Capecitabine (colorectal and biliary tract)

Indication

Adjuvant chemotherapy for colorectal and biliary tract cancer.
Treatment of metastatic colorectal cancer.

ICD-10 codes

Adjuvant Codes prefixed with C18-20 and C24
Metastatic Codes prefixed with C18-20.

Regimen details

Day	Drug	Dose	Route
1-14	Capecitabine	1250mg/m^2 BD *	PO

***Consider starting dose of 1000mg/m^2 for poor performance status or significant co-morbidity**

Cycle frequency

21 days

Number of cycles

Adjuvant 8
Metastatic continued until progression or unacceptable toxicity

Administration

Capecitabine is available as 150mg and 500mg tablets
Tablets should be taken after food and swallowed whole with a glass of water.

For patients who have difficulty swallowing, tablets may be dissolved in 200ml warm water. Stir until dissolved and drink immediately.

Pre-medication

Nil

Emetogenicity

This regimen has a moderate to low emetogenic potential

Additional supportive medication

Loperamide if required.
Metoclopramide 10mg tds prn.
Topical emollients to prevent PPE
H2 antagonist or proton pump inhibitor if required.

Extravasation

N/A

Investigations – pre first cycle

Investigation	Validity period
FBC	14 days
U+E (including creatinine)	14 days
LFTs (including AST)	14 days
Bone profile	14 days
CEA	14 days
DPYD mutation testing	none
Hepatitis B serology (HBsAG, HBcAb)	none
HbA1c	3 months
Random glucose	14 days

Investigations - pre subsequent cycles

FBC, U&E (including creatinine), LFT (including AST), 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
Neutrophils	≥ 1.5 x 10^9/L (discuss with consultant ≥ 1.0- <1.5)
Platelets	≥ 75 x 10^9/L
Bilirubin	< 1.5 x ULN
AST/ALT	< 2.5 x ULN
Creatinine Clearance (CrCl)	≥ 50mL/min

Dose modifications

- **Haematological toxicity**

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

Neutrophils	Platelets	Capecitabine dose
≥1.0 and	≥75	100%
0.5-0.9 or	50-74	75%
<0.5 and/or	25-49	50%
<0.5 and/or	<25	50%

- **Renal impairment**

CrCl (mL/min)	**Capecitabine dose**
≥ 50	100%
30-49	75% (closely monitored)
<30	Contraindicated

- **Hepatic impairment**

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.

- **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**

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	1st occurrence	2nd occurrence	3rd occurrence	4th 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.

Patients presenting with diarrhea 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
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.
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.

References

- Colorectal NICE guideline NG151 (updated 15 Dec 2021) accessed 11 May 2022
- 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-july-2020-final.pdf (theacp.org.uk)

THIS PROTOCOL HAS BEEN DIRECTED BY DR WILLIAMSON DESIGNATED LEAD CLINICIAN FOR COLORECTAL CANCER
RESPONSIBILITY FOR THIS PROTOCOL LIES WITH THE HEAD OF SERVICE

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