

Breast metastatic capecitabine

ID: 37 v.6 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.

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

This protocol is based on standard (first line) and limited evidence (second line); please refer to the evidence sections of this protocol for more information.

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



2022

Treatment schedule - Overview

Cycle 1 and further cycles

Drug	Dose	Route	Day
Capecitabine	1,000 mg/m ² TWICE a day *#	PO	1 to 14

^{*} Although most studies used a dose of capecitabine 1250 mg/m² twice daily, it is the consensus of the reference committee that a starting dose of 1000 mg/m² twice daily is more appropriate for this patient population. For frail or heavily pre-treated patients, consider reducing the dose. Careful monitoring during the initiation period is recommended.

An alternative dosing schedule is 650 mg/m² twice daily continuous.¹

Frequency: 21 days

Cycles: Continuous until disease progression or unacceptable toxicity

Drug status: Capecitabine is available on the PBS general schedule

Capecitabine is available as 150 mg and 500 mg tablets

Cost: ~ \$90 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.

Breast metastatic capecitabine Page 1 of 13

Cycle 1 and further cycles

Day 1 to 14		
Capecitabine	1,000 mg/m ² (PO)	TWICE a day *# within 30 minutes after the end of a meal

^{*} Although most studies used a dose of capecitabine 1250 mg/m² twice daily, it is the consensus of the reference committee that a starting dose of 1000 mg/m² twice daily is more appropriate for this patient population. For frail or heavily pre-treated patients, consider reducing the dose. Careful monitoring during the initiation period is recommended.

An alternative dosing schedule is 650 mg/m² twice daily continuous.¹

Frequency: 21 days

Cycles: Continuous until disease progression or unacceptable toxicity

Indications and patient population

· Metastatic breast cancer

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
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 minimal or low	No routine prophylaxis required. If patients experience nausea and/or vomiting, consider using the low emetogenic risk regimen. 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
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
Diarrhoea	Antidiarrhoeals (e.g. loperamide) are usually prescribed with this treatment. Read more about treatment induced diarrhoea
Hyperbilirubinaemia	Capecitabine can induce hyperbilirubinaemia which may require an interruption in treatment (see dose modifications).

Breast metastatic capecitabine Page 2 of 13

Blood tests	FBC, EUC and LFTs at baseline and prior to each cycle. INR as clinically indicated.
Hepatitis B screening and prophylaxis	Routine screening for HBsAg and anti-HBc is NOT usually recommended for patients receiving this treatment. 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)		
1.0 to less than 1.5	Refer to local institutional guidelines; it is the view of the expert clinicians that treatment should continue if patient is clinically well	
0.5 to less than 1.0	Delay treatment until recovery	
less than 0.5	Delay treatment until recovery and reduce capecitabine by 25% for subsequent cycles	
Febrile neutropenia	Delay treatment until recovery and reduce capecitabine by 25% for subsequent cycles	
Platelets x 10 ⁹ /L (pre-treatment blood test)		
75 to less than 100	The general recommendation is to delay, however if the patient is clinically well it may be appropriate to continue treatment; refer to treating team and/or local institutional	

Breast metastatic capecitabine Page 3 of 13

Haematological toxicity	
	guidelines
50 to less than 75	Delay treatment until recovery
less than 50	Delay treatment until recovery and reduce capecitabine by 25% for subsequent cycles

Renal impairment	
Creatinine clearance (mL/min)	
30 to 50	Reduce capecitabine by 25%
less than 30	Omit capecitabine

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

Mucositis and stomatitis		
Grade 2	Delay treatment until toxicity has resolved to Grade 1 or less and reduce the dose for subsequent cycles as follows: 1st occurrence: No dose reduction 2nd occurrence: Reduce capecitabine by 25% 3rd occurrence: Reduce capecitabine by 50% 4th 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: 1st occurrence: Reduce capecitabine by 50% 2nd 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: 1st occurrence: No dose reduction 2nd occurrence: Reduce capecitabine by 25% 3rd occurrence: Reduce capecitabine by 50% 4th 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 foot syndrome (link to Hand foot syndrome (Palmar-plantar erythrodysaesthesia)		
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	

Breast metastatic capecitabine Page 4 of 13

Hand foot syndrome (link to Hand foot syndrome (Palmar-plantar erythrodysaesthesia)	
	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

Capecitabine				
	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

Breast metastatic capecitabine Page 5 of 13

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

Breast metastatic capecitabine Page 6 of 13

Days 1 to 14

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.

Ochemotherapy - Time out

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
 - o 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)

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				
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.			
Taste and smell alteration	Read more about taste and smell changes			

Breast metastatic capecitabine Page 7 of 13

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			
Diarrhoea	Read more about triolinbocytoperna 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			
Actinic keratoses flare	Pre-existing actinic keratoses (AKs) can become more inflamed and scaly as a result of immunosuppression. Read more about actinic keratoses flare			
Anorexia	Loss of appetite accompanied by decreased food intake. Read more about anorexia			
Fatigue	Read more about fatigue			
Ocular changes	Symptoms may include eye pain, blurred vision, blepharitis, uveitis, optic neuritis, tear duct stenosis, conjunctivitis, hyperlacrimation, watery or dry eyes and photophobia.			
Photosensitivity	Increased sensitivity to ultraviolet (UV) light resulting in an exaggerated sunburn-like reaction accompanied by stinging sensations and urticaria.			
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			
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			
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 diarrhoed or constipation.			
Late (onset weeks to months)				
Anaemia	Abnormally low levels of red blood cells (RBCs) or haemoglobin in the blood. Read more about anaemia			
Hyperbilirubinaemia	An abnormal increase in the amount of bilirubin circulating in the blood which may result in jaundice.			
Delayed (onset months to year	rs)			
Menopausal symptoms	Irregular or absent periods, hot flushes, mood swings, sleep disturbance, night sweats, vaginal dryness, decreased libido and dyspareunia. This is caused by ovarian failure and may be temporary or permanent.			

Evidence

First line treatment

Breast metastatic capecitabine Page 8 of 13

The evidence supporting this protocol is provided by a phase 3 randomised controlled trial involving 325 patients comparing intermittent capecitabine or continuous capecitabine to classical cyclophosphamide methotrexate fluorouracil (CMF) in patients with metastatic breast cancer.¹

Between July 2001 and June 2005 325 patients who were not suitable for more intensive chemotherapy were randomised to receive intermittent capecitabine (1000 mg/m² twice daily on days 1-14 and repeated every 3 weeks), continuous capecitabine (650 mg/m² twice daily on days 1-21 and repeated every 3 weeks), or classical CMF (oral cyclophosphamide 100 mg/m² on days 1-14, methotrexate 40 mg/m², and fluorouracil 600 mg/m² on days 1-8, and repeated every 4 weeks). The primary endpoint was quality-adjusted progression-free survival (PFS); secondary endpoints included PFS, overall-survival (OS), objective tumour response, and adverse events.

Second line treatment

A search of the literature did not find strong evidence to support the use of capecitabine in the second line treatment of metastatic breast 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 phase II trial by Blum et al.²

Source	Study & year published	Supports use	Is the dose and regimen consistent with the protocol?	Comments
Phase II	Blum et al 1999 ²	Yes	No	
Meta-analysis	Ershler et al 2006 ³	N/A	N/A	
Guidelines	Date published/revised	Supports use	Is the dose and regiment consistent with the protocol	Comments
NCCN	N/A	N/A	N/A	First line treatment only
ссо	2003	Yes	No	-
BCCA	N/A	N/A	N/A	First line
ESMO	2018	Yes	N/A	

In the phase II study by Blum et al. 163 patients were enrolled into the study and 162 patients received treatment with capecitabine. All patients had received at least 2 but not more than 3 prior chemotherapy regimens, one of which had to have contained paclitaxel for metastatic disease.

Ershler et al. performed a systematic review of capecitabine monotherapy in 1st and 2nd line metastatic breast cancer patients.³ There were 28 studies which used single agent capecitabine in the 2nd line setting, but most were Phase 2 studies or conference abstracts and none were randomised controlled trials.

Overall, monotherapy capecitabine was active in previously treated patients. The median complete response rate was 3% and the median objective response rate was 28%. The median time to progression was 4.7 months and median overall survival was 11.0 months.

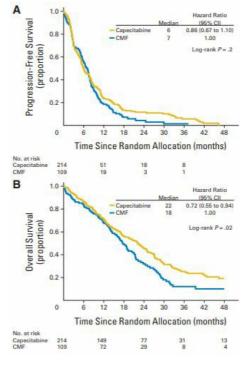
Efficacy

First line treatment

The overall response rate was 22% in the intermittent capecitabine arm, 20% in the continuous capecitabine arm, and 18% in the CMF arm. The quality-adjusted PFS was similar between capecitabine versus CMF (mean, 8.8 v 7.6 months). OS was longer in the capecitabine group (median, 22 v 18 months). There was no survival difference between the intermittent and continuous capecitabine arms.

Progression free survival and overall survival¹

Breast metastatic capecitabine Page 9 of 13



©Journal of Clinical Oncology 2011

Second line treatment

In the study by Blum et al, the overall response rate was 20%. 3 complete responses were seen and the median duration of response was 8.1 months, median survival time was 12.8 months and median time to disease progression was 93 days.²

Relationship between tumour response and survival ²

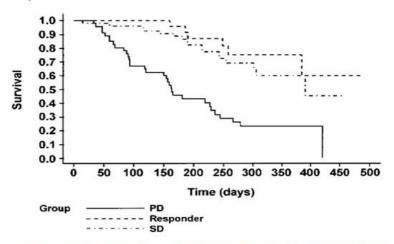


Fig 4. Patient survival was determined as a function of best overall tumor response achieved on study (n = 135). Abbreviations: Responder, objective responder (----); SD, stable disease (-----); PD, progressive disease (--).

© Journal of Clinical Oncology 1999

Toxicity

The most common treatment-related adverse events reported by both Stockler et al and Blum et al. were hand-foot syndrome (HFS), diarrhoea, nausea, vomiting, infection and fatigue.

Treatment related adverse events in first line treatment¹

Breast metastatic capecitabine Page 10 of 13

	18	Capecitabine (No. of patients)				
	Intern	nittent	Continuous		CMF (No. o	of patients)	P (capecitabine
Adverse Event	Grade 1-4	Grade 3-4	Any Grade	Grade 3-4	Any Grade	Grade 3-4	CMF) Grade 3-4
Fatigue	72	2	70	4	62	7	.1
Nausea	71	2	67	4	70	1	_4
Vomiting	41	2	48	4	32	3	1.0
Diarrhea	57	6	64	8	43	6	.8
Stomatitis	36	0	39	0	43	6	.001
Hand-foot syndrome	66	15	70	17	4	0	< .001
Tearing or conjunctivitis	33	1	28	0	34	0	1.0
Alopecia	14	0	9	0	54	0	1.0
Infection	46	6	45	3	44	9	.2
Fever without neutropenia	9	0	7	0	14	1	.3
Febrile neutropenia	1	0	0	0	11	11	< .001
Neutropenia	23	1	32	1	56	28	< .001
Leukopenia	31	0	38	0	74	5	.004
Anaemia	34	2	29	3	47	4	.5
Thrombocytopenia	6	3	12	3	32	3	1.0
Other	93	29	100	32	91	42	.08

© Journal of Clinical Oncology 2011

Frequently reported treatment-related adverse events in second line treatment ²

Adverse	T	otal	Mild		d Moderate		Severe		Life Threatening	
Event	No.	%	No.	%	No.	%	No.	%	No.	%
Hand-foot syn-										
drome	91	56.2	23	14.2	52	32.1	16	9.9	_	
Diarrhea	88	54.3	35	21.6	30	18.5	18	11.1	5	3.1
Nausea	84	51.9	40	24.7	37	22.8	7	4.3	_	
Vomiting	60	37.0	29	17.9	25	15.4	6	3.7	_	
Fatigue	59	36.4	19	11.7	28	17.3	12	7.4	_	
Constipation	25	15.4	15	9.3	8	4.9	2	1.2	-	
Dermatitis	25	15.4	17	10.5	6	3.7	2	1.2	-	
Abdominal pain	24	14.8	6	3.7	13	8.0	5	3.1	_	
Decreased										
appetite	18	11.1	10	6.2	7	4.3	1	0.6	_	
Pyrexia	18	11.1	11	6.8	6	3.7	1	0.6	_	
Erythematous										
rash	17	10.5	10	6.2	7	4.3	-			
Paresthesia	16	9.9	9	5.6	7	4.3	_		-	
Stomatitis	15	9.3	6	3.7	5	3.1	4	2.5	_	
Mucosal inflam-										
mation	15	9.3	5	3.1	3	1.9	7	4.3	_	
Dehydration	11	6.8	_		5	3.1	5	3.1	1	0.6
Coagulation										
disorder	1	0.6	_		_		_		1	0.6

© Journal of Clinical Oncology 1999

Ershler et al. reviewed the grade 3 or 4 adverse events reported in studies where capecitabine was used in the second-line or subsequent setting.³ Overall, the most frequently reported grade 3 or 4 non-haematological adverse events were hand-foot syndrome (median 13%, range 0% - 42%), diarrhoea (median 7.5%, range 0% - 30%), nausea (median 6.5%, range 0% - 35%), mucositis (median 6%, range 0% - 12%), and vomiting (median 4%, range 0% - 19%). Haematologic adverse events were uncommon (median neutropenia incidence of 1%, thrombocytopenia and leukopenia 0%).

References

1 Stockler, M. R., V. J. Harvey, P. A. Francis et al. 2011. "Capecitabine versus classical cyclophosphamide, methotrexate, and fluorouracil as first-line chemotherapy for advanced breast cancer." J Clin Oncol 29(34):4498-4504.

Breast metastatic capecitabine Page 11 of 13

- 2 Blum, J. L., S. E. Jones, A. U. Buzdar, et al. 1999. "Multicenter phase II study of capecitabine in paclitaxel-refractory metastatic breast cancer." J.Clin Oncol 17(2):485-493.
- **3** Ershler, W., B. 2006. "Capecitabine Monotherapy: Safe and Effective Treatment for Metastatic Breast Cancer." Oncologist 11(4):325-335

History

Version 6

Date	Summary of changes		
18/10/2019	Protocol reviewed at Medical Oncology Reference Committee meeting.		
	Indications changed to metastatic breast cancer. Alternative dosing schedule of 650 mg/m² twice daily continuous added to treatment schedule. Evidence updated with first and second line treatment. Version number change to V.6.		
13/08/2021	Protocol reviewed electronically by Medical Oncology Reference Committee. Nil changes. Review in 2 years.		
21/12/2021	Changed antiemetic clinical information block to minimal or low, to align with new categories. See ID 7 Prevention of anti-cancer therapy induced nausea and vomiting (AINV) v5.		

Version 5

Date	Summary of changes				
18/09/2006	Patient Information updated.				
28/06/2007	Reviewed and evidence updated.				
10/08/2009	Review, new dose modifications and transferred to eviQ				
28/06/2010	Haematological dose modifications updated (20% changed to 25% dose reduction).				
26/10/2010	Dose modifications updated: "consider reducing" changed to " reduce".				
18/01/2011	New format to allow for export of protocol information. Protocol version number changed to <i>V.2.</i> Antiemetics and premedications added to the treatment schedule. Additional Clinical Information, Key Prescribing table and Key Administration table combined into new section titled Clinical Considerations. Drug specific information placed behind the drug name link.				
27/04/2012	Protocol reviewed at Medical Oncology Reference Committee meeting. Group consensus to change fixed dosing of capecitabine to mg/m² dosing to reflect published evidence. Caveat that a lower dose may be required for frail or heavily pre treated patients added. Next review in 2 years.				
09/05/2014	Protocol reviewed by email survey. No change and next review in 2 years. PHC view removed.				
18/02/2016	Discussion with Medical Oncology Reference Committee Chairs and protocol to be reviewed every 5 years. Next review due in 3 years.				
16/12/2016	Dissolving capecitabine information added to administration and patient information.				
31/05/2017	Transferred to new eviQ website. Version number change to V.4. Link to the independent evaluation of the evidence completed in 2006/7 removed from the evidence section as no longer relevant. Hepatitis B screening changed to NOT recommended.				
10/05/2018	Haematological dose modifications updated as per consensus of the expert clinician group. Fluoropyrimidine overdose or overexposure warning added.				

Breast metastatic capecitabine Page 12 of 13

Date	Summary of changes				
	Fluoropyrimidine safety alert added in clinical information.				
	DPD enzyme deficiency wording in clinical information updated.				
Version number changed to V.5					

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

First approved: 15 February 2005 Last reviewed: 13 August 2021 Review due: 31 December 2023

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/37 07 Jun 2023

Breast metastatic capecitabine Page 13 of 13

Patient information - Breast cancer metastatic - Capecitabine



Patient's name:

Your treatment

The treatment schedule below explains how the drug for this treatment is given.

Capecitabi	Capecitabine					
This treatment cycle is repeated every 21 days. Your doctor will advise you of the number of treatments you will have.						
Day	Treatment How it is given					
1 to 14	Capecitabine (KAP-e-SYE-ta-been)	Take orally TWICE a day on days 1 to 14 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.				
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 hospital	Emergency contact details
---	---------------------------

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

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. 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 days)				
Nausea and vomiting	 You may feel sick (nausea) or be sick (vomit). Take your anti-sickness medication as directed even if you don't feel sick. Drink plenty of fluids (unless you are fluid restricted). Eat small meals more frequently. Try food that does not require much preparation. Try bland foods like dry biscuits or toast. Gentle exercise may help with nausea. Ask your doctor or nurse for eviQ patient information - Nausea and vomiting during cancer treatment. Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you have uncontrolled vomiting or feel dizzy or light-headed. 			
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. 			
Taste and smell changes	 You may find that food loses its taste or tastes different. These changes are likely to go away with time. Do your mouth care regularly. Chew on sugar-free gum or eat sugar-free mints. Add flavour to your food with sauces and herbs. Ask your doctor or nurse for eviQ patient information - Taste and smell changes during cancer treatment. 			

Early (onset days to weeks)

Infection risk (neutropenia)

- This treatment lowers the amount of white blood cells in your body. The type of white blood cells that help to fight infection are called neutrophils. Having low level of neutrophils is called neutropenia. If you have neutropenia, you are at greater risk of getting an infection. It also means that your body can't fight infections as well as usual. This is a serious side effect, and can be life threatening.
- · Wash your hands often.
- Keep a thermometer at home and take your temperature regularly, and if you feel unwell.
- Do your mouth care regularly.
- Inspect your central line site (if you have one) daily for any redness, pus or swelling.
- · Limit contact with people who are sick.
- Learn how to recognise the signs of infection.
- Ask your doctor or nurse for eviQ patient information Infection during cancer treatment.
- Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you get any of the following signs or symptoms:
 - a temperature of 38°C or higher
 - o chills, shivers, sweats or shakes
 - a sore throat or cough
 - uncontrolled diarrhoea
 - shortness of breath
 - a fast heartheat
 - 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.

- 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.

· You may have: Mouth pain and soreness o bleeding gums (mucositis) mouth ulcers a white coating on your tongue o 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: o 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. • Your skin may become dry, and you may notice changes to areas of your skin that have been Skin changes 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. · You may not feel like eating. Appetite loss (anorexia) 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. • You may feel very tired, have no energy, sleep a lot, and not be able to do normal activities or Tiredness and lack of energy things you enjoy. (fatigue) • 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. · You may get: Eye problems 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.

• After being out in the sun you may develop a rash like a bad sunburn. Skin that is more sensitive to • Your skin may become red, swollen and blistered. the sun (photosensitivity) · 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. • You may get a red, bumpy rash and dry, itchy skin. Skin rash · 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. • The palms of your hands and soles of your feet may become: Hand-foot syndrome o red and hot (palmar-plantar swollen erythrodysaesthesia) painful and tender o 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. · You may get: Stomach pain dull aches o 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.

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. 			
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. 			

Delayed (onset months to years)

Menopausal symptoms

- You may get:
 - hot flushes or night sweats
 - mood changes
 - vaginal dryness
 - o irregular or no periods.
- You may also:
 - have trouble sleeping
 - find sex painful or lose interest in sex
- These symptoms may go away after treatment, or the menopause may be permanent.
- If you have sex you should use contraception as there is still a risk of pregnancy. Talk to your doctor about what form of contraception is right for you.
- Talk to your doctor or nurse about ways to manage these symptoms.

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.

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.

Breast cancer information

- Australasian Lymphology Association lymphoedema.org.au
- Australasian Menopause Society menopause.org.au
- Breast Cancer Network Australia bcna.org.au
- National Breast Cancer Foundation nbcf.org.au
- YWCA Encore breast cancer exercise program ywcaencore.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 Igfb.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

First approved: 15 February 2005
Last reviewed: 13 August 2021
Review due: 31 December 2023

The currency of this information is guaranteed only up until the date of printing, for any updates please check:

https://www.eviq.org.au/pi/37

07 Jun 2023