

Capecitabine and Temozolomide (CAPTEM)

Indication

Palliative treatment of metastatic Grade 1 or 2 neuroendocrine tumours.

ICD-10 codes

Codes with a prefix C24,25

Regimen details

Days	Drug	Dose	Route
1-14	Capecitabine	750mg/m ² BD*	PO
10-14	Temozolomide	100mg/m ² BD** (or 200mg/m ² OD)	PO

* Total maximum **daily** dose of capecitabine is 2500mg/m².

** For patients who have received previous treatment with chemotherapy or extensive radiotherapy consider reducing **daily** temozolomide dose to 150mg/m².

Cycle frequency

28 days

Number of cycles

Maximum of 12 cycles

Administration

Capecitabine is available as 150mg and 500mg tablets. Tablets should be taken after food.

Temozolomide is available as 5mg, 20mg, 100mg, 140mg, 180mg, and 250mg capsules. Capsules should be taken on an empty stomach, swallowed whole with a glass of water. Capsules must **NOT** be opened or chewed. If vomiting occurs after the dose is administered, a second dose should not be administered that day.

Pre-medication

Nil

Emetogenicity

This regimen has low-moderate emetic potential, high on days 10-14.

Additional supportive medication

Antiemetics prior to temozolomide and if required.

Loperamide if required.

Topical emollients to prevent PPE.

H₂ 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	$\leq 3 \times$ ULN
AST/ALT	$\leq 2.5 \times$ ULN

Dose modifications

- Haematological toxicity

At start of each cycle:

Neutrophils ($\times 10^9/L$)		Platelets ($\times 10^9/L$)	Capecitabine and temozolomide doses			
			1 st occurrence	2 nd occurrence	3 rd occurrence	4 th occurrence
≥ 1.5	and	≥ 75	100%	100%	100%	100%
1-1.49	or	50-74	Delay until recovery then 100%	Delay until recovery then 75%	Delay until recovery then 50%	Discontinue
0.5-0.99	or	25-49	Delay until recovery then 75%	Delay until recovery then 50%	Discontinue	Discontinue
<0.5	or	<25	Discontinue or delay until recovery then 50%	Discontinue	Discontinue	Discontinue

- Renal impairment

Capecitabine

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

- Hepatic impairment

Capecitabine

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

*current evidence does NOT suggest dose modification is necessary

Temozolomide

Caution in patients with severe hepatic impairment – discuss with consultant if bilirubin > 3 x ULN and/or AST/ALT > 2.5 x ULN

- **Other toxicities**

Other toxicities should be managed by symptomatic treatment and/or dose modification (i.e. by treatment interruption or 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 for

Palmar Plantar Erythema (capecitabine)

Diarrhoea (capecitabine)

Stomatitis (capecitabine)

Nausea/vomiting (capecitabine and temozolomide)

Toxicity grade	1 st occurrence	2 nd occurrence	3 rd occurrence	4 th 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	Discontinue
4	Delay then 50%	Discontinue	Discontinue	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

Myopathy

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

Constipation

Anorexia, weight loss

Seizure, headache

- **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.

Sodium valproate - may decrease clearance of temozolomide.

Additional comments

Capecitabine is contraindicated if known or suspected dihydropyrimidine dehydrogenase (DPD) deficiency. Temozolomide is contraindicated in patients hypersensitive to dacarbazine (DTIC).

References

- Summary of Product Characteristics Capecitabine (Roche) accessed 22 June 2016 available at <http://www.medicines.org.uk>
- Summary of Product Characteristics Temozolomide (Janssen) accessed 22 June 2016 available at <http://www.medicines.org.uk>
- Fine RL, Gulati AP, Tsushima D, et al. Prospective phase II study of capecitabine and temozolomide (CAPTEM) for progressive, moderately, and well-differentiated metastatic neuroendocrine tumors. J Clin Oncol 2014;32:abstr 179
- Strosberg JR, Choi J, Gardner N and Kvols L. First-line Treatment of Metastatic Pancreatic Endocrine Carcinomas with Capecitabine and Temozolomide. J Clin Oncol 2008; 26 (May 20 Suppl) abstr 4612.

Written/reviewed by: Dr S Falk (Consultant Oncologist, UHBristol NHS Trust)

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: September 2016
