Colorectal metastatic cetuximab (weekly) and irinotecan (two weekly) SUPERSEDED

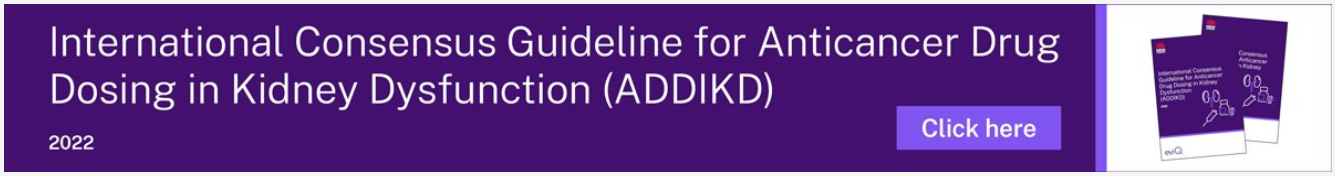
ID: 1567 v.5 **Superseded**

This protocol has been superseded as cetuximab two weekly is as efficacious and improves patient safety. The preferred regimen is ID 1681 Colorectal metastatic cetuximab (two weekly).

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

This protocol is based on limited evidence; refer to the evidence section of this protocol for more information.

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



Related pages:

- Colorectal metastatic cetuximab and irinotecan (two weekly)
- Colorectal metastatic cetuximab SUPERSEDED

Treatment schedule - Overview

Cycle 1

Drug	Dose	Route	Day
Cetuximab	400 mg/m^2 (loading dose only)	IV infusion	1
Cetuximab	250 mg/m^2 (subsequent doses)	IV infusion	8
Irinotecan	180 mg/m^2	IV infusion	1

Cycle 2 and further cycles

Drug	Dose	Route	Day
Cetuximab	250 mg/m^2	IV infusion	1 and 8
Irinotecan	180 mg/m^2	IV infusion	1

Frequency: 14 days

Cycles: Continuous until disease progression or unacceptable toxicity

Drug status: Irinotecan is on the PBS general schedule and cetuximab is PBS authority

Cost: ~ $2,840 per cycle

Treatment schedule - Detail

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

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

Cycle 1

Day 1		
Loratadine	10 mg (PO)	60 minutes before treatment
Dexamethasone	8 mg (PO)	60 minutes before treatment
Cetuximab	400 mg/m^2 (IV infusion)	over 2 hours *
Palonosetron	0.25 mg (IV bolus)	30 minutes before chemotherapy
Irinotecan	180 mg/m^2 (IV infusion)	in 250 mL to 500 mL glucose 5% over 90 minutes

Day 2 and 3		
Dexamethasone	8 mg (PO)	ONCE a day (or in divided doses) with or after food. Note: dexamethasone doses on day 2 and 3 may not be required and may be reduced or omitted at the clinicians discretion. **

Day 8		
Loratadine	10 mg (PO)	60 minutes before treatment
Dexamethasone	4 mg (PO)	60 minutes before treatment
Cetuximab	250 mg/m^2 (IV infusion)	over 60 minutes *

Cycle 2 and further cycles

Day 1		
Loratadine	10 mg (PO)	60 minutes before treatment
Dexamethasone	8 mg (PO)	60 minutes before treatment
Cetuximab	250 mg/m^2 (IV infusion)	over 60 minutes *
Palonosetron	0.25 mg (IV bolus)	30 minutes before chemotherapy
Irinotecan	180 mg/m^2 (IV infusion)	in 250 mL to 500 mL glucose 5% over 90 minutes

Day 2 and 3		
Dexamethasone	8 mg (PO)	ONCE a day (or in divided doses) with or after food. Note: dexamethasone doses on day 2 and 3 may not be required and may be reduced or omitted at the clinicians discretion. **

Day 8		
Loratadine	10 mg (PO)	60 minutes before treatment
Dexamethasone	4 mg (PO)	60 minutes before treatment
Cetuximab	250 mg/m^2 (IV infusion)	over 60 minutes *

* Although the product information recommends a maximum cetuximab infusion rate of 5 mg/min for the loading dose and 10 mg/min for subsequent doses, rates of 2 hours for the loading dose and 60 minutes for subsequent doses were used in clinical trials.[1, 2]

** Link to ID 7 Prevention of chemotherapy induced nausea and vomiting

Frequency: 14 days

Cycles: Continuous until disease progression or unacceptable toxicity

Indications and patient population

- RAS wild-type metastatic colorectal cancer refractory to first-line chemotherapy.

Notes:

- All patients should be tested for RAS mutations. Patients with mutant or unknown RAS status should not receive an EGFR antagonist as it may be harmful.
- Presence of a BRAF mutation has been identified as a marker of poorer prognosis, and potentially predictive of resistance to EGFR antagonists.[3]
- Consider side of primary tumour when prescribing treatment as patients with a right sided tumour may not benefit from the addition of an EGFR antagonist to chemotherapy.

Clinical information

Venous access required	IV cannula (IVC) or central venous access device (CVAD) is required to administer this treatment. Read more about central venous access device line selection
Hypersensitivity/infusion related reaction	High risk with cetuximab. The risk for anaphylactic reactions is increased in patients with a history of allergy to red meat or tick bites, or positive IgE antibody test results against cetuximab (α-1-3- galactose). Read more about Hypersensitivity reaction
Premedication	The product information states that premedication is required for this treatment. Please refer to the treatment schedule for suggested premedication regimen. This may be substituted to reflect institutional policy.
Premedication	Consider atropine 0.3 to 0.6 mg IV or SC prior to irinotecan administration as required to help prevent irinotecan induced cholinergic side effects (atropine should not be used in patients with glaucoma).
Emetogenicity MODERATE	Suggested default antiemetics have been added to the treatment schedule, and may be substituted to reflect institutional policy. A steroid has been included both as an antiemetic and premedication for hypersensitivity in this protocol. For patients with a prior episode of chemotherapy induced nausea or vomiting, a NK1 receptor antagonist may be available on the PBS in combination with a $5HT_3$ antagonist and steroid. 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
Diarrhoea (early onset) and cholinergic syndrome	Early onset diarrhoea and other cholinergic symptoms such as rhinitis, hypersalivation, miosis, lacrimation, diaphoresis, flushing, and abdominal cramping can occur during or within 24 hours of administration of irinotecan. Symptoms may be treated with atropine 0.3 to 0.6 mg IV or SC as needed, repeated up to a maximum dose of 1.2 mg (unless clinically contraindicated). Patients 65 years of age and above should be closely monitored due to a greater risk of early diarrhoea observed in this population. Read more about treatment induced diarrhoea

Diarrhoea (late onset)	Irinotecan induced diarrhoea can be life threatening and requires immediate management. Ensure patients have sufficient antidiarrhoeal (e.g. loperamide) and appropriate instructions should this adverse event occur. Note: If prescribing loperamide, the recommended maximum daily dose of 16 mg of loperamide can be exceeded. Read more about treatment induced diarrhoea
Gilbert's syndrome	Patients with Gilbert's syndrome should have their dose of irinotecan reduced. There is no clear dosing strategy; however based on the area under the concentration-time curve of SN-38, Innocenti et al (2006) recommend a 20% dose reduction of irinotecan. Read more about Gilbert's syndrome
Acneiform rash	EGFR targeted therapies are commonly associated with acneiform rash. The rash may peak in the first 2 to 4 weeks. Ensure advice on skin care (i.e. moisturisers) and sunscreen is provided. Prophylactic or early therapy with a tetracycline antibiotic (e.g. doxycycline) and 1% hydrocortisone cream to affected areas may be considered. Patients developing skin rash should be monitored for infectious sequelae, dose reductions and/or delay or cessation of treatment may be required. Read more about acneiform rash associated with EGFR inhibitors
Pulmonary toxicity	Interstitial lung disease (ILD) has been reported in patients treated with EGFR inhibitors. Read more about pulmonary toxicity associated with anti-cancer drugs.
Blood tests	FBC, EUC, LFTs, calcium and magnesium at baseline and monthly during treatment or as clinically indicated. Magnesium wasting syndrome is associated with this therapy and patients should be monitored for hypomagnesaemia and accompanying hypocalcaemia for up to 8 weeks after completion of treatment.
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 consider reducing irinotecan by 25% for subsequent cycles
Febrile neutropenia	Delay treatment until recovery and consider reducing irinotecan 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 guidelines.
50 to less than 75	Delay treatment until recovery
less than 50	Delay treatment until recovery and consider reducing irinotecan by 25% for subsequent cycles

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

Hepatic impairment	
Hepatic dysfunction	
Minimal	Reduce irinotecan by 25%
Mild	Reduce irinotecan by 50%
Moderate/Severe	Omit irinotecan
Gilbert's syndrome	Reduce irinotecan by 20%

Diarrhoea	
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 irinotecan by 25% 3rd occurrence: Reduce irinotecan by 50% 4th occurrence: Omit irinotecan
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:

Diarrhoea	
	1st occurrence: Reduce irinotecan by 50% 2nd occurrence: Omit irinotecan

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

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*

Cetuximab		
	Interaction	**Clinical management**
Chemotherapeutic agents	Increased incidence of specific adverse reactions when used in combination	Monitor closely (e.g. for cardiac toxicity and hand-foot syndrome when combined with fluoropyrimidines; for severe diarrhoea with capecitabine and oxaliplatin)

Irinotecan		
	Interaction	**Clinical management**
CYP3A4 and P-gp inhibitors (e.g. amiodarone, aprepitant, azole-antifungals, ritonavir, lapatinib, nilotinib, sorafenib, macrolides, ciclosporin, grapefruit juice etc.)	Increased toxicity of irinotecan possible due to reduced clearance	Avoid combination or monitor for irinotecan toxicity (Ketoconazole contraindicated and should be discontinued at least 1 week prior to irinotecan)
CYP3A4 and P-gp inducers (e.g. carbamazepine, phenytoin, phenobarbitone, rifampicin, St John's wort, dexamethasone etc.)	Reduced efficacy of irinotecan possible due to increased clearance	Avoid combination or monitor for decreased clinical response to irinotecan (St John's wort contraindicated; substituting non-enzyme inducing antiepileptics (e.g. clonazepam, diazepam, lorazepam) at least 1 week prior to irinotecan should be considered)
Atazanavir	Increased toxicity of irinotecan possible due to reduced clearance caused by inhibition of both CYP3A4 and UGT1A1 by atazanavir	Avoid combination or monitor for irinotecan toxicity
Smoking	Reduced efficacy of irinotecan possible due to increased clearance caused by induction of both CYP3A4 and UGT1A1 by smoking	Monitor for decreased clinical response to irinotecan in patients who continue to smoke; no specific dosing recommendations are available

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

Administration

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

product information monographs via the TGA website for further information.

Day 1

Approximate treatment time: 3 hours

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.

Prime IV line(s).

Insert IV cannula or access TIVAD or CVAD.

Pre treatment medication

Verify premedication taken or administer as prescribed.

Verify dexamethasone taken or administer as prescribed.

Treatment - Time out

Cetuximab

- administer via IV infusion over 2 hours (loading dose only)
- if well tolerated subsequent doses over 60 minutes
- although the product information recommends a maximum cetuximab infusion rate of 5 mg/min for the loading dose and 10 mg/min for subsequent doses, rates of 2 hours for the loading dose and 60 minutes for subsequent doses were used in clinical trials
- observe for hypersensitivity reaction
- flush with ~ 50 mL of sodium chloride 0.9%
- patient should be observed for an hour post infusion. If patient has a hypersensitivity reaction – stop infusion immediately. Review by medical officer; if re-challenge indicated, pre medicate patient and recommence infusion over 2 hours, then patient should be observed for an hour post infusion.

The product information recommends waiting one hour post completion of the cetuximab infusion, before commencing concomitant chemotherapy. However, to reflect clinical practice, if no reactions are observed with the first two doses, concomitant chemotherapy may be administered immediately following cetuximab at the discretion of the treating physician.

Pre treatment medication

Verify antiemetics taken or administer as prescribed.

Chemotherapy - Time out

Irinotecan

Prior to administration:

- administer atropine premedication if required
- patient vital signs should be closely monitored post atropine administration as atropine can cause tachycardia, heart arrhythmias, hypertension and angina.

Administer irinotecan (irritant):

- via IV infusion over 90 minutes
- protect from light
- flush with ~ 100 mL of sodium chloride 0.9%
- observe patient for cholinergic symptoms
- if patient develops early onset diarrhoea and other cholinergic symptoms (such as rhinitis, increased salivation, miosis, lacrimation, diaphoresis, flushing) - stop infusion, monitor vital signs and review by medical officer.

Remove IV cannula and/or deaccess TIVAD or CVAD.

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

Day 8

Approximate treatment time: 2 hours

Handling of monoclonal antibodies and waste management

Safe administration

General patient assessment prior to each day of treatment.

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

Prime IV line(s).

Insert IV cannula or access TIVAD or CVAD.

Pre treatment medication

Verify premedication taken or administer as prescribed.

Verify dexamethasone taken or administer as prescribed.

Treatment - Time out

Cetuximab

- administer via IV infusion
- if first dose was well tolerated, administer over 60 minutes
- although the product information recommends a maximum cetuximab infusion rate of 5 mg/min for the loading dose and 10 mg/min for subsequent doses, rates of 2 hours for the loading dose and 60 minutes for subsequent doses were used in clinical trials
- flush with ~ 50 mL of sodium chloride 0.9%
- observe for hypersensitivity reaction
- If patient has a hypersensitivity reaction – stop infusion immediately. Review by medical officer; if re-challenge indicated, pre medicate patient and recommence infusion over 2 hours, then patient should be observed for an hour post infusion.

Remove IV cannula and/or deaccess TIVAD or CVAD.

Discharge information

Antiemetics

- Antiemetics as prescribed.

Antidiarrhoeals

- Antidiarrhoeals (e.g. loperamide) as prescribed with written instructions on how to manage this side effect and 24 hour emergency contact.

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)	
Hypersensitivity reaction	Anaphylaxis and infusion related reactions can occur with this treatment. Read more about hypersensitivity reaction
Nausea and vomiting	Read more about prevention of treatment induced nausea and vomiting
Diarrhoea and cholinergic syndrome (early onset) associated with irinotecan	Cholinergic syndrome can occur during or shortly after commencing the irinotecan infusion, or within 24 hours of administration of the drug. It is characterised by diarrhoea, rhinitis, hypersalivation, miosis, lacrimation, diaphoresis, flushing, and abdominal cramping. Read more about treatment induced diarrhoea

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 (late onset) associated with irinotecan	Late onset of diarrhoea after 24 hours post irinotecan administration can be life threatening and requires immediate treatment. Read more about treatment induced diarrhoea
Fatigue	Read more about fatigue
Anorexia	Loss of appetite accompanied by decreased food intake. Read more about anorexia
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
Acneiform rash	A skin rash, characterised by papules and pustules affecting the face and upper body. This is commonly associated with small molecule EGFR inhibitors and some monoclonal antibodies (e.g. cetuximab, panitumumab). Read more about acneiform rash associated with EGFR inhibitors

Late (onset weeks to months)	
Anaemia	Abnormally low levels of red blood cells (RBCs) or haemoglobin in the blood. Read more about anaemia
Alopecia - partial	Hair thinning and/or patchy hair loss. Patients can also experience mild to moderate discomfort of the hair follicles, and rarely pain as the hair is falling out. Read more about alopecia and scalp cooling
Paronychia	An inflammatory reaction involving the folds of the skin surrounding the fingernail. Read about nail toxicities
Pulmonary toxicity	Pulmonary toxicity may include damage to the lungs, airways, pleura and pulmonary circulation. Read more about pulmonary toxicity associated with anti-cancer drugs

Evidence

A search of the literature did not find strong evidence to support the use of cetuximab and irinotecan in the treatment of metastatic colorectal cancer. The expert reference panel supported publication of the protocol on the basis of the information summarised below.

Monoclonal antibodies (mABs) targeting the epidermal growth factor receptor (EGFR) prolong survival in patients with metastatic

colorectal cancer (mCRC) harbouring KRAS exon 2 wild type tumours. Recent evidence suggest that other RAS mutations (exon 3 and 4 of KRAS and exons 2, 3, 4 of NRAS) may also be predictive of resistance[4,5] and many studies suggest that anti-EGFR mAB treatment may have a detrimental effect on PFS and OS in patients with NRAS mutations.[6] As such, cetuximab should not be used in patients with any RAS mutations.

The 2 weekly schedule of irinotecan used in this protocol is preferred to 3 weekly irinotecan as it is associated with less toxicity and is the schedule currently used in clinical trials.

The incremental benefit and additional toxicity attributable to combination treatment compared with best supportive care in individuals with RAS wild type tumours has not been determined in a head to head study. Conclusions regarding the benefit of combination treatment rely on a series of indirect comparisons and extrapolations, each of which raises uncertainty regarding benefit and risk.

The FOLFIRI regimen is preferred to single agent irinotecan as second-line therapy for mCRC as it is associated with less toxicity in particular grade3/4 diarrhoea and alopecia.[7] (link to FOLFIRI + Cetuximab ID 1212 protocol)

Source	Study and year published	Supports use	Is the dose and regimen consistent with the protocol?	Comments
Phase III trials	EPIC 2008[1]	**Yes**	No	Irinotecan 350 mg/m^2 q21 days + weekly cetux 250 mg/m^2 No selection for KRAS; subset analysis not representative for overall efficacy results No OS benefit possibly due to crossover
Phase II trials	BOND 2004[8]	**Yes**	Yes	Various schedules of irinotecan used (weekly, 2 weekly and 3 weekly) No selection for KRAS No OS benefit
	MABEL 2008[2]	**Yes**	Yes	Various schedules of irinotecan used (weekly, 2 weekly and 3 weekly)
Observational studies	-	**N/A**	-	-
Case series	-	**N/A**	-	-
Guidelines	**Date published/revised**	**Supports use**	**Is the dose and regimen consistent with the protocol?**	**Comments**
NCCN	v.1 2014	**Yes**	Yes	
BCCA	Sept 2013	**Yes**	No	Irinotecan 180 mg/m^2 + cetux 500 mg/m^2 q14 days
CCO	March 2013	**Yes**	Yes	

N/A = not available

Efficacy

The rate of response in the combination-therapy group was significantly higher than that in the monotherapy group (22.9% vs.

10.8%; p=0.007). The median time to progression was significantly greater in the combination-therapy group (4.1 vs 1.5 months; p<0.001). The median survival was 8.6 months in the combination-therapy group and 6.9 months in the monotherapy group (p=0.48).[8]

Kaplan-Meier curves for (A) time to disease progression and (B) overall survival[8]

(A)

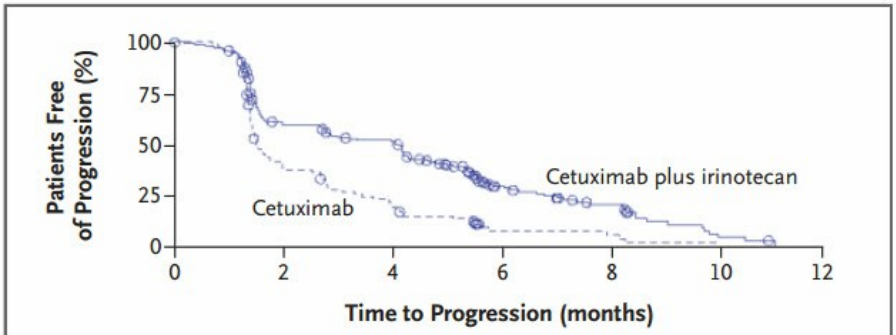


Figure 2. Time to Disease Progression in the Two Study Groups.
The hazard ratio for disease progression in the combination-therapy group as compared with the monotherapy group was 0.54 (95 percent confidence interval, 0.42 to 0.71) (P<0.001 by the log-rank test). The points on the curves represent the dates on which a patient's data were censored.

(B)

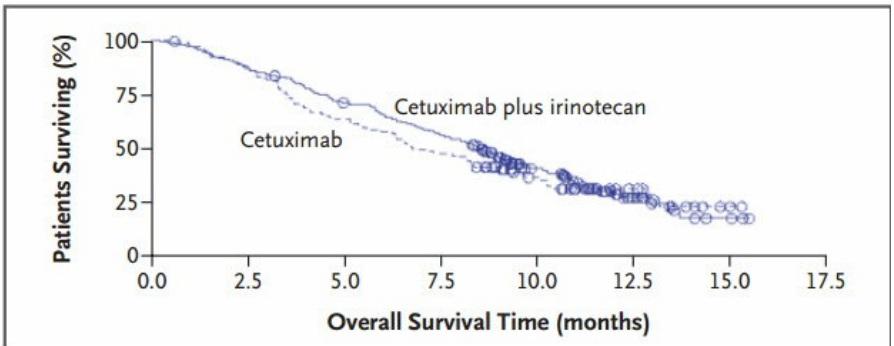


Figure 3. Overall Survival in the Two Study Groups.
The hazard ratio for death in the combination-therapy group as compared with the monotherapy group was 0.91 (95 percent confidence interval, 0.68 to 1.21) (P=0.48 by the log-rank test). The points on the curves represent the dates on which a patient's data were censored.

Toxicity

Grade 3 or 4 Adverse Events[8]	Cetuximab + Irinotecan (n=212) (%)	Cetuximab (n=115) (%)	*p*-value
Anaemia	4.7	2.6	0.55
Neutropenia	9.4	0	<0.001
Thrombocytopenia	0.5	0.9	1.00
Diarrhoea	21.2	1.7	<0.001
Asthenia	13.7	10.4	0.49
Acne-like rash	9.4	5.2	0.20
Nausea and vomiting	7.1	4.3	0.47

Grade 3 or 4 Adverse Events[8]	Cetuximab + Irinotecan (n=212) (%)	Cetuximab (n=115) (%)	*p*-value
Abdominal pain	3.3	5.2	0.39
Stomatitis	2.4	0.9	0.67
Dyspnoea	1.4	13.0	<0.001
Fever	2.4	0	0.17
Hypersensitivity reaction	0	3.5	0.01
Death	0	0	1.00

Note: 4 patients randomly assigned to combination group did not receive irinotecan and were evaluated for safety in the monotherapy group. 2 patients randomly assigned to combination group did not receive any study medication.

References

1 Sobrero, A. F., J. Maurel, L. Fehrenbacher, et al. 2008. "EPIC: phase III trial of cetuximab plus irinotecan after fluoropyrimidine and oxaliplatin failure in patients with metastatic colorectal cancer." J Clin Oncol 26(14):2311-2319.

2 Wilke, H., R. Glynne-Jones, J. Thaler, et al. 2008. "Cetuximab plus irinotecan in heavily pretreated metastatic colorectal cancer progressing on irinotecan: MABEL Study." J Clin Oncol 26(33):5335-5343.

3 Nott, L., M. Khattak, T. Price, et al. Molecular pathology and biomarkers – implications for systemic therapy. Available from https://wiki.cancer.org.au/australia/Guidelines:Colorectal_cancer/Systemic_therapy_molecular_pathology. In: Cancer Council Australia Colorectal Cancer Guidelines Working Party.

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History

Version 5

Date	Summary of changes
24/03/2021	Cetuximab infusion rate information in detailed treatment schedule and administration section updated to include maximum infusion rates as per product information. Version number increased to V.5.
20/10/2022	Protocol reviewed electronically by Medical Oncology Reference Committee. No changes. Next review in 4 years.

Version 4

Date	Summary of changes

04/12/2020	Protocol reviewed by the Medical Oncology Reference Committee meeting on 23rd October 2020. Group consensus was to supersede this protocol as cetuximab two weekly is as efficacious and improves patient safety. Version number updated to V.4. Next review in 2 years.

Version 3

Date	Summary of changes
13/09/2013	New protocol discussed at the Medical Oncology Reference Committee meeting.
09/10/2013	Approved and published on eviQ.
20/06/2014	Indication updated 'K-RAS wild type' replaced with 'RAS wild type'. PHC view removed.
27/03/2015	Protocol reviewed by email survey. Evidence updated to include statement on RAS mutations. Next review in 2 years.
18/02/2016	Discussion with Medical Oncology Reference Committee Chairs and protocol to be reviewed every 5 years. Next review due in 4 years.
07/11/2016	The following change made post Medical Oncology Reference Committee meeting held on 21 October 2016: link to AGTIG and ANZCTR added.
19/12/2016	The following sentence added to Indications and Patient population after discussion at Medical Oncology Reference Committee meeting held on 21 October 2016: Consider BRAF mutation status and side of primary tumour when prescribing treatment as patients with a BRAF mutation and/or right sided tumour may not benefit from the addition of cetuximab to chemotherapy and another regimen should be considered.
31/05/2017	Transferred to new eviQ website. Version number change to V.2. Hepatitis screening changed to not recommended.
16/02/2018	BRAF note in indication updated by Medical Oncology Reference Committee.
10/05/2018	Haematological dose modifications updated as per consensus of the expert clinician group. Version number changed to V.3.
22/06/2018	Antiemetics updated to be in line with international guidelines. Note to dexamethasone added.
04/07/2018	Indications reworded for consistency across all colorectal EGFR monoclonal antibody protocols.
25/09/2020	Protocol reviewed electronically by the Medical Oncology Reference committee. Nil changes. Next review in 2 years.

First approved: 9 October 2013
Last reviewed: 20 October 2022
Review due: 31 December 2026
Superseded: 4 December 2020

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/1567
16 Jul 2023

Patient information - Bowel cancer metastatic - Cetuximab (weekly) and irinotecan (two weekly)

Patient's name:

Your treatment

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

Cetuximab and irinotecan			
This treatment cycle is repeated every 14 days. Your doctor will advise you of the number of treatments you will have.			
Day	**Treatment**	**How it is given**	**How long it takes**
1	**Cetuximab** (*se-TUK-see-mab*) **Irinotecan** (*eye-ri-noe-TEE-kan*)	By a drip into a vein	About 4 to 5 hours
8	**Cetuximab**	By a drip into a vein	About 2 hours

When to get help

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

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

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

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

Other information about your treatment

Changes to your dose or treatment delays

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

Blood tests and monitoring

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

Other medications given during this treatment

- **Anti-sickness (anti-nausea) medication:** you may be given some anti-sickness medication. Make sure you take this medication as your doctor or nurse tells you, even if you don't feel sick. This can help to prevent the sickness starting.
- **Antidiarrhoeals:** you will be given some medication called loperamide to treat the diarrhoea. See the *Side effects* section below for further information about diarrhoea and for instructions on how and when to take the loperamide.
- **Medication for skin rash:** you may be given some medication (which may include a steroid cream, an antibiotic cream and/or oral antibiotics) to prevent or treat skin rash. Your doctor or nurse will tell you how to take or use these medications.
- **Cetuximab premedication:** before your treatment with cetuximab you will need to take some tablets called a premedication to help prevent you from having a reaction to the cetuximab.

Superseded treatments

This treatment is superseded meaning that better treatments have taken its place. Uncommonly superseded treatments are still used. Your doctor will explain why this treatment has been selected for you.

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)	

Allergic reaction	• Allergic reactions are uncommon but can be life threatening.
	• **If you feel unwell during the infusion or shortly after it, or:**
	  ◦ **get a fever, shivers or shakes**
	  ◦ **feel dizzy, faint, confused or anxious**
	  ◦ **start wheezing or have difficulty breathing**
	  ◦ **have a rash, itch or redness of the face**
	
	<u>While you are in hospital:</u> Tell your doctor or nurse immediately.
	<u>After you leave:</u> Contact your doctor or nurse immediately, or go to the nearest hospital Emergency Department.

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.**

Diarrhoea (early onset)	• You may get bowel motions (stools, poo) that are more frequent or more liquid (diarrhoea).
	• You may also get:
	  ◦ bloating, cramping or pain
	  ◦ increased saliva, a runny nose or watery eyes
	  ◦ sweating or flushing.
	• These symptoms are caused by the drug irinotecan. They can occur during or shortly after the drug has been given.
	• **Tell your doctor or nurse immediately if you develop any of these symptoms.**

Early (onset days to weeks)	

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

Low platelets (thrombocytopenia)	• This treatment lowers the amount of platelets in your blood. Platelets help your blood to clot. When they are low, you are at an increased risk of bleeding and bruising. • Try not to bruise or cut yourself. • Avoid contact sport or vigorous exercise. • Clear your nose by blowing gently. • Avoid constipation. • Brush your teeth with a soft toothbrush. • Don't take aspirin, ibuprofen or other similar anti-inflammatory medications unless your doctor tells you to. • Tell your doctor or nurse if you have any bruising or bleeding. • **Tell your doctor or nurse immediately, or go to your nearest hospital Emergency Department if you have any uncontrolled bleeding.**
Diarrhoea (late onset)	• You may get bowel motions (stools, poo) that are more frequent or more liquid (diarrhoea). • You may also get bloating, cramping or pain. • These symptoms are caused by the drug irinotecan. This can become very serious and life threatening if not treated quickly and properly. • Take your antidiarrhoea medication, loperamide, as prescribed: When the diarrhoea starts, take 4 mg (this is 2 tablets/capsules), then take one tablet/capsule (2 mg) every 2 hours during the day and 2 tablets/capsules (4 mg) every 4 hours at night while you still have diarrhoea and until the diarrhoea has stopped for 12 hours. You should not take loperamide at these doses for more than 48 hours. • 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 if you get any of the symptoms listed above.** • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you have diarrhoea for more than 24 hours, any blood in your bowel motions, or a temperature of 38°C or higher.**
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.**
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.

Mouth pain and soreness (mucositis)	• You may have: ◦ bleeding gums ◦ mouth ulcers ◦ a white coating on your tongue ◦ pain in the mouth or throat ◦ difficulty eating or swallowing. • Avoid spicy, acidic or crunchy foods and very hot or cold food and drinks. • Try bland and soft foods. • Brush your teeth gently with a soft toothbrush after each meal and at bedtime. If you normally floss continue to do so. • Rinse your mouth after you eat and brush your teeth, using either: ◦ 1/4 teaspoon of salt in 1 cup of warm water, or ◦ 1/4 teaspoon of bicarbonate of soda in 1 cup of warm water • Ask your doctor or nurse for eviQ patient information - Mouth problems during cancer treatment. • **Tell your doctor or nurse if you get any of the symptoms listed above.**
Skin rash (acneiform rash)	• You may get an acne-like skin rash. • Your skin may become red and dry. • Moisturise your skin with a gentle non-perfumed moisturising cream like sorbolene or aqueous cream. • Do not scratch your skin. • Do not use over-the-counter acne treatments as these can make the rash worse. • Protect your skin from the sun by wearing sun-protective clothing, a wide-brimmed hat, sunglasses and sunscreen of SPF 50 or higher. • You may be given medications to prevent the rash. • **Tell your doctor or nurse as soon as possible if you notice any changes to the rash like itching, pain or pus forming**

Late (onset weeks to months)	
Low red blood cells (anaemia)	• You may feel dizzy, light-headed, tired and appear more pale than usual. • Tell your doctor or nurse if you have any of these signs or symptoms. You might need a blood transfusion. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you have any chest pain, trouble breathing, or feel like your heart is racing.**
Hair thinning	• Your hair may become dry and may break easily. • You may lose some of your hair. • Use a gentle shampoo and a soft hairbrush. • Take care with hair products like hairspray, hair dye, bleaches and perms. • Protect your scalp from the cold with a hat or scarf. • Protect your scalp from the sun with a hat and sunscreen of SPF 50 or higher. • Ask your doctor or nurse about the Look Good Feel Better program (www.lgfb.org.au)
Swelling and pain around the fingernails or toenails (paronychia)	• The skin around your nails may swell and become painful. • Apply a warm compress or soak your nails for 15 minutes, 3 or 4 times a day, in warm water or a mixture of equal parts vinegar and water. • Keep your nails clean and short. • Avoid things like biting your fingernails, getting a manicure, pedicure or false nails. • Wear gloves when you wash the dishes, work in the garden, or clean the house. • Tell your doctor or nurse if you get any of the symptoms listed above.
Lung problems	• Lung problems are rare, but can be serious. They may occur throughout treatment or after the completion of treatment. • You may get: ◦ shortness of breath ◦ fever ◦ dry cough ◦ wheezing ◦ fast heartbeat ◦ chest pain. • Your doctor will monitor how well your lungs are working during your treatment. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you have chest pain or become short of breath.**

General advice for people having cancer treatment

Chemotherapy safety

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

Blood clot risk

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

Medications and vaccinations

- Before you start treatment, tell your doctor about any medications you are taking, including vitamins or herbal supplements.
- Don't stop or start any medications during treatment without talking to your doctor and pharmacist first.
- Paracetamol is safe to take if you have a headache or other mild aches and pains. It is recommended that you avoid taking aspirin, ibuprofen and other anti-inflammatory type medications for pain while you are having treatment. However, if these medications have been prescribed by your doctor, do not stop taking them without speaking with your doctor.
- Vaccinations such as flu and tetanus vaccines are safe to receive while having treatment. Do not have any live vaccines during

your treatment or for 6 months after it finishes. If you are unsure, check with your doctor before you have any vaccinations.
- People you live with should be fully vaccinated, including having live vaccines according to the current vaccination schedule. Extra care needs to be taken with hand washing and careful disposal of soiled nappies for infants who have recently received the rotavirus vaccine.

Other medical and dental treatment

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

Diet

- While you are receiving this treatment it is important that you try to maintain a healthy diet.
- Grapefruit and grapefruit juice can interact with your medication and should be avoided while you are on this treatment.
- Speak to your doctor or nurse about whether drinking alcohol is safe with your treatment.
- If you have any concerns about recent weight loss or weight gain or questions about your diet, ask to speak to a dietitian.

Fertility

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

Pregnancy and breastfeeding

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

Sex life and sexuality

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

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

Bowel cancer information

- Australian Council of Stoma Associations – australianstoma.com.au
- Australian Government Bladder and Bowel – bladderbowel.gov.au
- Australian Government Department of Health & Ageing Stoma appliance scheme – health.gov.au/internet/main/publishing.nsf/Content/Stoma+Appliance+Scheme-1

- Bowel Cancer Australia – bowelcanceraustralia.org
- National Public Toilet map – toiletmap.gov.au
- Recovering after Pelvic Radiation Therapy: A guide for women – https://www.targetingcancer.com.au/useful-resources/recovering-after-pelvic-radiation-therapy-a-guide-for-women/

General cancer information and support

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

Quit smoking information and support

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

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

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