

Adjuvant CAPOX (XELOX) (capecitabine and oxaliplatin)

ID: 4019 v.4 Endorsed Essential Medicine List

A Fluoropyrimidine overdose or overexposure:

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

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

Some indications in this protocol are based on limited evidence; please refer to the individual evidence sections for more information.

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

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

Click here



Related pages:

- Colorectal adjuvant FOLFOX6 (modified) (fluorouracil leucovorin oxaliplatin)
- Gastric adjuvant MacDonald (modified) (fluorouracil and radiation therapy) SUPERSEDED
- · Gastric oesophageal neoadjuvant/adjuvant ECF (epirubicin ciSplatin fluorouracil) DISCONTINUED
- Rectal adjuvant FOLFOX6 (modified) (fluorouracil leucovorin oxaliplatin)
- · Colorectal rectum adjuvant EBRT chemoradiation post-operative

Treatment schedule - Overview

Cucle 1 to 8

Drug	Dose	Route	Day
Oxaliplatin	130 mg/m ²	IV infusion	1
Capecitabine	1,000 mg/m ² TWICE a day	PO	1 to 14

Frequency: 21 days

Cycles: 8

Notes:

Evidence from a meta-analysis examining duration of oxaliplatin-based therapy in stage III colon cancer^{1, 2} has demonstrated:

• in the overall population shorter therapy (3 months) was not equivalent to longer (6 months) therapy, but for lower risk patients (T1-3N1) shorter CAPOX therapy was equivalent to longer therapy with less neurotoxicity. Non oxaliplatin-based adjuvant therapy was not examined in this study and should be given for 6 months.

Drug status: All drugs are on the PBS general schedule

Capecitabine is available as 150 mg and 500 mg tablets

Cost: ~ \$190 per cycle

Treatment schedule - Detail

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

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

Cycle 1 to 8

Day 1		
Netupitant	300 mg (PO)	60 minutes before chemotherapy (fixed dose preparation with palonosetron)
Palonosetron	0.5 mg (P0)	60 minutes before chemotherapy (fixed dose preparation with netupitant)
Dexamethasone	8 mg (PO)	60 minutes before chemotherapy
Oxaliplatin	130 mg/m ² (IV infusion)	in 250 mL to 500 mL glucose 5% over 2 hours
Capecitabine	1,000 mg/m ² (PO)	TWICE a day within 30 minutes after the end of a meal

Day 2 and 3		
Dexamethasone	8 mg (PO)	ONCE a day (or in divided doses) with or after food.*
Capecitabine	1,000 mg/m ² (P0)	TWICE a day within 30 minutes after the end of a meal

Day 4 to 14		
Capecitabine	1,000 mg/m ² (PO)	TWICE a day within 30 minutes after the end of a meal

^{*} 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: 21 days

Cycles: 8

Indications and patient population - Colon

• Adjuvant stage III (Dukes C) colon cancer after complete resection of the primary tumour.

Indications and patient population - Gastric

- Adjuvant stage II/III gastric adenocarcinoma post D2 gastrectomy
 - ECOG performance status of 0 to 2 and adequate oral absorption after gastrectomy.

Note: limited evidence in non-Asian populations.

Indications and patient population - Rectal

- Resected stage II or III rectal cancer
 - ECOG performance status 0 to 1.

Clinical information

Safety alert fluoropyrimidines	Fluoropyrimidines can be administered by different routes and schedules with each method having associated increased risk of certain side effects. Fluoropyrimidine overdose or overexposure is a rare but potentially life threatening side effect of this drug class and can occur by any route of administration. An antidote is available and highly effective if given within 96 hours. Read more about the medication safety alert for infusional fluorouracil and fluoropyrimidine overdose or overexposure
Caution with oral anti-cancer drugs	Select links for information on the safe prescribing, dispensing and administration of orally administered anti-cancer drugs. Read more about the COSA guidelines and oral anti-cancer therapy
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 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	Angina-like chest pain, tachycardia, arrhythmias, heart failure, myocardial infarction and cardiac arrest may occur with capecitabine especially in patients with a prior history of coronary artery disease. Cardiac symptoms may require cessation of capecitabine and referral to a cardiologist for symptomatic treatment. Re-challenge is controversial and generally not recommended. Read more about cardiac toxicity associated with anti-cancer drugs
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
Diarrhoea	Antidiarrhoeals (e.g. loperamide) are usually prescribed with this treatment. Read more about treatment induced diarrhoea
Hyperbilirubinaemia	Capecitabine can induce hyperbilirubinaemia which may require an interruption in treatment (see dose modifications).
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

Growth factor support	G-CSF (short or long-acting) is available on the PBS for chemotherapy induced neutropenia depending on clinical indication and/or febrile neutropenia risk. Access the PBS website
Blood tests	FBC, EUC and LFTs at baseline and prior to each cycle. INR as clinically indicated.
Hepatitis B screening and prophylaxis	Routine screening for HBsAg and anti-HBc is recommended prior to initiation of treatment. Prophylaxis should be determined according to individual institutional policy. Read more about hepatitis B screening and prophylaxis in cancer patients requiring cytotoxic and/or immunosuppressive therapy
Vaccinations	Live vaccines are contraindicated in cancer patients receiving immunosuppressive therapy and/or who have poorly controlled malignant disease. Refer to the recommended schedule of vaccination for immunocompromised patients, as outlined in the Australian Immunisation Handbook. Read more about COVID-19 vaccines and cancer.
Fertility, pregnancy and lactation	Cancer treatment can have harmful effects on fertility and this should be discussed with all patients of reproductive potential prior to commencing treatment. There is a risk of foetal harm in pregnant women. A pregnancy test should be considered prior to initiating treatment in females of reproductive potential if sexually active. It is important that all patients of reproductive potential use effective contraception whilst on therapy and after treatment finishes. Effective contraception methods and adequate contraception timeframe should be discussed with all patients of reproductive potential. Possibility of infant risk should be discussed with breastfeeding patients. Read more about the effect of cancer treatment on fertility

Dose modifications

Evidence for dose modifications is limited, and the recommendations made on eviQ are intended as a guide only. They are generally conservative with an emphasis on safety. Any dose modification should be based on clinical judgement, and the individual patient's situation including but not limited to treatment intent (curative vs palliative), the anti-cancer regimen (single versus combination therapy versus chemotherapy versus immunotherapy), biology of the cancer (site, size, mutations, metastases), other treatment related side effects, additional co-morbidities, performance status and patient preferences. Suggested dose modifications are based on clinical trial findings, product information, published guidelines and reference committee consensus. The dose reduction applies to each individual dose and not to the total number of days or duration of treatment cycle unless stated otherwise. Non-haematological gradings are based on Common Terminology Criteria for Adverse Events (CTCAE) unless otherwise specified. Renal and hepatic dose modifications have been standardised where possible. For more information see dosing considerations & disclaimer.

The dose recommendations in kidney dysfunction (i.e.renal impairment) displayed may not reflect those in the ADDIKD guideline and have been included for historical reference only. Recommendations will be updated once the individual protocol has been evaluated by the reference committee, with this version of the protocol then being archived. Clinicians are expected to refer to the ADDIKD guideline prior to prescribing in kidney dysfunction.

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

Note: all dose reductions are calculated as a percentage of the starting dose.

Haematological toxicity		
ANC x 10 ⁹ /L (pre-treatment	blood test)	
0.5 to less than 1.0	Delay treatment until recovery	
less than 0.5	Delay treatment until recovery and consider reducing oxaliplatin and capecitabine by 25% for subsequent cycles	
Febrile neutropenia	Delay treatment until recovery and consider reducing oxaliplatin and capecitabine by 25% for subsequent cycles	

Haematological toxicity Platelets x 10 ⁹ /L (pre-treatment blood test)	
75 to less than 100	Refer to local institutional guidelines; it is the view of the expert clinicians that treatment should continue if patient is clinically well
50 to less than 75	Delay treatment until recovery
less than 50	Delay treatment until recovery and consider reducing oxaliplatin and capecitabine by 25% for subsequent cycles

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

Hepatic impairment	
Hepatic dysfunction	
Mild	No dose modifications necessary
Moderate	Reduce capecitabine by 25%
Severe	Reduce capecitabine by 50%
Treatment related Grade 3 or Grade 4 hyperbilirubinaemia	Delay treatment until toxicity resolves to Grade 2 or less and reduce the dose of capecitabine for subsequent cycles as recommended above

Acute laryngopharyngeal dysaesthesia

No dose reductions necessary. Patients should be advised to avoid exposure to cold and to avoid ingesting cold food and/or beverages during and for at least 48 hours following oxaliplatin administration. If symptoms are severe and/or distressing, subsequent infusions should be administered over a longer period (e.g. 6 hours).

Peripheral neuropathy	
Grade 2 which is present at the start of the next cycle	Reduce oxaliplatin by 25%; if persists, consider omitting oxaliplatin
Grade 3 or Grade 4	Omit oxaliplatin

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 capecitabine by 25% 3rd occurrence: Reduce oxaliplatin and capecitabine 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 capecitabine by 50% 2nd occurrence: Withhold chemotherapy

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

<u>Diarrhoea</u>					
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 capecitabine by 50% 2nd occurrence: Withhold 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 capecitabine 25% 3rd occurrence: Reduce capecitabine by 50% 4th occurrence: Omit capecitabine			
Grade 3	Delay treatment until toxicity has resolved to Grade 1 or less and reduce the dose for subsequent cycles as follows: 1 st occurrence: Reduce capecitabine by 50% 2 nd occurrence: Omit capecitabine			

Interactions

Drug interactions in eviQ protocols are under review and being updated to align with current literature. Further site-wide updates and changes will occur in due course. References & Disclaimer

The drug interactions shown below are not an exhaustive list. For a more comprehensive list and for detailed information on specific drug interactions and clinical management, please refer to the specific drug product information and the following key resources:

- MIMS interactions tab (includes link to a CYP-450 table) (login required)
- Australian Medicines Handbook (AMH) interactions tab (login required)
- Micromedex Drug Interactions (login required)
- Cancer Drug Interactions
- Cytochrome P450 Drug Interactions

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

^{*} currently not marketed in Australia

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

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

Dau 1 (IV)

Approximate treatment time: 3 to 4 hours

Safe handling and waste management

Safe administration

General patient assessment prior to each day of treatment.

Peripheral neuropathy assessment tool

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

Prime IV line(s) with glucose 5%.

Insert IV cannula or access TIVAD or CVAD.

Pre treatment medication

Verify antiemetics taken or administer as prescribed.

Verify dexamethasone taken or administer as prescribed.

Ochemotherapy - 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
 - o 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).

Remove IV cannula and/or deaccess TIVAD or CVAD.

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

Days 1 to 14 (PO)

This is an oral treatment

Safe handling and waste management

Safe administration

General patient assessment prior to each treatment.

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

Ochemotherapy - Time out

Capecitabine

- administer orally TWICE a day on days 1 to 14
- · to be swallowed whole with a glass of water; do not break, crush or chew
- to be taken morning and night (approximately 12 hours apart) within thirty minutes after the end of a meal
- tablets may also be dispersed in water if patient has swallowing difficulties:

- place the required number of tablets in a disposable cup and fill with approximately 200mL of water, leave the tablets to dissolve (approximately 15 minutes) and swallow immediately
- o mix any residues in the cup with water and swallow
- o avoid direct contact of the tablets or solution with the skin or mucous membrane. If such contact occurs, wash thoroughly.

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

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

Discharge information

Capecitabine tablets

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

Antiemetics

· Antiemetics as prescribed.

Antidiarrhoeals

· Antidiarrhoeals as prescribed.

Patient information

· Ensure patient receives patient information sheet.

Side effects

The side effects listed below are not a complete list of all possible side effects for this treatment. Side effects are categorised into the approximate onset of presentation and should only be used as a guide.

Immediate (onset hours to days)				
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			
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.			
Nausea and vomiting	Read more about prevention of treatment induced nausea and vomiting			
Taste and smell alteration	Read more about taste and smell changes			

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				
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				
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				
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				
Fatigue	Read more about fatigue				
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				
mi					
Photosensitivity	Increased sensitivity to ultraviolet (UV) light resulting in an exaggerated sunburn-like reaction accompanied by stinging sensations and urticaria.				
Ocular changes	Symptoms may include eye pain, blurred vision, blepharitis, uveitis, optic neuritis, tear duct stenosis, conjunctivitis, hyperlacrimation, watery or dry eyes and photophobia.				
Abdominal pain	Dull ache, cramping or sharp pains are common with some anti-cancer drugs. These are caused by either increased or decreased gastrointestinal motility and can be associated with diarrhoea or constipation.				
Late (onset weeks to months)					
Anaemia	Abnormally low levels of red blood cells (RBCs) or haemoglobin in the blood.				
	Read more about anaemia				
Nail changes	Hyperpigmentation, paronychia, onycholysis, splinter haemorrhage, pyogenic granuloma formation, subungal haematoma and subungal hyperkeratosis are some of the nail changes associated with anti-cancer drugs.				
	Read more about nail toxicities				

Late (onset weeks to months)	
Anaemia	Abnormally low levels of red blood cells (RBCs) or haemoglobin in the blood. Read more about anaemia
Nail changes	Hyperpigmentation, paronychia, onycholysis, splinter haemorrhage, pyogenic granuloma formation, subungal haematoma and subungal hyperkeratosis are some of the nail changes associated with anti-cancer drugs. Read more about nail toxicities
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
Hyperbilirubinaemia	An abnormal increase in the amount of bilirubin circulating in the blood which may result in jaundice.

Evidence - Colon

The evidence supporting the use of XELOX in the adjuvant setting is based on a multicentre international, open label phase III study (NO16968) involving 1,886 patients. This study compared capecitabine (1000 mg/m² BD days 1-14) and oxaliplatin (130 mg/m² day 1) given every 21 days, with bolus fluorouracil and folinic acid (FU/FA, given as either Mayo or Roswell Park regimen) in patients with resected stage III colon cancer. Non-inferiority of XELOX compared with FOLFOX has been demonstrated in the metastatic but not specifically in the adjuvant setting but may be extrapolated to extend to this patient population.

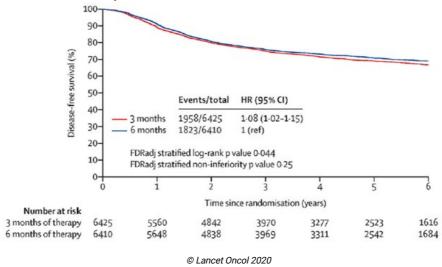
The International Duration Evaluation of Adjuvant Chemotherapy (IDEA) Collaboration in 2020 published analysed data from 6 phase III randomised trials to determine if a 3 month course of oxaliplatin-based adjuvant treatment (FOLFOX4/mFOLFOX6 or XELOX) is non-inferior to the current standard 6 month treatment for stage III colon cancer. In the overall population shorter therapy (3 months) was not equivalent to longer (6months) therapy, but for lower risk patients (T1-3N1) shorter CAPOX therapy was equivalent to longer therapy with less neurotoxicity. Non oxaliplatin-based adjuvant therapy was not examined in this study and monotherapy is recommended to be given for 6 months. 2

Efficacy

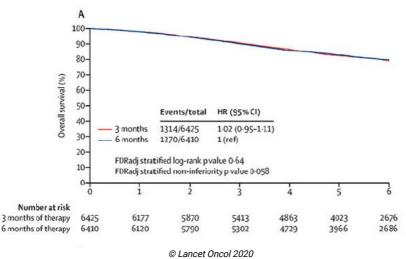
At a median follow-up of 57.0 months, the difference in the proportion of patients that had died (20.9% in the XELOX group vs 23.9% in the 5FU/FA group) was not statistically significant (HR, 0.87; 95% CI, 0.72 to 1.05; P = 0.1486). XELOX was superior to bolus FU/FA in terms of disease-free survival (DFS) (HR 0.80; 95% CI, 0.69 to 0.93; P = 0.0045) with 3 year DFS rates of 70.9% and 66.5% respectively. The 5-year overall survival (OS) for XELOX and FU/FA were 77.6% and 74.2% respectively.

In the IDEA analysis, patients received adjuvant chemotherapy (ACT) 39.5% received CAPOX and the remainder received FOLFOX. In the overall population, the 5-year OS was 82.4% with 3 months of therapy and 82.8% with 6 months of therapy, with an estimated OS HR of 1.02 (95% CI 0.95 to 1.11). The absolute difference in 5-year OS rate was -0.4% (95% CI -2.1-1.3%). Five-year OS rate in 3 compared to 6 months treatment in CAPOX was $82\cdot1\%$ versus $81\cdot2\%$ with an estimated HR of 0.96 (95% CI, $0.85\cdot1.08$; NI FDRadj p, 0.033), and FOLFOX was $82\cdot6\%$ and $83\cdot8\%$, estimated HR of 1.07 (95% CI, 0.97-1.18; NI FDRadj p, 0.34). CAPOX had considerably less toxicity, especially neuro toxicity.

Kaplan-Meier curves IDEA Collaboration - 5 year DFS, 3 months versus 6 months ACT 2



Kaplan-Meier curves IDEA Collaboration - combined 5 year OS for 3 months versus 6 months ACT ²



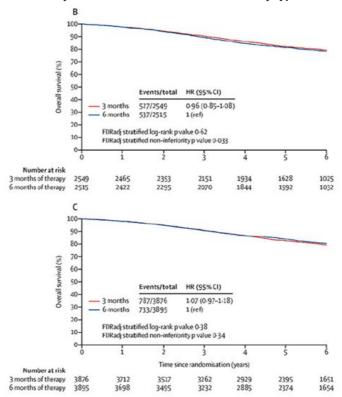
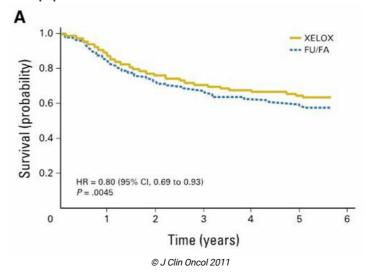


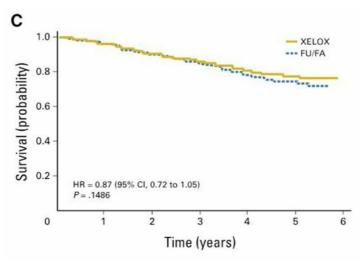
Figure 2: Overall survival with three months versus six months of adjuvant therapy; 2A: Overall mITT population; 2B: CAPOX; 2C: FOLFOX;

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Disease-free survival, intent-to-treat population³



Overall survival, intent-to-treat population³



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Toxicity

Overall, patients receiving XELOX experienced less diarrhoea and alopecia, but more vomiting and hand-foot syndrome than those patients treated with FU/LV. With the addition of oxaliplatin, the XELOX regimen was associated with more neurosensory toxicity compared to FU/LV (78% vs 7%).

An analysis of the safety profiles of XELOX and 5FU/LV between patients younger than 65 and those \geq 65 years showed that while many adverse events showed similar rates between both younger and older patients in both treatment arms, adverse events such as diarrhoea and dehydration showed elevated rates in the elderly patients treated with XELOX.⁵

Treatment-related adverse events⁵

				Pa	tients			
			FU/LV					
	XELOX (n = 938)		All Patients (N = 926)		Mayo (n = 657)		RP (n = 269)	
Event	No.	%	No.	%	No.	%	No.	%
Patients with at least 1 AE	520	55	439*	47	312*	47	127*	47
Diarrhea	177	19	187	20	108	16	79*	29
Neurosensory toxicity†	105	11	1*	< 1	1*	< 1	_*	77—
Neutropenia	81	9	144*	16	133*	20	11*	4
Vomiting	58	6	29°	3	14"	2	15	6
Nausea	48	5	41	4	18"	3	23*	9
Hand-foot syndrome	51	5	4*	< 1	2*	< 1	2*	< 1
Thrombocytopenia	45	5	1*	< 1	1*	< 1	-*	-
Stomatitis	6	< 1	81*	9	81*	12		-
Abdominal pain	17	2	22	2	9	1	13*	5
Dehydration	30	3	25	3	7*	1	18*	7
Hypokalemia	21	2	19	2	6*	< 1	13*	5
Febrile neutropenia	4	< 1	39*	4	36*	5	3	1

Abbreviations: AE, adverse event; XELOX, capecitabine and oxaliplatin; FU/LV, fluorouracil/leucovorin; Mayo, Mayo clinic regimen; RP, Roswell Park regimen. *P value for comparison with XELOX < .05.
†Pooled term; see Patients and Methods for definition.

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Grade 3/4 treatment-related/unrelated adverse events⁵

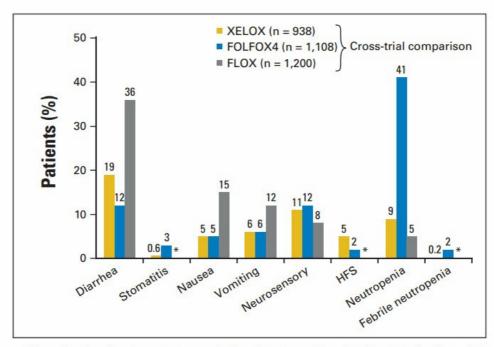


Fig 1. Grade 3/4 adverse events (related and unrelated) with capecitabine plus oxaliplatin (XELOX), oxaliplatin, fluorouracil (FU), and folinic acid (FOLFOX4), and bolus FU/leucovorin plus oxaliplatin (FLOX)—cross trial comparison. (*) Not reported. HFS, hand-foot syndrome.

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Evidence - Gastric

The evidence supporting this protocol is provided by an open label, phase 3 multicentre international randomised trial (CLASSIC) involving 1035 patients comparing adjuvant XELOX after D2 gastrectomy with D2 gastrectomy alone in Asian patients with stage II or III gastric adenocarcinoma.^{6, 7}

Between June 2006 and June 2009, 520 patients were randomised to receive adjuvant chemotherapy post D2 gastrectomy with capecitabine (1000 mg/m² BD PO days 1-14) and oxaliplatin (130 mg/m² day 1) given every 21 days for 8 cycles while 515 patients were randomised to receive D2 gastrectomy alone. A D2 gastrectomy includes the regional lymphatics: perigastric (D1) and those along the named vessels of the coeliac axis (D2), with a goal of examining at least 15 or greater lymph nodes.

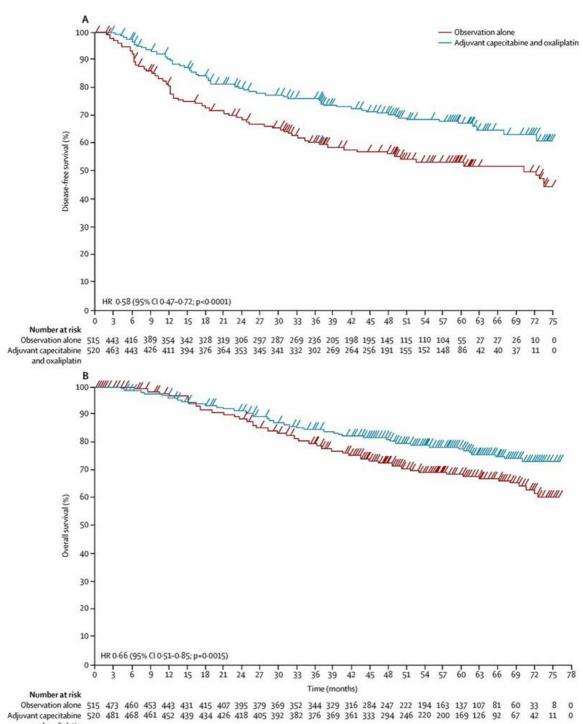
The primary end point was 3 year disease free survival (DFS) and secondary end points were overall survival (OS) and safety.^{6,7}

Adjuvant XELOX post D2 gastrectomy reduced both locoregional recurrence and distant metastases compared with D2 gastrectomy alone but was associated with greater grade 3 and 4 toxicities. As the study did not include non Asian populations or patients with less extensive surgery, the data may not be relevant to all patients due to possible variation in disease characteristics and side effect profiles.

Efficacy

At a median follow up of 34.2 months, the estimated 3 year DFS was 74% in the adjuvant capecitabine and oxaliplatin group vs 59% in the observation group (hazard ratio 0.56, 95% CI 0.44-0.72, p<0.0001). At a median follow up of 62.4 months, the estimated 5 year OS was 78% and 69% respectively (hazard ratio 0.66, 95% CI 0.51-0.85, p=0.0015).

(A) Disease-free survival and (B) overall survival in the intent-to-treat population⁶



and oxaliplatin

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Disease-free survival and overall survival by disease stage in the intent-to treat population⁶

		5-year DFS		5-year OS			
Disease stage	Adjuvant capecitabine and oxaliplatin (%, 95% CI)	Observation alone (%, 95% CI)	Hazard ratio	Adjuvant capecitabine and oxaliplatin (%, 95% CI)	Observation alone (%, 95% CI)	Hazard ratio	
II (n=515)	80 (74-85)	68 (61-74)	0.55 (0.38- 0.80)	88 (83-92)	79 (73-84)	0.54 (0.34- 0.87)	
IIIA (n=377)	58 (50-67)	44 (35-53)	0.61 (0.44- 0.84)	70 (62-77)	63 (55-71)	0.75 (0.52- 1.10)	
IIIB (n=143)	52 (40-65)	21 (9-33)	0.52 (0.33- 0.82)	66 (54-78)	45 (31-58)	0.67 (0.39- 1.13)	

Quality of life data were not recorded in this trial.

Toxicity

Adverse events ⁷	Surgery alone (n=478)		Capecitabine and oxaliplatin (n=496)	
	All grades (%)	Grade 3 or 4 (%)	All grades (%)	Grade 3 or 4 (%)
Nausea	4	0	66	8
Neutropenia	<1	<1	60	22
Decreased appetite	4	<1	59	5
Peripheral neuropathy	0	0	56	2
Diarrhoea	11	<1	48	2
Vomiting	3	0	39	7
Fatigue	2	0	31	5
Thrombocytopenia	0	0	26	8
Hand-foot syndrome	0	0	19	1
Asthenia	1	0	18	2
Abdominal pain	9	<1	17	2
Constipation	4	0	13	<1
Dizziness	5	0	13	<1
Stomatitis, all	0	0	12	<1
Weight decreased	3	<1	12	<1
Peripheral sensory neuropathy	0	0	10	<1

Evidence - Rectal

A search of the literature did not find strong evidence to support the use of CAPOX in the adjuvant treatment of rectal cancer. The expert reference committee supported publication of the protocol on the basis of the information summarised below. The committee was most strongly influenced by the multicentre, single-arm, phase 2 CORONA II study, involving 40 patients with resectable stage II (n=21) or stage III (n=19) rectal cancer who were enrolled to receive CAPOX (every 3 weeks for 8 cycles, or until disease progression/unacceptable toxicity) after total mesorectal excision (TME) or tumour-specific mesorectal excision (TSME). The primary endpoint was relapse-free survival (RFS). Secondary endpoints were overall survival (OS), cumulative local and distant recurrence rates, R0 resection and safety.

Source	Study & year published	Supports use	Is the dose and regimen consistent with the protocol?	Comments
Phase II trial	Hattori et al 2019 ⁹	Yes	Yes	-
Guidelines	Date published/revised	Supports use	Is the dose and regimen consistent with the protocol?	Comments
NCCN	V.1 2021	Yes	Yes	Recommends FOLFOX and CAPOX as preferred options or only options for higher risk patients
ССО	March 2019	Yes	No doses stated	-

Source	Study & year published	Supports use	Is the dose and regimen consistent with the protocol?	Comments
Source	Study & year published	Supports use	Is the dose and regimen consistent with the protocol?	Comments
Phase II trial	Hattori et al 2019 ⁹	Yes	Yes	-
Guidelines	Date published/revised	Supports use	Is the dose and regimen consistent with the protocol?	Comments
ESMO	2018	Yes	No doses stated	Supports use in stage III and high-risk stage II
BCCA	October 2012	Yes	Yes	Supports use in patients with resected stage III (node positive) rectal cancer

Efficacy

A summary of the evidence supporting this protocol:

Study	Outcome			
	3-year RFS (%, 95% CI)	3-year OS rate (%, 95% CI)	3-year cumulative recurrence rate (%)	R0 resection rate
Hattori et al ⁹ (n=40; safety	Intent to treat population: 80 (64-89)	Intent to treat population: 97 (83-99)	Distant recurrence rate: 21 (10-39)	97.5%
population n=32, median follow-up duration: 46 months)	Per protocol population: 75 (57-86)	Per protocol population: 96 (80-99)	Local recurrence rate: 9.3 (3-2.5)	

In the prognosis of each staging, 3-year RFS rate was 93% (95% CI 64–99%) in stage II and 52% (95% CI 30–74%) in stage III, the 3-year OS rate was 100% in stage II and 93% (95% CI 66–99%) in stage III. Combined three-year cumulative rates for local recurrence and distant recurrence were 9.3% (95% CI 3.0–25%) and 21% (95% CI 10–39%) respectively. 9

Toxicity

A summary of the toxicities associated with this protocol are included in the table below. The most clinically significant Grade ≥ 3 toxicities for this treatment are thrombocytopenia (12.5%) and peripheral sensory neuropathy (15.6%). The incidence of toxicity-related treatment discontinuation was 73% with peripheral sensory neuropathy as the most common adverse event leading to discontinuation (38%).

Treatment-related adverse events⁹

Table 5 Frequency of common toxicities

	N=32			
	All grade		≥Grade 3	
	n	%	n	%
Hematologic toxicity	21	65.6	6	19
Neutropenia	17	53.1	3	9.3
Anemia	21	65.6	1	3.1
Thrombocytopema	21	65.6	4	12.5
Febrile neutropenia	0	0	0	0
Non-hematologic toxicity	26	81.2	12	38
Anorexia	18	56.2	4	12.5
Diarrhea	8	25	1	3.1
Nausea/vomiting	17	53.1	3	9.3
Mucositis	5	15.6	0	0
Hand-foot syndrome	11	34.3	1	3.1
Peripheral neuropathy	26	81.2	5	15.6
Allergy	3	9.3	1	3.1

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History

Version 4

Date Summary of changes

Date	Summary of changes
12/05/2023	Protocol reviewed electronically by Medical Oncology Reference committee 2022. Evidence section updated to
	align with new 5 year available data. Version number changed to V.4. Next review in 2 years.

Version 3

Date	Summary of changes
20/01/2022	Treatment schedule notes updated with final results of IDEA collaboration study. Number of cycles added to gastric evidence section as per trial. Version changed to V.3.

Version 2

Date	Summary of changes
14/10/2021	Existing approved protocol ID 1707 incorporated in the protocol.

Version 1

ID 4019 Adjuvant CAPOX (XELOX) (capecitabine and oxaliplatin)		
Date	Summary of changes	
12/08/2021	New multi-indication protocol approved by reference committee and published on eviQ. Note that this protocol	
	replaces the existing approved protocol ID 1211. Next review in one year.	

As ID 4019 Adjuvant CAPOX (XELOX) (capecitabine and oxaliplatin) replaces the existing approved protocols ID 1211 and ID 1707, their individual History sections are included below for consistency in documentation.

Date	Summary of changes
25/11/2011	New protocol taken to Medical Oncology Reference Committee meeting.
24/01/2012	Approved and published on eviQ.
15/3/2012	PHC Omis view updated.
01/05/2012	Palonosetron added as the preferred 5HT ₃ antagonist for moderate emetogenicity.
27/09/2012	Change to calcium gluconate and magnesium sulphate dilution and administration time details due to stability reasons (100 mL sodium chloride 0.9% changed to to 250 mL glucose 5%).
12/06/2013	Calcium and magnesium removed as no protective benefit against oxaliplatin-induced neurotoxicity.
13/09/2013	Protocol reviewed by reference committee via email. No changes and next review in 2 years.
24/08/2014	PHC view removed.
18/02/2016	Discussion with Medical Oncology Reference Committee Chairs and protocol to be reviewed every 5 years. Nex review due in 3 years.
09/11/2016	The following changes made post Medical Oncology Reference Committee meeting held on 21 October 2016. Link to AGTIG and ANZCTR added. Title changed from XELOX to CAPOX.
16/12/2016	Dissolving capecitabine information added to administration and patient information.
31/05/2017	Transferred to new eviQ website. Version number changed to V.3.
	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.
16/02/2018	Protocol reviewed electronically by Medical Oncology Reference Committee. Note regarding the IDEA evidence on 3 vs 6 months treatment added. Fluoropyrimidine warning added. Review in 2 years.
10/05/2018	Haematological dose modifications updated as per consensus of the expert clinician group. Version number changed to V.4.
22/06/2018	Antiemetics updated to be in line with international guidelines. Note to dexamethasone added.

08/10/2019	Clinical information updated with PBS expanded indications for GCSF.
25/10/2020	Protocol reviewed electronically by the Medical Oncology Reference committee. ID 637 Colorectal adjuvant FOLFOX6 (modified) (fluorouracil leucovorin oxaliplatin) added as a related page. Evidence updated to include
	IDEA evidence and to align with ID 637. Version number changed to V.6. Next review in 2 years.

ID 1707 Gast	ric adjuvant CAPOX (XELOX) (capecitabine and oxaliplatin) version 4
Date	Summary of changes
27/03/2015	New protocol taken to Medical Oncology Reference Committee meeting.
14/04/2015	Approved and published on eviQ.
09/11/2016	The following changes made post Medical Oncology Reference Committee meeting held on 21 October 2016. Title changed from XELOX to CAPOX. Link to AGITG and ANZCTR added.
16/12/2016	Dissolving capecitabine information added to administration and patient information.
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.
16/02/2018	Protocol reviewed electronically by Medical Oncology Reference Committee. Fluoropyrimidine overdose or overexposure warning added. Review in 2 years
10/05/2018	Haematological dose modifications updated as per consensus of the expert clinician group. DPD enzyme deficiency wording in clinical information updated. Fluoropyrimidine safety alert in clinical information added. Version number changed to V.3.
22/06/2018	Antiemetics updated to be in line with international guidelines. Note to dexamethasone added.
08/10/2019	Clinical information updated with PBS expanded indications.
25/09/2020	Protocol reviewed electronically by the Medical Oncology Reference committee. Nil changes. Next review in 2 years.

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

First approved: 6 August 2021 Last reviewed: 12 May 2023 Review due: 30 June 2025

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https://www.eviq.org.au/p/4019

12 Jul 2023

Patient information - Adjuvant - CAPOX (XELOX) (capecitabine and oxaliplatin)



Patient's name:

Your treatment

This treatment may be used to treat different types of cancer. Your doctor will advise you why you are receiving this treatment.

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

CAPOX (you may also hear this called XELOX) (capecitabine and oxaliplatin) This treatment cycle is repeated every 21 days. Your doctor will advise you of the number of treatments you will have. Day **Treatment** How it is given How long it takes 1 Oxaliplatin By a drip into a vein About 3 hours (ox-AL-ih-pla-tin) 1 to 14 Capecitabine Take orally TWICE a day on days 1 to 14 with a glass of water within 30 minutes of (KAP-e-SYE-ta-been) finishing a meal (just after breakfast and then again after evening meal). Do not break, crush or chew tablets. If you are unable to swallow the tablets whole they may be dissolved in water and the solution swallowed (see directions in Other information about your treatment). If you forget to take a tablet or vomit a

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

Do not take capecitabine tablets from day 15 to 21

tablet, take your normal dose the next time it is due. Do not take an extra dose.

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

When to get help

15 to 21

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

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

· diarrhoea - passing an extra 4 to 6 bowel motions per day, or passing bowel motions through the night

- vomiting 2 to 5 episodes of vomiting in a 24 hour period
- · a sore mouth which is making it difficult to eat
- pain and redness on the palms of your hands and the soles of your feet.

IMMEDIATELY go to your nearest hospital Emergency 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. 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.

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.

Instructions for dissolving capecitabine tablets:

- Capecitabine tablets should never be crushed, cut or broken.
- You (or whoever is dissolving the tablets) should wear disposable gloves and try to minimise touching the tablets.
- Put the tablet(s) needed for the dose into a disposable cup with a lid, if possible. If using a non-disposable cup, ensure the cup is kept only for this purpose.
- Fill the cup with approximately 200 mL of water and cover with lid if available.

- Leave the tablets in the water to dissolve, this may take up to 15 minutes. Gentle agitation of the solution may assist in the dissolving process, being careful not to spill the solution.
- Once the tablets have fully dissolved, swallow the solution immediately.
- In case of any spillages to skin, immediately wash the affected area thoroughly with warm soapy water. If spillage occurs to
 work surface or floor, wash area with warm soapy water and dry with absorbent paper towel or cloth. Dispose of cloth in a
 cytotoxic bag.
- The tablets have a bitter taste. The solution may be made more palatable by dissolving the tablets in fruit juice (not citrus juice) or by adding cordial or flavouring.
- To ensure that the whole dose is taken, swirl the cup with water and swallow. Repeat if necessary.
- The disposable cup and gloves should be disposed of in a cytotoxic waste bag. Non-disposable cups should be washed thoroughly with warm soapy water.

Side effects

Cancer treatments can cause damage to normal cells in your body, which can cause side effects. Everyone gets different side effects, and some people will have more problems than others.

The table below shows some of the side effects you may get with this treatment. You are unlikely to get all of those listed and you may also get some side effects that have not been listed.

Tell your doctor or nurse about any side effects that worry you. Follow the instructions below and those given to you by your doctor or nurse.

Immediate (onset hours to days) • Allergic reactions are uncommon but can be life threatening. **Allergic reaction** • If you feel unwell during the infusion or shortly after it, or: o 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 While you are in hospital: Tell your doctor or nurse immediately. After you leave: Contact your doctor or nurse immediately, or go to the nearest hospital **Emergency Department.** · You may get discomfort or tightness in the back of the throat, or the feeling like you cannot Breathing or swallowing breathe or swallow. problems • 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. • You may get: **Heart problems** · chest pain or tightness o 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. • You may feel sick (nausea) or be sick (vomit). Nausea and vomiting • 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 • 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. • You may find that food loses its taste or tastes different. Taste and smell changes • These changes are likely to go away with time. · Do your mouth care regularly. • Chew on sugar-free gum or eat sugar-free mints. • Add flavour to your food with sauces and herbs. Ask your doctor or nurse for eviQ patient information - Taste and smell changes during cancer treatment.

Early (onset days to weeks)

Infection risk (neutropenia)

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

Mouth pain and soreness (mucositis)

- You may have:
 - bleeding gums
 - mouth ulcers
 - a white coating on your tongue
 - o pain in the mouth or throat
 - difficulty eating or swallowing.
- Avoid spicy, acidic or crunchy foods and very hot or cold food and drinks.
- · Try bland and soft foods.
- Brush your teeth gently with a soft toothbrush after each meal and at bedtime. If you normally floss continue to do so.
- Rinse your mouth after you eat and brush your teeth, using either:
 - o 1/4 teaspoon of salt in 1 cup of warm water, or
 - 1/4 teaspoon of bicarbonate of soda in 1 cup of warm water
- Ask your doctor or nurse for eviQ patient information Mouth problems during cancer treatment.
- Tell your doctor or nurse if you get any of the symptoms listed above.

Hand-foot syndrome (palmar-plantar erythrodysaesthesia)

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

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.

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.

Skin changes	 Your skin may become dry, and you may notice changes to areas of your skin that have been exposed to the sun. Keep your skin moisturised with a cream such as sorbolene or aqueous cream. Avoid direct sunlight. Protect your skin from the sun by wearing a wide-brimmed hat, sun-protective clothing, sunglasses and sunscreen of SPF 50 or higher. 				
	Tell your doctor or nurse if you notice any skin changes.				
Skin that is more sensitive to the sun (photosensitivity)	 After being out in the sun you may develop a rash like a bad sunburn. Your skin may become red, swollen and blistered. Avoid direct sunlight. Protect your skin from the sun by wearing sun-protective clothing, a wide-brimmed hat, sunglasses and a sunscreen of SPF 50 or higher. Tell your doctor or nurse if you get any of the symptoms listed above. 				
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. 				
Stomach pain	 You may get: dull aches cramping or pain bloating or flatulence (gas). Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you have stomach pain that you are unable to control. 				

Late (onset weeks to months	s)
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.
Nail changes	 Your nails may: grow more slowly become darker develop ridges or white lines become brittle and flaky In some cases, you may lose your nails completely. Keep your nails clean and short. Avoid things like biting your fingernails, getting a manicure, pedicure or false nails. Wear gloves when you wash the dishes, work in the garden, or clean the house.
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)
High blood bilirubin levels (hyperbilirubinaemia)	 You may get: yellowing of your skin or eyes itchy skin pain or tenderness in your stomach nausea and vomiting loss of appetite. You will have regular blood tests to check how well your liver is working. Tell your doctor or nurse as soon as possible if you notice that your urine is a dark colour, the whites of your eyes look yellow, or if you have stomach pain.

General advice for people having cancer treatment

Chemotherapy safety

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

Blood clot risk

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

Medications and vaccinations

- Before you start treatment, tell your doctor about any medications you are taking, including vitamins or herbal supplements.
- Don't stop or start any medications during treatment without talking to your doctor and pharmacist first.
- Paracetamol is safe to take if you have a headache or other mild aches and pains. It is recommended that you avoid taking aspirin, ibuprofen and other anti-inflammatory type medications for pain while you are having treatment. However, if these medications have been prescribed by your doctor, do not stop taking them without speaking with your doctor.
- Vaccinations such as flu and tetanus vaccines are safe to receive while having treatment. Do not have any live vaccines during your treatment or for 6 months after it finishes. If you are unsure, check with your doctor before you have any vaccinations.

People you live with should be fully vaccinated, including having live vaccines according to the current vaccination schedule. Extra
care needs to be taken with hand washing and careful disposal of soiled nappies for infants who have recently received the
rotavirus vaccine.

Other medical and dental treatment

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

Diet

- · While you are receiving this treatment it is important that you try to maintain a healthy diet.
- · Speak to your doctor or nurse about whether drinking alcohol is safe with your treatment.
- If you have any concerns about recent weight loss or weight gain or questions about your diet, ask to speak to a dietitian.

Fertility

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

Pregnancy and breastfeeding

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

Sex life and sexuality

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

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 - Colorectal

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

Where to get more information - Gastric

Telephone support

• Call Cancer Council on 13 11 20 for cancer information and support

Stomach and oesophageal cancer information

• Pancare Foundation - pancare.org.au

General cancer information and support

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

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- iCanQuit iCanQuit.com.au
- Patient Information patients.cancer.nsw.gov.au/coping-with-cancer/physical-wellbeing/quitting-smoking
- Quitnow quitnow.gov.au

Additional notes:		

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

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