Capecitabine (breast)

Indication

Palliative therapy for advanced breast cancer where anthracyclines and single-agent docetaxel have either failed or are not appropriate.

(NICE CG81)

ICD-10 codes

Codes with a prefix C50

Regimen details

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

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

For some patients it may be acceptable to switch to alternate week dosing; 1250mg/m^2 BD for 7 days, on alternate weeks (i.e. one week 'on' one week 'off'). Please note this dosing schedule is unlicensed.

Cycle frequency

21 days

Number of cycles

Until disease progression or intolerable toxicity.

Administration

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

Doses should be prescribed as per the following table:

Body surface area (m^2)	100% dose (**1250mg/m^2**)	75% dose (**950mg/m^2**)	50% dose (**625mg/m^2**)
≤ 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 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	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

- Blum. J.L., et al. Capecitabine in paclitaxel refractory metastaic breast cancer. JCO. 1999. 17; (2):485 – 493
- Summary of Product Characteristics Capecitabine (Roche) accessed 2 July 2014 via www.medicines.org.uk
- NICE CG81 – Advanced breast cancer. Accessed 2 July 2014 via www.nice.org.uk

Written/reviewed by: Dr M Beresford (Consultant Oncologist, Royal United Hospital, Bath)

Checked by: Sarah Murdoch (Senior Oncology Pharmacist, SW Strategic Clinical Network)

Authorised by: Dr J Braybrooke (Consultant Oncologist, UHBristol NHS Trust, SW Strategic Clinical Network)

Date: 14 January 2015