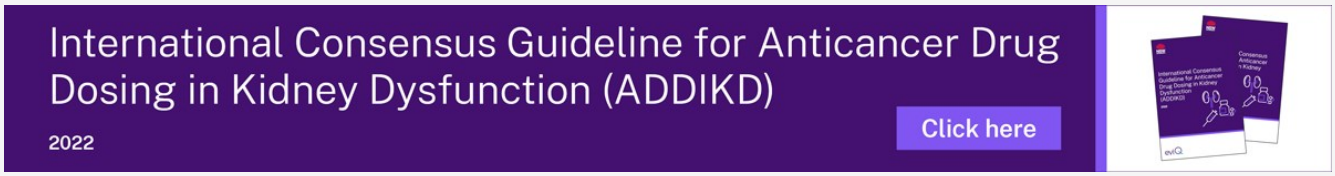
Colorectal metastatic FOLFOX6 (modified) (fluorouracil leucovorin oxaliplatin) and pANITUMumab

ID: 1542 v.5 **Endorsed**

⚠ 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

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 pANITUMumab
- Colorectal metastatic FOLFOX6 (modified) (fluorouracil leucovorin oxaliplatin)

Treatment schedule - Overview

Cycle 1 and further cycles

Drug	Dose	Route	Day
pANITUMumab	6 mg/kg	IV infusion	1
Oxaliplatin	85 mg/m^2 *	IV infusion	1
Calcium folinate (Leucovorin)	50 mg *	IV bolus	1
Fluorouracil	400 mg/m^2	IV	1
Fluorouracil	2,400 mg/m^2	CIV via pump over 46 hours	1

* The dose of oxaliplatin and calcium folinate (Leucovorin®) in this protocol have been modified from the original clinical trial doses (100 mg/m² to 85 mg/m² for oxaliplatin and 200 mg/m² to 50 mg for calcium folinate (Leucovorin®) based on reference committee consensus. Refer to discussion on FOLFOX protocols , calcium folinate (Leucovorin®)) and evidence section for more information. Consideration should be given to limiting oxaliplatin to 6 cycles.[1] If oxaliplatin is continued, oxaliplatin should be limited to 12 cycles. Maintenance therapy may be continued in patients who are stable or responding to treatment.

Frequency: 14 days

Cycles: Continuous until disease progression or unacceptable toxicity

Notes:
Although the PRIME trial used FOLFOX4 as the chemotherapy backbone,[2] the FOLFOX6 (Modified) regimen is comparable to the FOLFOX4 regimen and is widely accepted (link to discussion on FOLFOX protocols).

Drug status: Fluorouracil, leucovorin and oxaliplatin are on the PBS general schedule

Panitumumab is PBS authority

Cost: ~ $2,650 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 and further cycles

Day 1		
Netupitant	300 mg (PO)	60 minutes before chemotherapy (fixed dose preparation with palonosetron)
Palonosetron	0.5 mg (PO)	60 minutes before chemotherapy (fixed dose preparation with netupitant)
Dexamethasone	8 mg (PO)	60 minutes before chemotherapy
pANITUMumab	6 mg/kg (IV infusion)	in 100 mL sodium chloride 0.9% over 60 minutes (for doses over 1g dilute in 150mL sodium chloride 0.9% and infuse over 90 minutes). If first dose is tolerated, subsequent infusions over 30 to 60 minutes
Oxaliplatin	85 mg/m^2 (IV infusion)	in 250 mL to 500 mL glucose 5% over 2 hours *
Calcium folinate (Leucovorin)	50 mg (IV bolus)	over 1 to 2 minutes *
Fluorouracil	400 mg/m^2 (IV)	over 3 to 5 minutes
Fluorouracil	2,400 mg/m^2 (CIV)	via ambulatory infusion pump over 46 hours
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 **

* The dose of calcium folinate (Leucovorin®) and oxaliplatin have both been modified in this protocol from the original FOLFOX6 doses (200 mg/m² to 50 mg for leucovorin and 100 mg/m² to 85 mg/m² for oxaliplatin). A discussion regarding the effect of dosing on outcome can be found in the calcium folinate dose document. Consideration should be given to limiting oxaliplatin to 6 cycles.[1] If oxaliplatin is continued, oxaliplatin should be limited to 12 cycles. Maintenance therapy may be continued in patients who are stable or responding to treatment.

** Dexamethasone doses on day 2 and 3 may not be required and may be reduced or omitted at the clinicians discretion. Link to Prevention of chemotherapy induced nausea and vomiting.

Frequency: 14 days

Cycles: Continuous until disease progression or unacceptable toxicity

Indications and patient population

- First-line treatment of RAS wild-type metastatic colorectal cancer.

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.
- Not recommended for patients who have progressed on cetuximab therapy.

Clinical information

Safety alert fluoropyrimidines	Fluoropyrimidines can be administered by different routes and schedules with each method having associated increased risk of certain side effects. Fluoropyrimidine overdose or overexposure is a rare but potentially life threatening side effect of this drug class and can occur by any route of administration. An antidote is available and highly effective if given within 96 hours. Read more about the medication safety alert for infusional fluorouracil and fluoropyrimidine overdose or overexposure
Venous access	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 oxaliplatin. Read more about Hypersensitivity reaction
Emetogenicity MODERATE	Suggested default antiemetics have been added to the treatment schedule, and may be substituted to reflect institutional policy. A NK1 receptor antagonist and a 5HT3 receptor antagonist in combination with dexamethasone are available on the PBS for primary prophylaxis of oxaliplatin induced nausea and vomiting. Ensure that patients also have sufficient antiemetics for breakthrough emesis: Metoclopramide 10 mg three times a day when necessary (maximum of 30 mg/24 hours, up to 5 days) OR Prochlorperazine 10 mg PO every 6 hours when necessary. Read more about preventing anti-cancer therapy induced nausea and vomiting
Cardiac toxicity	Cardiac toxicity is a serious complication that can occur during treatment with fluorouracil. Patients treated with fluorouracil, especially those with a prior history of cardiac disease or other risk factors, should be carefully monitored during therapy. Read more about cardiac toxicity associated with anti-cancer drugs
Laryngopharyngeal dysaesthesia associated with oxaliplatin	Sensation of loss of breathing related to oxaliplatin without objective evidence of respiratory distress. Symptoms are often precipitated by exposure to cold. Read more about laryngopharyngeal dysaesthesia associated with oxaliplatin
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
Severe enteropathy associated with fluoropyrimidine	Severe enteropathy has been reported among patients with stage II/III colon cancer treated with fluoropyrimidine chemotherapy with or without oxaliplatin. Patients treated with fluoropyrimidine should be closely monitored for diarrhoea and aggressively managed. Read more about severe enteropathy associated with fluorouracil in colorectal cancer
Diarrhoea	Antidiarrhoeals (e.g. loperamide) are usually prescribed with this treatment. Read more about treatment induced diarrhoea

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
Peripheral neuropathy	Assess prior to each treatment and dose reduce if appropriate. Read more about peripheral neuropathy Link to chemotherapy-induced peripheral neuropathy screening tool
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.
Thromboembolism	Venous thromboembolic events have been observed in patients with this treatment.
Blood tests	FBC, EUC, LFT's, calcium and magnesium at baseline and prior to each cycle. INR 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.
- The dose of calcium folinate (Leucovorin®) remains fixed at 50 mg and is delayed or omitted if fluorouracil bolus is delayed or omitted.

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 oxaliplatin and fluorouracil by 25% for subsequent cycles
Febrile neutropenia	Delay treatment until recovery and consider reducing oxaliplatin and fluorouracil 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 oxaliplatin and fluorouracil by 25% for subsequent cycles

Renal impairment	
Creatinine clearance (mL/min)	
30 to 50	Reduce fluorouracil by 25%
less than 30	Omit oxaliplatin and reduce fluorouracil by 50% or withhold chemotherapy

Hepatic impairment	
Hepatic dysfunction	
Mild	No dose modifications necessary
Moderate	Reduce fluorouracil by 25%
Severe	Reduce fluorouracil by 50%

Peripheral neuropathy	
Grade 2 which is present at the start of the next cycle	Reduce oxaliplatin by 25%; if persistent, reduce oxaliplatin by 50%
Grade 3 or Grade 4	Omit oxaliplatin
Acute laryngo-pharyngeal dysaesthesia	Increase oxaliplatin infusion time to 6 hours

Mucositis and stomatitis	
Grade 2	Delay treatment until toxicity has resolved to Grade 1 or less and reduce doses for subsequent cycles as follows: 1st occurrence: No dose reduction 2nd occurrence: Reduce oxaliplatin and fluorouracil by 25%

Mucositis and stomatitis	
	3rd occurrence: Reduce oxaliplatin and fluorouracil by 50% 4th occurrence: Withhold chemotherapy
Grade 3 or Grade 4	Delay treatment until toxicity has resolved to Grade 1 or less and reduce doses for subsequent cycles as follows: 1st occurrence: Reduce oxaliplatin and fluorouracil by 50% 2nd occurrence: Withhold chemotherapy

Diarrhoea	
Grade 2	Delay treatment until toxicity has resolved to Grade 1 or less and reduce doses for subsequent cycles as follows: 1st occurrence: No dose reduction 2nd occurrence: Reduce oxaliplatin, fluorouracil and panitumumab by 25% 3rd occurrence: Reduce oxaliplatin, fluorouracil and panitumumab by 50% 4th occurrence: Cease chemotherapy
Grade 3 or Grade 4	Delay treatment until toxicity has resolved to Grade 1 or less and reduce doses for subsequent cycles as follows: 1st occurrence: Reduce oxaliplatin, fluorouracil and panitumumab by 50% 2nd occurrence: Cease chemotherapy

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

Rash acneiform	
Grade 3 or greater	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 panitumumab by 25% 3rd occurrence: Reduce panitumumab by 50% 4th occurrence: Omit panitumumab

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*

Fluorouracil		
	Interaction	**Clinical management**
Folic acid	Increased toxicity of fluorouracil due to stabilisation of its bond to thymidylate synthetase (folic acid is a precursor of folinic acid/leucovorin)	Advise patients not to take folic acid supplements (inc. multivitamins) around the time of receiving treatment with fluorouracil
Metronidazole, tinidazole	Increased toxicity of fluorouracil due to reduced clearance	Avoid combination or monitor for fluorouracil toxicity
Warfarin and other drugs metabolised by CYP2C9 (e.g. warfarin, phenytoin etc.)	Increased effect/toxicity of these drugs due to inhibition of CYP2C9 by fluorouracil resulting in reduced clearance	Avoid combination or monitor for increased effect/toxicity of these drugs (e.g. for bleeding/elevated INR with warfarin, elevated phenytoin serum levels or signs of toxicity such as ataxia, tremor etc.)
Allopurinol	Reduced efficacy of fluorouracil possible due to reduced conversion to the active metabolites	Avoid combination or monitor for reduced fluorouracil efficacy

Oxaliplatin		
	Interaction	**Clinical management**
Nephrotoxic drugs (e.g. aminoglycosides, amphotericin, contrast dye, frusemide, NSAIDs)	Additive nephrotoxicity	Avoid combination or monitor kidney function closely
Neurotoxic drugs (e.g. vincristine, paclitaxel)	Additive neurotoxicity	Monitor closely for neuropathy if combination used

Panitumumab
No specific clinically significant drug-drug interactions

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

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

Administration

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

product information monographs via the TGA website for further information.

Day 1

Approximate treatment time: 4 to 5 hours

Safe handling and waste management

Safe administration

General patient assessment prior to each day of treatment.

Peripheral neuropathy assessment tool

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

Prime IV line(s).

Access TIVAD or CVAD.

Pre treatment medication

Verify antiemetics taken or administer as prescribed.

Verify dexamethasone taken or administer as prescribed.

Treatment - Time out

Panitumumab

- a low protein binding 0.2 micron or 0.22 micron inline filter must be used
- panitumumab is incompatible with glucose solutions, ensure IV administration sets are flushed with sodium chloride 0.9% pre and post administration.

Administer panitumumab:

- via IV infusion over 60 minutes
- observe for hypersensitivity reaction
- flush with 50 mL of sodium chloride 0.9%
- if well tolerated
  - subsequent doses over 30 to 60 minutes
- doses greater than 1000 mg should be diluted in 150mL sodium chloride 0.9% and infused over 90 minutes.

Stop infusion at first sign of reaction:

- if symptoms are mild and resolve when infusion is stopped, consider recommencing infusion after review by medical officer at a slower rate of 50%.
- for severe reactions seek medical assistance immediately and do not restart infusion.

Chemotherapy - Time out

Oxaliplatin

- Oxaliplatin is only compatible with glucose 5%, ensure IV lines are flushed with glucose 5% pre and post administration.

Administer oxaliplatin (irritant with vesicant properties):

- via IV infusion over 2 hours
- risk of laryngopharyngeal dysaesthesia
  - patients should not drink cold fluids
- monitor for signs of hypersensitivity
- flush with ~ 100 mL glucose 5%
- if patient has laryngopharyngeal dysaesthesia or a hypersensitivity reaction - stop infusion and obtain medical officer review. If rechallenge indicated, premedicate patient and administer oxaliplatin at a slower rate (up to 6 hours).

Calcium Folinate (Leucovorin)

- administer by IV bolus via a side port of the IV line over 1 to 2 minutes
- flush with ~ 50mL of sodium chloride 0.9%.

Fluorouracil

Administer fluorouracil (irritant):

- over 3 to 5 minutes
  - via a minibag **OR**
  - by IV bolus via a side port of a freely flowing IV infusion
- flush with ~ 100 mL of sodium chloride 0.9%.

Fluorouracil continuous infusion (irritant)

Connect pump containing fluorouracil and administer over the correct time for the amount of drug in the pump:

- ⚠ safety alert issued for administration of infusional fluorouracil
- verify the correct rate of infusion via the ambulatory infusion pump
- read more information about the different ambulatory infusion pumps.

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

Day 3

Approximate treatment time: 30 minutes

Safe handling and waste management

Disconnection of ambulatory infusion pump/infusor

Verify the ambulatory infusion pump/infusor is complete.

Disconnect the ambulatory infusion pump/infusor as per recommended procedure for type of pump/infusor.

Read more about ambulatory infusion pumps/infusors.

Deaccess TIVAD or CVAD.

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

Discharge information

Antiemetics

- Antiemetics as prescribed.

Antidiarrhoeals

- Antidiarrhoeals as prescribed.

Patient information

- Ensure patient receives patient information sheet.

Infusion pumps

- CADD-Legacy® 1 ambulatory infusion pump patient information sheet.
- CADD-Legacy® Plus ambulatory infusion pump patient information sheet.
- CADD® Solis VIP ambulatory infusion pump patient information sheet.
- Elastomeric infusion system 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
Laryngopharyngeal dysaesthesia	The sensation of difficulty breathing or an inability to swallow. This is associated with oxaliplatin and can occur during, and for up to 48 hours after treatment. Read more about laryngopharyngeal dysaesthesia
Nausea and vomiting	Read more about prevention of treatment induced nausea and vomiting
Taste and smell alteration	Read more about taste and smell changes
Cardiotoxicity	Coronary artery spasm is a temporary, sudden narrowing of one of the coronary arteries that may present at any time during treatment with fluoropyrimidines. It most commonly manifests as angina.

Early (onset days to weeks)	
Neutropenia	Abnormally low levels of neutrophils in the blood. This increases the risk of infection. Any fever or suspicion of infection should be investigated immediately and managed aggressively. Read more about immediate management of neutropenic fever
Thrombocytopenia	A reduction in the normal levels of functional platelets, increasing the risk of abnormal bleeding. Read more about thrombocytopenia
Diarrhoea	Read more about treatment induced diarrhoea
Fatigue	Read more about fatigue
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
Ocular changes	Symptoms may include eye pain, blurred vision, blepharitis, uveitis, optic neuritis, tear duct stenosis, conjunctivitis, hyperlacrimation, watery or dry eyes and photophobia.
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
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
Photosensitivity	Increased sensitivity to ultraviolet (UV) light resulting in an exaggerated sunburn-like reaction accompanied by stinging sensations and urticaria.
Peripheral neuropathy	Typically symmetrical sensory neuropathy, affecting the fingers and toes, sometimes progressing to the hands and feet. It is associated with several classes of anti-cancer drugs. These include taxanes, platinum-based compounds, vinca alkaloids and some drugs used to treat multiple myeloma. Read more about peripheral neuropathy
Hypomagnesaemia, hypokalaemia, hypocalcaemia	Abnormally low levels of magnesium, potassium and calcium in the blood.

Late (onset weeks to months)	
Anaemia	Abnormally low levels of red blood cells (RBCs) or haemoglobin in the blood. Read more about anaemia
Abnormal hair growth	Hair may become fine, brittle and curly. Eyelashes and eyebrows may grow more quickly and become unusually long.
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
Hyperpigmentation	Darkening of an area of skin caused by the overproduction of melanin.
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

Although there are no RCTs which provide a comparison between FOLFOX regimens, the FOLFOX6 (modified) regimen is widely accepted and is currently used as the control arm in most clinical trials (link to discussion on FOLFOX protocols).

Due to the lack of conclusive evidence to identify the optimum dose of calcium folinate (Leucovorin®), it is the consensus of the eviQ reference committee to adopt flat dosing of calcium folinate (Leucovorin®) as a 50 mg IV bolus when used with bolus 5FU across all colorectal and upper gastrointestinal protocols. A discussion regarding the effect of dosing on outcome can be found in the calcium folinate (Leucovorin®) dose document.

The evidence supporting this protocol is provided by a phase III multicentre international randomised trial 'PRIME' involving 1183 patients comparing panitumumab-FOLFOX4 with FOLFOX4 alone in patients with metastatic colorectal cancer.

Between August 2006 and February 2008, 593 patients were randomised to receive panitumumab 6mg/kg IV every two weeks along with FOLFOX4 and 590 patients were randomised to receive FOLFOX4 alone every two weeks.

The primary end point was PFS and secondary end point was OS, objective response rate and safety.[2]

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, panitumumab should not be used in patients with any RAS mutations.

Efficacy

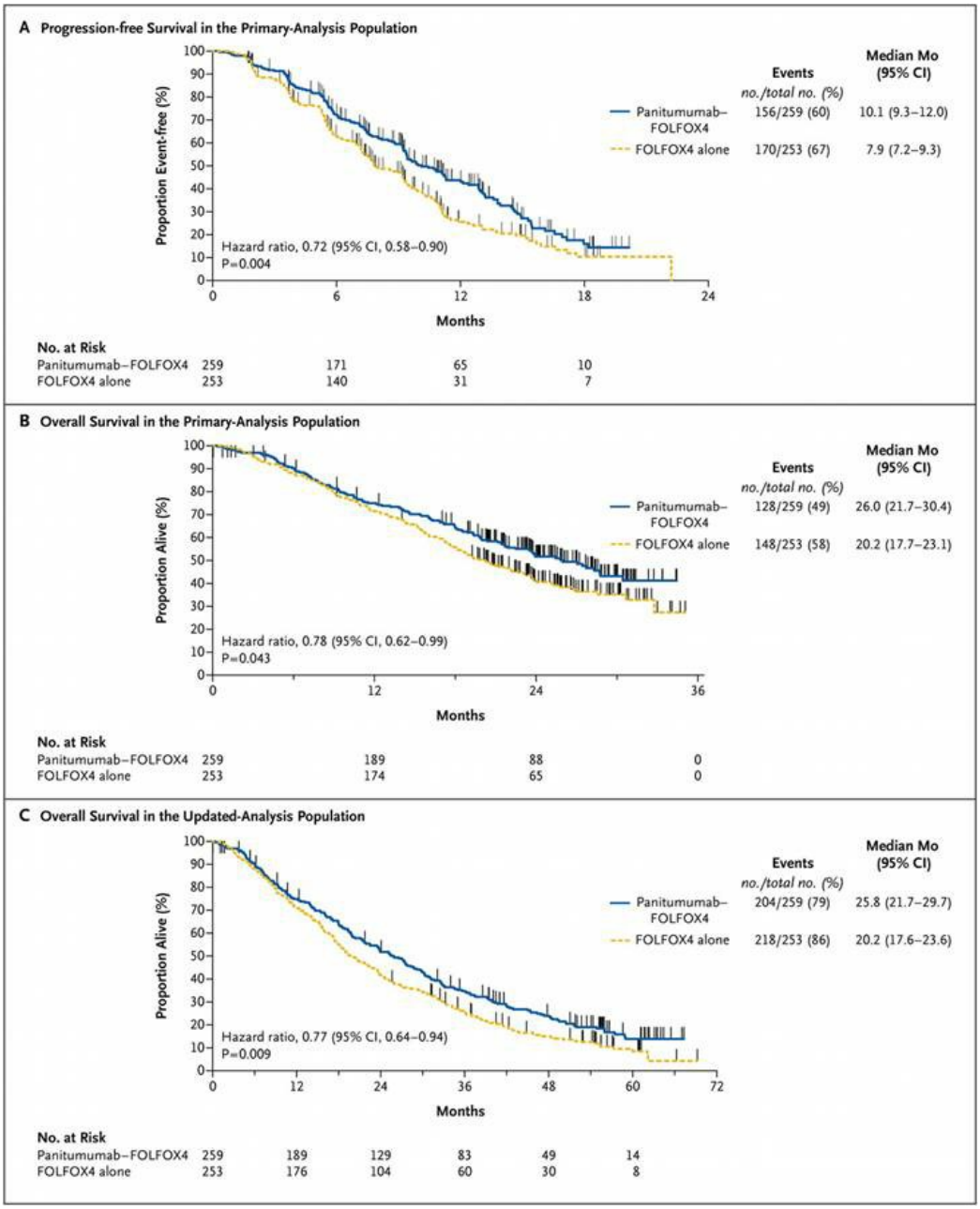
The trial was originally designed to test the treatment effect on all randomised patients but was amended to compare PFS and OS according K-RAS status before any efficacy analyses. 656 patients (60%) had wild type K-RAS in this trial.

In the wild type K-RAS population, after a median follow up of 13.2 months, the median PFS was 9.6 months in the panitumumab+FOLFOX4 group vs 8.0 months in the FOLFOX4 group (HR=0.80; CI 95% 0.66 to 0.97 ; p=0.02).[2]

In an updated analysis, panitumumab+FOLFOX4, compared with FOLFOX4 alone, was associated with a 4.4-month improvement in overall survival (23.8 months vs. 19.4 months; p=0.03).[6]

Among patients without RAS mutations, the overall survival was 26.0 months in the panitumumab-FOLFOX group vs 20.2 months in the FOLFOX4 alone group (HR=0.78; 95% CI, 0.62 to 0.99; p=0.04). Patients with non-mutated KRAS exon 2 who had other RAS mutations were associated with inferior progression-free survival and overall survival with panitumumab-FOLFOX treatment.[6]

(A) Kaplan-Meier Estimates of Progression-free Survival and (B) Overall Survival in the Primary Analysis Population[6]



Toxicity

Grade 3 and 4 Adverse Events[2]

Table 2. Grade 3 and 4 Adverse Events of Interest

	WT *KRAS* (n = 649)				MT *KRAS* (n = 435)			
	Panitumumab-FOLFOX4 (n = 322)		FOLFOX4 (n = 327)		Panitumumab-FOLFOX4 (n = 217)		FOLFOX4 (n = 218)	
Adverse Event by MedDRA Term	No. of Patients	%	No. of Patients	%	No. of Patients	%	No. of Patients	%
Patients with any event	270	84	227	69	173	80	159	73
Neutropenia	136	42	134	41	81	37	103	47
Skin toxicity	116	36	7	2	66	30	3	1
Diarrhea	59	18	29	9	43	20	21	10
Neurologic toxicities	52	16	51	16	36	17	37	17
Hypokalemia	32	10	15	5	19	9	8	4
Fatigue	30	9	10	3	16	7	11	5
Mucositis*†	28	9	2	< 1	12	6	6	3
Hypomagnesemia	20	6	1	< 1	13	6	1	< 1
Paronychia†	11	3	0	0	4	2	0	0
Pulmonary embolism	9	3	5	2	7	3	8	4
Febrile neutropenia	8	2	7	2	7	3	7	3
Infusion-related reaction (panitumumab)†	2	< 1	—	—	0	0	—	—

NOTE. All events are included, regardless of relatedness to therapy.
Abbreviations: MedDRA, Medical Dictionary for Regulatory Activities; WT, wild type; MT, mutant; FOLFOX4, infusional fluorouracil, leucovorin, and oxaliplatin.
*Results are based on the following prespecified list of preferred terms: stomatitis, mucosal inflammation, aphthous stomatitis, mouth ulceration, mucosal dryness, and mucosal ulceration.
†No grade 4 events.

References

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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.

4 Van Cutsem, E., H. J. Lenz, C. H. Kohne, et al. 2015. "Fluorouracil, Leucovorin, and Irinotecan Plus Cetuximab Treatment and RAS Mutations in Colorectal Cancer." J Clin Oncol 33(7):692-700.

5 Heinemann, V., L. F. von Weikersthal, T. Decker, et al. 2014. "FOLFIRI plus cetuximab versus FOLFIRI plus bevacizumab as first-line treatment for patients with metastatic colorectal cancer (FIRE-3): a randomised, open-label, phase 3 trial." Lancet Oncol 15(10):1065-1075.

6 Douillard, J. Y., K. S. Oliner, S. Siena, et al. 2013. "Panitumumab-FOLFOX4 treatment and RAS mutations in colorectal cancer." N Engl J Med 369(11):1023-1034.

History

Version 5

Date	Summary of changes
26/03/2021	Indications and patient population section updated to add the note "Not recommended for patients who have progressed on cetuximab therapy". Version number increased to V.5.
20/10/2022	Protocol reviewed electronically by Medical Oncology Reference Committee. No changes. Next review 2 years.

Version 4

Date	Summary of changes
16/12/2020	Treatment schedule note added regarding number of oxaliplatin cycles as per Medical Oncology Reference Committee consensus. Version number increased to V.4. Next review in 2 years.

Version 3

Date	Summary of changes
13/09/2013	New protocol taken to 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'.
27/03/2015	Protocol reviewed by email survey. Evidence updated to include analysis 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.
16/10/2016	Patient information sheet updated to include more fluorouracil toxicity symptom warnings.
18/10/2016	Sentence relating to oxaliplatin dose: "the dose may be escalated for individual patients at the discretion of the

Date	Summary of changes
	treating clinician." deleted due to toxicity concerns.
09/11/2016	The following changes made post Medical Oncology Reference Committee meeting held on 21 October 2016. Link to AGTIG and ANZCTR added. Sentence in dose modifications regarding omitting leucovorin if fluorouracil is delayed or omitted changed to specify fluorouracil bolus.
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 panitumumab to chemotherapy and another regimen should be considered.
31/05/2017	Transferred to new eviQ website. Version number changed to V.2. Antiemetic change: A NK1 receptor antagonist and a $5HT_3$ receptor antagonist in combination with dexamethasone has been added as available on the PBS for primary prophylaxis of oxaliplatin induced nausea and vomiting. Hepatitis screening changed to not required.
10/05/2018	Haematological dose modifications updated as per consensus of the expert clinician group. Fluoropyrimidine overdose or overexposure warning added. Fluoropyrimidine safety alert and DPD enzyme deficiency wording in clinical information updated. 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.
25/09/2018	Treatment schedule note and evidence section updated with Leucovorin® dosing information as per reference committee consensus.
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 2024

The currency of this information is guaranteed only up until the date of printing, for any updates please check:
https://www.eviq.org.au/p/1542
16 Jul 2023

Patient information - Bowel cancer metastatic - FOLFOX6 modified (fluorouracil, leucovorin, oxaliplatin) and panitumumab

Patient's name:

Your treatment

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

FOLFOX6 modified (fluorouracil, leucovorin, oxaliplatin) and panitumumab			
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	**Panitumumab** (*pan-i-TUE-moo-mab*) **Oxaliplatin** (*ox-AL-ih-pla-tin*) **Calcium folinate (Leucovorin)** *(loo-koe-VOR-in)* **Fluorouracil** *(Flure-oh-YOOR-a-sill)*	By a drip into a vein	About 4 to 5 hours
	Fluorouracil *(Flure-oh-YOOR-a-sill)*	By a pump slowly into a vein	For 2 days (46 hours) by pump at home
3	**Disconnect pump**		About 30 minutes

When to get help

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

IMMEDIATELY go to your nearest hospital Emergency Department, or contact your doctor or nurse if you have any of the following at any time:	**Emergency contact details** Ask your doctor or nurse from your treating team who to contact if you have a problem
• 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 • leaking from your pump • 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. 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.

Pumps and central venous access devices (CVADs)

This treatment involves having chemotherapy through a pump. To have this, you will also need a central venous access device (CVAD). Your doctor or nurse will explain this to you. For more information see the eviQ patient information sheets on pumps and CVADs. At home you will need to look at your pump 3 to 4 times a day to check it is working. Your nurse will teach you how to do this.

Treatment with oxaliplatin

You should avoid cold drinks, cold food and ice on the day of and for up to 2 days after treatment with oxaliplatin. If you have cold food or drinks you may get discomfort or tightness in the back of the throat, or the feeling like you cannot breathe or swallow.

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.
- **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.

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.

Breathing or swallowing problems	• You may get discomfort or tightness in the back of the throat, or the feeling like you cannot breathe or swallow. • This can happen during an infusion of oxaliplatin, and for up to 48 hours after. • These symptoms are temporary. • They can be distressing but they are not usually harmful and will disappear. • If symptoms develop, cup your hands over your mouth and breathe normally. The warm air will help relieve the feeling. • Avoid cold temperature, cold drinks and ice cubes before having oxaliplatin and for 2 days after, as this can increase the risk. • **Tell your doctor or nurse as soon as possible if your symptoms don't go away.**
Nausea and vomiting	• You may feel sick (nausea) or be sick (vomit). • Take your anti-sickness medication as directed even if you don’t feel sick. • Drink plenty of fluids (unless you are fluid restricted). • Eat small meals more frequently. • Try food that does not require much preparation. • Try bland foods like dry biscuits or toast. • Gentle exercise may help with nausea. • Ask your doctor or nurse for eviQ patient information - Nausea and vomiting during cancer treatment. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you have uncontrolled vomiting or feel dizzy or light-headed.**
Taste and smell changes	• You may find that food loses its taste or tastes different. • These changes are likely to go away with time. • Do your mouth care regularly. • Chew on sugar-free gum or eat sugar-free mints. • Add flavour to your food with sauces and herbs. • Ask your doctor or nurse for eviQ patient information - Taste and smell changes during cancer treatment.

Heart problems	• You may get:
	  ◦ chest pain or tightness
	  ◦ shortness of breath
	  ◦ an abnormal heartbeat
	• Tell your doctor if you have a history of heart problems or high blood pressure.
	• **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you get any of the symptoms listed above.**

Early (onset days to weeks)	

Infection risk (neutropenia)	• This treatment lowers the amount of white blood cells in your body. The type of white blood cells that help to fight infection are called neutrophils. Having low level of neutrophils is called neutropenia. If you have neutropenia, you are at greater risk of getting an infection. It also means that your body can't fight infections as well as usual. This is a serious side effect, and can be life threatening. • Wash your hands often. • Keep a thermometer at home and take your temperature regularly, and if you feel unwell. • Do your mouth care regularly. • Inspect your 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	• 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.**
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.**

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 changes	• Your skin may become dry, and you may notice changes to areas of your skin that have been exposed to the sun. • Keep your skin moisturised with a cream such as sorbolene or aqueous cream. • Avoid direct sunlight. • Protect your skin from the sun by wearing a wide-brimmed hat, sun-protective clothing, sunglasses and sunscreen of SPF 50 or higher. • **Tell your doctor or nurse if you notice any skin changes.**
Eye problems	• You may get: ◦ eye pain ◦ red, sore or swollen eyes ◦ blurred vision ◦ watery or gritty eyes ◦ changes in your eyesight ◦ sensitivity to sunlight. • Protect your eyes from the weather (sun and wind) by wearing sunglasses, especially if you have lost your eyelashes. • **Tell your doctor or nurse if you get any of the symptoms listed above. Eye drops may help with your symptoms.**
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**

Hand-foot syndrome (palmar-plantar erythrodysaesthesia)	• The palms of your hands and soles of your feet may become:
	  ◦ red and hot
	  ◦ swollen
	  ◦ painful and tender
	  ◦ blistered.
	• The skin in the area may also peel.
	• Moisturise your hands and feet daily with sorbolene or aqueous cream.
	• Keep your hands and feet clean and dry.
	• Avoid hot water, instead use lukewarm water to bathe.
	• Avoid direct sunlight.
	• Avoid unnecessary walking, jogging or exercise.
	• Wear cotton socks and avoid tight-fitting shoes.
	• **Tell your doctor or nurse as soon as possible if you notice any skin changes on your hands or feet.**

Skin that is more sensitive to the sun (photosensitivity)	• After being out in the sun you may develop a rash like a bad sunburn. • Your skin may become red, swollen and blistered. • Avoid direct sunlight. • Protect your skin from the sun by wearing sun-protective clothing, a wide-brimmed hat, sunglasses and a sunscreen of SPF 50 or higher. • **Tell your doctor or nurse if you get any of the symptoms listed above.**

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

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

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 changes	• Your hair may become fine or curly and may break easily. • Your eyelashes and eyebrows may grow more than normal. • Use a gentle shampoo and a soft hairbrush. • Take care with hair products like hairspray, hair dye, bleaches and perms. • Ask your doctor or nurse about the Look Good Feel Better program (www.lgfb.org.au).
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.
Skin colour changes	• You may have darkening of your skin, especially in areas that are exposed to the sun. • You may also notice darkening of your tongue, gums and over your finger joints. • These skin changes may fade over time. • Protect your skin from the sun by wearing sun-protective clothing, a wide-brimmed hat, sunglasses and a sunscreen of SPF 50 or higher.
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.
- 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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