

CapOX 2 Weekly

Indication

Palliative chemotherapy for colorectal cancer in patients unsuitable for central line experiencing significant oxaliplatin infusion related complications

ICD-10 codes

Codes prefixed with C20

Regimen details

Day	Drug	Dose	Route
1	Oxaliplatin	85mg/m ²	IV infusion
1-9	Capecitabine	800mg/m ² twice daily	PO

Cycle frequency

14 days

Number of cycles

Treat until disease progression

Administration

Oxaliplatin is administered in 500ml of 5% glucose over 2 hours. Oxaliplatin is not compatible with sodium chloride 0.9%. Lines must not be pig-backed or flushed with sodium chloride 0.9% immediately after the infusion.

Patients should be observed closely for platinum hypersensitivity reactions, particularly during the first and second infusions. Hypersensitivity reactions may occur within a few minutes following the initiation of the infusion of oxaliplatin. Facilities for the treatment of hypotension and bronchospasm must be available.

If hypersensitivity reactions occur, minor symptoms such as flushing or localized cutaneous reactions do not require discontinuation of therapy: the infusion may be temporarily interrupted and when symptoms improve re-started at a slower infusion rate. Chlorpheniramine 10mg IV may be administered.

Severe reactions such as hypotension, bronchospasm or generalized rash/erythema require immediate discontinuation of oxaliplatin, and appropriate therapy should be initiated.

Oxaliplatin may cause transient paraesthesia of hands and feet and laryngopharyngeal dysaesthesia (unpleasant sensations in the throat). Onset is during or within hours of infusion and resolves within minutes to a few days. Symptoms are exacerbated by cold, so patients should be well advised on precautions to be taken. This does not require treatment or dose reduction, but subsequent infusions should be given over 6 hours.

Capecitabine is available as 150mg and 500mg tablets.

Tablets should be taken after food and swallowed whole with a glass of water.

Pre-medication

Antiemetics as per local policy.

Patients who have previously experienced Grade 1 or Grade 2 platinum hypersensitivity should receive the following pre-medication:

- 30 minutes prior to oxaliplatin: Dexamethasone 20mg IV
- 30 minutes prior to oxaliplatin: Chlorpheniramine 10mg IV and Ranitidine 50mg IV

Emetogenicity

Moderate- high emetogenic potential

Additional supportive medication

Mouthwashes as per local policy.

Loperamide if required.

Metoclopramide 10mg tds prn.

Extravasation

Oxaliplatin is an exfoliant (group 4)

Investigations – pre first cycle

Investigation	Validity period
FBC	14 days
U+E (including creatinine)	14 days
LFT (including AST)	14 days
Calcium	14 days
Magnesium	14 days
CEA	14 days
DPYD mutation testing	none
Hep B serology (HBsAG, HBcAb)	none
HbA1c	3 months
Random glucose	14 days

Investigations –pre subsequent cycles

FBC, U&E (including creatinine), LFT (including AST), calcium, magnesium, random glucose, CEA

Standard limits for administration to go ahead

If blood results not within range, authorisation to administer **must** be given by prescriber/ consultant.

Investigation	Limit
Neutrophil count	$\geq 1.5 \times 10^9/L$ (discuss with consultant ≥ 1.0 - <1.5)
Platelet count	$\geq 75 \times 10^9/L$
Creatinine clearance	≥ 50 mL/min
Bilirubin	$\leq 1.5 \times$ ULN
AST/ALT	$< 2.5 \times$ ULN

Dose modifications

Haematological toxicity

Defer treatment for 1 weeks if neutrophil count $<1.0 \times 10^9/L$ and/or platelets $<75 \times 10^9/L$ and delay next cycle until recovery. Recommence with dose modifications as below:

Neutrophils	Platelets	Oxaliplatin dose	Capecitabine dose
≥ 1.0 and	≥ 75	100%	100%
0.5-0.9 or	50-74	65mg/m ²	100%
<0.5 and/or	25-49	65mg/m ²	100%
<0.5 and/or	<25	40mg/m ²	100%

If febrile neutropenia (neutrophils $<0.5 \times 10^9/L$ and fever requiring IV antibiotics)- reduce all subsequent doses of oxaliplatin to 100mg/m²

Renal Impairment

CrCl (mL/min)	Oxaliplatin dose	Capecitabine dose
≥ 50	100%	100%

30- 49	75%	75%
<30	Omit	contraindicated

Hepatic impairment

Capecitabine:

Lack of information available. In patients with mild to moderate hepatic dysfunction (bilirubin <3 x ULN and/or AST/ALT <5 x ULN) probably no dose reduction necessary, consultant decision.

Oxaliplatin:

Little information available. Probably no dose reduction necessary, consultant decision. Note that significantly impaired hepatic function may be a sign of disease progression and require cessation of, or change in, treatment

DPYD variants

All patients due to receive fluoro-pyrimidine based therapy should have a DPD test prior to starting treatment. Dihydropyrimidine dehydrogenase (DPD) deficiency can result in severe toxicity secondary to reduced fluorouracil metabolism (this can present as severe diarrhoea and/or severe stomatitis early in the first cycle).

Any patient who has not had a DPD test should be discussed with the consultant prior to going ahead. Patients with variants should be considered for a dose modification following national advice for recommended dose adjustments.

[dpd-testing-ukcb-july-2020-final.pdf \(theacp.org.uk\)](#)

Where a patient has had significant toxicities but the DPD test has shown none of the variants to be present, a further test can be conducted to test the presence of rarer variants.

Other Toxicities

Capecitabine: Other toxicities should be managed by symptomatic treatment and/or dose modification (e. by treatment interruption or undertaking a dose reduction). Once the dose has been reduced, it should not be increased at a later time.

Dose modifications should be made as per the following table:

Toxicity grade	1 st occurrence	2 nd occurrence	3 rd occurrence	4 th occurrence
0-1	100%	100%	100%	100%
2	Delay then 100%	Delay then 75%	Delay then 50%	Discontinue
3	Delay then 75%	Delay then 50%	Discontinue	
4	Delay then 50%	Discontinue		

Any delays should be until the toxicity has resolved to grade 0-1.

Oxaliplatin:

Neurological toxicity: Dose related peripheral neuropathy can occur with oxaliplatin. It usually occurs after a cumulative dose of 800mg/m². It can occur once oxaliplatin is completed.

If neurological symptoms occur, use the following oxaliplatin dose adjustments:

Toxicity Grade	Oxaliplatin
1 (any duration) or grade 2 longer than 7 days	100%
2 paraesthesia persisting until next cycle	65mg/m ²
3 paraesthesia lasting longer than 7 days	65mg/m ²
3 paraesthesia persisting until next cycle	Discontinue permanently
4 of any duration	Discontinue permanently

In grade 3 or 4 stomatitis or diarrhoea, delay until recovers to ≤ grade 2 then reduce oxaliplatin dose to 100mg/m². Patients presenting with diarrhoea must be carefully monitored until the symptoms have disappeared as a rapid deterioration can occur. Any delays should be until toxicity has resolved to grade 0-1

Adverse effects –

for full details consult product literature/ reference texts

• Serious side effects

Myelosuppression Infertility

Allergic reactions

Neurotoxicity

Nephrotoxicity

Coronary artery spasm*

*Coronary artery spasm is a recognised complication of capecitabine treatment, although the evidence base regarding aetiology, management and prognosis is not particularly strong. Should a patient receiving capecitabine present with chest pains, stop the treatment. Standard investigation and treatment of angina may be required. If re-challenge is deemed necessary, this can be performed under close supervision, but should symptoms redevelop, the capecitabine should be permanently discontinued.

• Other side effects

Headache

Dizziness

Dysgeusia

Transient cerebellar syndrome

Confusion

Significant drug interactions

– for full details consult product literature/ reference texts

Warfarin/coumarin anticoagulants: Avoid use due to elevations in INR. Switch to low molecular weight heparin during treatment.

Oxaliplatin:

Avoid **nephrotoxic agents** as these may increase toxicity of oxaliplatin

Capecitabine:

Folinates: Avoid concomitant use of folinic and folic acid – enhanced toxicity of capecitabine.

Co-trimoxazole/trimethoprim: Avoid if possible – enhances antifolate effect. If essential, monitor FBC regularly.

Phenytoin and fosphenytoin: Toxicity has occurred during concomitant therapy- monitor levels regularly

Sorivudine and its analogues: Co-administration can cause increased toxicity which may be fatal.

Allopurinol: A decrease in capecitabine activity has been shown when taken in combination with allopurinol. Avoid if possible

Antacids: the use of antacids with capecitabine can decrease absorption-avoid.

Additional comments

Fertility/Contraception

Patients should agree to use an acceptable method of birth control to avoid pregnancy for the duration of treatment and for 6 months afterwards. Breastfeeding should be discontinued during treatment. Oxaliplatin may have an anti-fertility effect

References

- Colorectal NICE guideline NG151 (updated 15 Dec 2021) accessed 11 May 2022
- Summary of Product Characteristics (Oxaliplatin) accessed 11 May 2022 via www.medicines.org.uk
- Summary of Product Characteristics (Capecitabine) accessed 11 May 2022 via www.medicines.org.uk
- Personalised Medicine Approach for Fluoro-pyrimidine-based Therapies. UK Chemotherapy Board July 2020 accessed 11 May 2022 via dpd-testing-ukcb-july2020-final.pdf (theacp.org.uk)

THIS PROTOCOL HAS BEEN DIRECTED BY DR WILLIAMSON, DESIGNATED LEAD CLINICIAN FOR

RESPONSIBILITY FOR THIS PROTOCOL LIES WITH THE HEAD OF SERVICE

Date: May 2022

Review: May 2024

VERSION: 2.0
