Capecitabine

Indication
Adjuvant treatment of biliary tract cancer following surgical resection.

ICD-10 codes
Codes with a prefix C23

Regimen details

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

* consider reducing dose to 1000mg/m^2 BD for patients ≥ 70 years old.

Treatment should commence within 16 weeks of surgery.

Cycle frequency
21 days

Number of cycles
8 cycles

Administration
Capecitabine is available as 150mg and 500mg tablets.
Tablets should be taken twice a day, ideally 12 hours apart. They should be taken after food, within 30 minutes of a meal, and swallowed whole with a glass of water.

Pre-medication
Nil

Emetogenicity
This regimen has moderate-low emetic potential

Additional supportive medication
Loperamide if required.
Topical emollients to prevent palmar plantar erythema.
H_2 antagonist or proton pump inhibitor if required.

Extravasation
N/A

Investigations – pre first cycle

Investigation	**Validity period** (or as per local policy)
FBC	14 days
U+E (including creatinine)	14 days
LFTs	14 days

Investigations – pre subsequent cycles

Investigation	**Validity period** (or as per local policy)
FBC	96 hours
U+E (including creatinine)	7 days
LFTs	7 days

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	≥ 1.0 x 10^9/L
Platelets	≥ 100 x 10^9/L
Creatinine clearance (CrCl)	>50 mL/min
Bilirubin	≤ 3 x ULN
AST/ALT	≤ 2.5 x ULN

Dose modifications

- **Haematological toxicity**

If neutrophils <1.0 x 10^9/L and/or platelets <100 x 10^9/L delay 1 week or until recovery.

- **Renal impairment**

CrCl (mL/min)	**Capecitabine dose**
>50	100%
30-50	75% (with close monitoring)
<30	Contra-indicated

- **Hepatic impairment**

AST +/or ALT (x ULN)		**Bilirubin (x ULN)**	**Capecitabine dose**
≤ 2.5	and	≤ 3	100%
> 2.5	or	> 3	Consultant decision*

*current evidence does NOT suggest dose modification is necessary.
Capecitabine is contra-indicated in severe hepatic impairment.

- **Other toxicities**

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

For those toxicities considered unlikely to become serious or life-threatening (e.g. alopecia, altered taste or nail changes) treatment can be continued at the same dose without reduction or interruption.

Patients should be informed of the need to interrupt treatment immediately if they develop moderate or severe side effects particularly diarrhoea – not controlled by loperamide, palmar-plantar erythema or infection.

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	Discontinue or Delay then 50%	Discontinue		

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

Adverse effects - for full details consult product literature/ reference texts

- **Serious side effects**

Cardiotoxicity
Myelosuppression
Diarrhoea
Thrombus/embolism
Severe toxicity due to DPD deficiency (see comments below)

- **Frequently occurring side effects**

Nausea and vomiting
Stomatitis/Mucositis
Myelosuppression
PPE
Fatigue
Skin reactions
Nail changes
Taste disturbance

- **Other side effects**

Myalgia
Fluid retention
Alopecia
Rash
Deranged liver function

Significant drug interactions – for full details consult product literature/ reference texts

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

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

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

Sorivudine, Allopurinol, Phenytoin: close monitoring is necessary if prescribed with any of these agents.

Antacids: Aluminium hydroxide and magnesium hydroxide containing antacids have been shown to produce a slight increase in plasma concentration of capecitabine.

Additional comments

This regimen is contraindicated if known or suspected dihydropyrimidine dehydrogenase (DPD) deficiency.

References

- Summary of Product Characteristics Capecitabine (Roche) accessed 1 May 2019 via www.medicines.org.uk
- Primrose, J., et al. Capecitabine compared with observation in resected biliary tract cancer. The Lancet Oncology. Published March 2019 https://doi.org/10.1016/S1470-2045(18)30915-X

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