TEMOZOLOMIDE CAPECITABINE

INDICATION (ICD10) M-8246/3

1. Neuroendocrine tumour
PS 0, 1, 2

REGIMEN

Days 1 to 14	CAPECITABINE	1000mg twice daily orally (14 days)
Days 10 to 14	TEMOZOLOMIDE	200mg/m^2 once daily orally (5 days)

CYCLE FREQUENCY AND NUMBER OF CYCLES

Every 28 days for 6 cycles

ADMINISTRATION

Capecitabine
Tablets should be taken 12 hours apart.
Swallowed with water within 30 minutes after a meal, or dissolve in 200ml luke warm water, stir thoroughly (squash may be added if unpalatable).

Temozolomide
Available as various strength capsules
Take on an empty stomach

ANTI-EMETICS

Low risk days 1 to 9
Moderate risk days 10 to 14

CONCURRENT MEDICATION REQUIRED

Capecitabine	Mouth and bowel support eg Loperamide, benzydamine mouthwash
Temozolomide	-

EXTRAVASATION AND TYPE OF LINE / FILTERS

Not applicable

INVESTIGATIONS

Blood results required before SACT administration
FBC, U&E and LFTs every cycle
Neutrophils x 10^9/L ≥1.5
Platelets x 10^9/L ≥100
Serum creatinine every cycle
DPD test
Baseline weight and every cycle

MAIN TOXICITES AND ADVERSE REACTIONS

Capecitabine	Palmar plantar (handfoot syndrome) causing red palms and soles – treat with pyridoxine 50mg tds Diarrhoea – treat with loperamide or codeine Cardiotoxicity – monitor cardiac function. To minimise risk of anthracycline induced cardiac failure signs of cardiotoxicity e.g. cardiac arrhythmias, pericardial effusion, tachycardia with fatigue. All patients should be told to report any cardiac symptoms immediately and should be told to stop the medication immediately if any suspicion of cardiac problems. Stomatitis
Temozolomide	Myelosuppression Hepatic toxicity – may still occur several weeks after end of treatment

INTERACTIONS WHICH MAY REQUIRE DOSE MODIFICATIONS (not exhaustive list check SPC/BNF/Stockleys)

Capecitabine	Brivudine and analogues should be avoided Warfarin and caution with all oral anticoagulants Phenytoin Allopurinol

DOSE MODIFICATIONS

Haematological

Temozolomide

Dose range 150-200mg/m² days 10 to 14 of each 28 day cycle.
if neutrophils <1.5 AND the platelets <100 on day 28 consider delaying treatment
if neutrophils <1.0 OR the platelets <50 during any cycle the next cycle should be reduced to the next dose level; 150mg/m² then 100mg/m²

Non-haematological

Capecitabine

Dose limiting toxicities include diarrhoea, abdominal pain, nausea, stomatitis and handfoot syndrome.

Toxicity can be managed by symptomatic treatment and/or modification of the dose (treatment interruption or dose reduction).

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

When capecitabine is stopped for toxicity, the doses are omitted and not delayed.

Toxicity Grades	Dose changes within a treatment cycle	Dose adjustment for next cycle/dose (% of starting dose)
Grade 2 - 1st appearance	Interrupt until resolved to grade 0-1	100%
Grade 2 - 2nd appearance	Interrupt until resolved to grade 0-1	75%
Grade 2 - 3rd appearance	Interrupt until resolved to grade 0-1	50%
Grade 2 - 4th appearance	Discontinue treatment permanently	Not applicable
Grade 3 - 1st appearance	Interrupt until resolved to grade 0-1	75%
Grade 3 - 2nd appearance	Interrupt until resolved to grade 0-1	50%
Grade 3 - 3rd appearance	Discontinue treatment permanently	Not applicable
Grade 4 - 1st appearance	Discontinue permanently OR if physician deems it to be in the patient's best interest to continue, interrupt until resolved to grade 0-1	50%
Grade 4 - 2nd appearance	Discontinue treatment permanently	Not applicable

Hepatic impairment

Capecitabine

Bilirubin of >3xULN or ALT/AST >2.5xULN	Interrupt Capecitabine Treatment may be resumed when bilirubin decreases to <3xULN or hepatic aminotransferases decrease to <2.5xULN.

Temozolomide

Stop temozolomide if there is a progressive rise in transaminases eg ALT >200 or rise in bilirubin.

Renal impairment

Capecitabine

CrCl >50ml/min	give 100% dose
CrCl 30-50ml/min	give 75% dose
CrCl <30ml/min	contraindicated

Temozolomide

Stop temozolomide if there is a significant rise in serum creatinine (more common in patients with pre-existing renal impairment).

REFERENCES

1. JCO abstract vol.24 No.3 2006.