

## Capecitabine (colorectal)

### Indication

First line treatment of metastatic colorectal cancer.

(NICE TA61)

Adjuvant therapy for stage III (Dukes C) colon cancer.

(NICE TA100)

### ICD-10 codes

Codes with a prefix C18-20

### Regimen details

Days	Drug	Dose	Route
1-14	Capecitabine	1250*mg/m <sup>2</sup> BD	PO

\* Consider a starting dose of 950-1000mg/m<sup>2</sup> for elderly, poor performance status or significant co-morbidity.

### Cycle frequency

21 days

### Number of cycles

Metastatic – 6 cycles

Adjuvant – 8 cycles

### Administration

Capecitabine is available as 150mg and 500mg tablets.

Tablets should be taken after food.

Doses should be prescribed as per the following table:

Body surface area (m <sup>2</sup> )	100% dose (1250mg/m <sup>2</sup> )	75% dose (950mg/m <sup>2</sup> )	50% dose (625mg/m <sup>2</sup> )
≤ 1.26	1500 BD	1150 BD	800 BD
1.27-1.38	1650 BD	1300 BD	800 BD
1.39-1.52	1800 BD	1450 BD	950 BD
1.53-1.66	2000 BD	1500 BD	1000 BD
1.67-1.78	2150 BD	1650 BD	1000 BD
1.79-1.92	2300 BD	1800 BD	1150 BD
1.93-2.06	2500 BD	1950 BD	1300 BD
2.07-2.18	2650 BD	2000 BD	1300 BD
≥2.19	2800 BD	2150 BD	1450 BD

### Pre-medication

Nil

### Emetogenicity

This regimen has moderate-low emetic potential

### Additional supportive medication

Loperamide if required.

Topical emollients to prevent PPE

H<sub>2</sub> 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	$\geq 1.0 \times 10^9/L$
Platelets	$\geq 100 \times 10^9/L$
Creatinine clearance (CrCl)	>50 mL/min
Bilirubin	$\leq 3 \times \text{ULN}$

### Dose modifications

- Haematological toxicity**

If neutrophils  $<1.0 \times 10^9/L$  and/or platelets  $<100 \times 10^9/L$  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
$\leq 2.5$	and	$\leq 3$	100%
$> 2.5$	or	$> 3$	Consultant decision*

\*current evidence does NOT suggest dose modification is necessary

- 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 erythrodyesthesia or infection.

Dose modifications should be made as per the following table:

Toxicity grade	1 <sup>st</sup> occurrence	2 <sup>nd</sup> occurrence	3 <sup>rd</sup> occurrence	4 <sup>th</sup> 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.

### 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.

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### References

- Summary of Product Characteristics Capecitabine - Xeloda® (Roche) accessed 11 June 2014 available at <http://www.medicines.org.uk>
  - NICE TA100 (Capecitabine and oxaliplatin in the adjuvant treatment of stage III colon cancer) accessed 11 June 2014 via [www.nice.org.uk](http://www.nice.org.uk)
  - NICE TA61 (Capecitabine and tegafur uracil for metastatic colorectal cancer) accessed 11 June 2014 via [www.nice.org.uk](http://www.nice.org.uk)
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