Capecitabine and radiotherapy (rectal)

Indication
Pre-operative use in rectal cancer to down stage the tumour prior to surgery.

ICD-10 codes
Codes with a prefix C20

Regimen details

Days	Drug	Dose	Route
1-35*	Capecitabine	825mg/m^2 BD	PO

* Continuously for 35 days whilst on radiotherapy, from the first to the last day, including weekends.

In elderly or frail patients consider reducing starting dose to 625mg/m^2 BD.

Cycle frequency
As above

Number of cycles
One cycle only.

Administration
Capecitabine is available as 150mg and 500mg tablets.
Tablets should be taken after food.
Ideally the first dose should be taken 1-2- hours before radiotherapy treatment.

Doses should be prescribed as per the following table:

Body surface area (m^2)	**Dose** 825mg/m^2 BD
≤ 1.26	1000
1.27-1.38	1100
1.39-1.48	1150
1.49-1.66	1300
1.67-1.78	1450
1.79-1.92	1500
1.93-2.06	1650
2.07-2.18	1750
≥2.19	1800

Pre-medication
Nil

Emetogenicity
This regimen has moderate-low emetic potential

Additional supportive medication

Loperamide if required.
Topical emollients to prevent PPE
H_2 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	14 days

Investigations – pre subsequent cycles

Investigation	Validity period
FBC	Weekly during treatment
U+E (including creatinine)	Day 1 and during week 3
LFTs	Day 1 and during week 3

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

Dose modifications

Once a dose has been reduced it should not be increased at a later time.

- **Haematological toxicity**

If neutrophils <1.0 x 10^9/L and/or platelets <100 x 10^9/L delay 1 week (continue radiotherapy). If FBC recovered after 1 week then restart at 75% dose.

If further delays are needed then consider further dose reduction or discontinue capecitabine (consultant decision).

- **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

- **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 erythrodyaesthesia (PPE) 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	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 Caepcitabine - Xeloda®(Roche) accessed 11 June 2014 available at http://www.medicines.org.uk
- Rich, T, Shepard, R and Mosley, S. Four Decades of Continuing Innovation with 5FU: Current and Future Approaches to 5 Fluorouracil Chemoradiation Therapy. JCO (2004) 22; 11: 2214 - 2232.

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