take up to 15 minutes. Gentle agitation of the solution may assist in the dissolving process, being careful not to spill the solution.
- Once the tablets have fully dissolved, swallow the solution immediately.
- In case of any spillages to skin, immediately wash the affected area thoroughly with warm soapy water. If spillage occurs to work surface or floor, wash area with warm soapy water and dry with absorbent paper towel or cloth. Dispose of cloth in a cytotoxic bag.
- The tablets have a bitter taste. The solution may be made more palatable by dissolving the tablets in fruit juice (not citrus juice) or by adding cordial or flavouring.
- To ensure that the whole dose is taken, swirl the cup with water and swallow. Repeat if necessary.
- The disposable cup and gloves should be disposed of in a cytotoxic waste bag. Non-disposable cups should be washed thoroughly with warm soapy water.

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 day	/s)
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.
raste and smen changes	 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.
Heart problems	You may get:
	 chest pain or tightness
	 shortness of breath
	 an abnormal heartbeat
	• Tell your doctor if you have a history of heart problems or high blood pressure.
	• Tell your doctor or nurse immediately, or go to the nearest hospital Emergency
	Department if you get any of the symptoms listed above.
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 constraint inspect (if you have one) doily for any reduces have or evaluating
	 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 core threat or court
	 a sore throat or cough upcontrolled disprace
	uncontrolled diarrhoea shortness of breath
	 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.
Stomach pain	 You may get: dull aches cramping or pain bloating or flatulence (gas). Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you have stomach pain that you are unable to control.
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.
Eye problems	 You may get: eye pain red, sore or swollen eyes blurred vision watery or gritty eyes changes in your eyesight sensitivity to sunlight. Protect your eyes from the weather (sun and wind) by wearing sunglasses, especially if you have lost your eyelashes. Tell your doctor or nurse if you get any of the symptoms listed above. Eye drops may help with your symptoms.

Oesophagus inflammation (oesophagitis)	 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.
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.
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.
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.
Skin changes	 Your skin may become dry, and you may notice changes to areas of your skin that have been exposed to the sun. Keep your skin moisturised with a cream such as sorbolene or aqueous cream. Avoid direct sunlight. Protect your skin from the sun by wearing a wide-brimmed hat, sun-protective clothing, sunglasses and sunscreen of SPF 50 or higher. Tell your doctor or nurse if you notice any skin changes.
Skin that is more sensitive to the sun (photosensitivity)	 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.
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.

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.
Hand-foot syndrome (palmar-plantar erythrodysaesthesia)	 The palms of your hands and soles of your feet may become: red and hot swollen painful and tender blistered. The skin in the area may also peel. Moisturise your hands and feet daily with sorbolene or aqueous cream. Keep your hands and feet clean and dry. Avoid hot water, instead use lukewarm water to bathe. Avoid direct sunlight. Avoid unnecessary walking, jogging or exercise. Wear cotton socks and avoid tight-fitting shoes. Tell your doctor or nurse as soon as possible if you notice any skin changes on your hands or feet.
Appetite loss (anorexia)	 You may not feel like eating. Try to avoid drinking fluids at meal times. Try to eat small meals or snacks regularly throughout the day. Try to eat food that is high in protein and calories. If you are worried about how much food you can eat, or if you are losing weight, ask to speak to a dietitian.
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.

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 loss (alopecia)	 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
High blood bilirubin levels (hyperbilirubinaemia)	 You may get: yellowing of your skin or eyes itchy skin pain or tenderness in your stomach nausea and vomiting loss of appetite. You will have regular blood tests to check how well your liver is working. Tell your doctor or nurse as soon as possible if you notice that your urine is a dark colour, the whites of your eyes look yellow, or if you have stomach pain.

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

Stomach and oesophageal cancer information

• Pancare Foundation – pancare.org.au

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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