CAPECITABINE AND TEMOZOLOMIDE (CAPTEM)

[Capecitabine + Temozolomide]

INDICATION

Palliative treatment of metastatic Grade 1 or 2 neuroendocrine tumours

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TREATMENT INTENT

- Palliative

TREATMENT CONTEXT

- SACT only

DRUG REGIMEN

Cycle frequency every 28 days

Drug	Dose	Route	Frequency	Cycles
Capecitabine	750mg/m2	Oral	BD days 1-14	All cycles
Temozolomide	150mg/m2	Oral	OD Days 10-14	Cycle 1
	200mg/m2	Oral	OD Days 10-14	Cycle 2+

ADDITIONAL DOSE INFORMATION

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

ADDITIONAL ADMINISTRATION INFORMATION

- Capecitabine is available as 150mg and 500mg tablets. Tablets should be taken 12 hours apart 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.

EXTRAVASATION RISK

- Not applicable

SUPPORTIVE MEDICATIONS

Take home (outpatient setting):

- Ondansetron 8mg 15-30 min prior to each dose of temozolomide
- Metoclopramide 10mg when required for nausea
- Oral loperamide when required for diarrhoea
- Consider mouthwashes according to local or national policy on the treatment of mucositis.
- Consider gastric protection in patients at high risk of GI ulceration or bleed.
- Consider topical emollients to prevent PPE

CONTRAINDICATIONS

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

INVESTIGATIONS PRE-FIRST CYCLE

Investigation	Validity period
FBC	14 days (or at consultant discretion)
U&E	14 days (or at consultant discretion)
LFTs	14 days (or at consultant discretion)
Baseline height and weight	14 days (or at consultant discretion)
Consider HbA1c	Baseline
Consider ECHO and/or MUGA	Baseline
DPD test	Baseline

INVESTIGATIONS PRE-CYCLE 2 ONWARDS

Investigation	Validity period
FBC	96 hours
U&E	7 days
LFTs	7 days
Weight	7 days (or at consultant discretion)

DOSE MODIFICATIONS

Please discuss all dose reductions / delays with the relevant consultant before prescribing, if appropriate. The approach may be different depending on the clinical circumstances. All dose reductions to be discussed with the Consultant.

In principle any dose reduction due to adverse drug reactions **should not** be re-escalated in subsequent cycles without consultant approval. It is also a general rule that if a third dose reduction is necessary treatment should be stopped.

Dose modifications listed are for haematological, hepatic function, renal function and limited drug specific toxicities. Adjustments may be necessary for other toxicities as well.

Haematological toxicities on the day of treatment		
Neutrophils [x10^9/L]	<1.5	Delay until recovery
Platelets [x10^9/L]	<75	Delay until recovery

	Drug	CrCl (mL/min)	Adjustment
Renal	**Capecitabine**	30 – 50	75% dose (with close monitoring)
		< 30	Contra-indicated
	Temozolomide	< 30	Advised caution, stop if there is a significant rise in serum creatinine

	Drug	Level	Adjustment
Hepatic	**Capecitabine**	ALT > 2.5 or Bilirubin > 3	Consultant decision, advised caution*
	Temozolomide		Consultant decision, advised caution. Stop temozolomide if there is a progressive rise in transaminases (eg ALT >200) or rise in bilirubin

*Current evidence does not suggest that dose reduction is necessary

Other drug specific 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.

The following drug specific toxicities may require treatment interruption and/or dose reduction. Most adverse reactions are reversible and do not require permanent discontinuation of therapy, although doses may need to be withheld or reduced:

Drug	Toxicities
Capecitabine	Diarrhoea, abdominal pain, nausea, stomatitis and Palmar Plantar Erythema (PPE)
Temozolomide	Nausea

Dose modifications and treatment interruptions should be made as per the following table. Treatment should only be restarted once the toxicity has resolved to grade 0-1

Toxicity grade	Dose modification advised			
	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	N/A
4	Delay then 50%	Discontinue	N/A	N/A

ADVERSE EFFECTS/REGIMEN SPECIFIC COMPLICATIONS

The adverse effects listed are not exhaustive. For full details consult product literature/ reference texts.

ADVERSE EFFECTS			
Drug	**Common (> 10%)**	**Uncommon (1-10%)**	**Rare (<1%)**
Capecitabine	Palmar Plantar Erythema (PPE), Diarrhoea, Abdominal pain, Stomatitis, Nausea / Vomiting, Myelosuppression, Myopathy, Fatigue, Skin reactions, Nail Changes, Taste disturbances, Anorexia, Fluid retention, Alopecia, Deranged liver function	Cardiotoxicity, Thromboembolisms	Hepatic failure, severe skin reactions, angioedema
Temozolomide	Myelosuppression, Infections, stomatitis, allergic reaction, hyperglicaemia, anorexia, psychiatric disorders, eye disorders, tinnitus, vertigo, Thromboembolisms, hypertension, Dyspnoea, diarrhoea, constipation, nausea, vomiting, skin reactions, Myopathy, arthralgia, myalgia, deranged liver function	Sepsis, Secondary malignancies, palpitation, respiratory failure, nasal congestion, hepatitis	Severe skin reactions

SIGNIFICANT DRUG INTERACTIONS

- **Folinates:** Avoid concomitant use of folinic and folic acid – enhanced toxicity of fluorouracil.
- **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.

REFERENCES

- J. Herrstedt, R. Clark-Snow, C. H. Ruhlmann and A. Molassiotis et al. on behalf of the participants of the MASCC/ESMO Consensus Conference 2022. 2023 MASCC and ESMO guideline update for the prevention of chemotherapy- and radiotherapy-induced nausea and vomiting. ESMO Open. 2024;9(2):102195. Available at https://www.esmoopen.com/action/showPdf?pii=S2059-7029%2823%2901436-9 (Accessed June 2026)
- 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.
- Summary of Product Characteristics Capecitabine accessed 03 August 2026 available at http://www.medicines.org.uk
- Summary of Product Characteristics Temozolamide accessed 03 August 2026 available at http://www.medicines.org.uk

DOCUMENT CONTROL

Version	Date	Amendment	Written By	Approved By
1.0	03/08/2026		Alexandre Guedes (Pharmacist)	Dr Luke Nolan

This SACT protocol has been developed by the Wessex Cancer Alliance SACT protocol development group. These documents have been approved on behalf of the following Trusts;

Hampshire Hospitals NHS Foundation Trust
NHS Isle of Wight
Portsmouth Hospitals NHS Trust
Salisbury NHS Foundation Trust
University Hospital Southampton NHS Foundation Trust
Western Sussex Hospitals NHS Foundation Trust
University Hospitals of Dorset

All actions have been taken to ensure these protocols are correct. However, no responsibility can be taken for errors which occur as a result of following these guidelines.

The regimen summary that follows is to facilitate building the protocols in the Aria prescribing system for those Trusts that utilise this system.

REGIMEN SUMMARY

Capecitabine (14 day)

Cycle 1

Take Home Medicines

1. Capecitabine 750mg/m^2 twice a day for 14 days oral
   Administration Instructions
   Take on days 1 to 14 of each cycle. Tablets should be taken 12 hours apart after food

2. Temozolomide 150mg/m2 oral once a day for 5 days
   Administration Instructions
   Take on days 10-14 of each cycle. Take on an empty stomach, swallow whole, do not chew

3. Ondansetron 8mg once a day 15-30 minutes prior to the temozolomide
   Administration Instructions
   Take 15 to 30 minutes prior to each dose of temozolomide. An additional 8mg may be taken 12 hours later if required for the relief of nausea or vomiting. Please supply an original pack (10 tablets) or nearest appropriate equivalent

4. Metoclopramide 10mg three times a day when required oral
   Administration Instructions
   Please dispense 28 tablets or nearest equivalent pack size

Cycle 2–12

Take Home Medicines

5. Capecitabine 750mg/m^2 twice a day for 14 days oral
   Administration Instructions
   Take on days 1 to 14 of each cycle. Tablets should be taken 12 hours apart after food

6. Temozolomide 200mg/m2 oral once a day for 5 days
   Administration Instructions
   Take on days 10-14 of each cycle. Take on an empty stomach, swallow whole, do not chew

7. Ondansetron 8mg once a day 15-30 minutes prior to the temozolomide
   Administration Instructions
   Take 15 to 30 minutes prior to each dose of temozolomide. An additional 8mg may be taken 12 hours later if required for the relief of nausea or vomiting. Please supply an original pack (10 tablets) or nearest appropriate equivalent

8. Metoclopramide 10mg three times a day when required oral
   Administration Instructions
   Please dispense 28 tablets or nearest equivalent pack size