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.
** For patients who have received previous treatment with chemotherapy or extensive radiotherapy consider reducing **daily** temozolomide dose to 150mg/m^2.

All patients must have documented DPYD status. Adjust capecitabine doses as per local practice.

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 further dose should not be administered to make up for this.

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.
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

DPYD status must be available prior to starting capecitabine treatment as per local practice.

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**

At start of each cycle:

Neutrophils (x 10^9/L)		**Platelets** (x 10^9/L)	**Capecitabine and temozolomide doses**			
			1st occurrence	**2nd occurrence**	**3rd occurrence**	**4th 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

Temozolomide

No need for dose adjustment is expected in renal impairment.

- **Hepatic impairment**

Capecitabine

AST / 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

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	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	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 capecitabine.

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

Temozolomide is contraindicated in patients with known hypersensitivity to dacarbazine (DTIC).

References

- Summary of Product Characteristics Capecitabine (Glenmark) accessed 21 September 2023 available at http://www.medicines.org.uk
- Summary of Product Characteristics Temozolomide (Ranbaxy) accessed 21 September 2023 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, UHBW NHS Trust)

Checked by: Kate Gregory (Lead Pharmacist for SACT Protocols, SWAG Cancer Alliance)

Authorised by: Dr J Braybrooke (Consultant Oncologist, UHBW NHS Trust and SWAG Cancer Alliance)

Date: September 2023