CAPECITABINE (1000)

INDICATION (ICD10) C50, E34, M-8246/3

1. Monotherapy of metastatic or locally advanced breast cancer after failure of taxanes and an anthracycline-containing chemotherapy regimen or for whom further anthracycline therapy is not indicated.
2. Neuroendocrine tumour (unlicensed indication)
3. Carcinoid syndrome (unlicensed indication)
4. Monotherapy of adjuvant breast cancer in patients with triple negative breast cancer and an incomplete response to neo-adjuvant chemotherapy (unlicensed indication)

PS 0, 1, 2

REGIMEN

Days 1 to 14 CAPECITABINE 1000mg/m^{2*} twice daily (2000mg/m^2/day) oral followed by a 7 day rest

*Neuroendocrine, carcinoid dose may be increased to 1250mg/m^2 twice daily (2500mg/m^2/day)
*Breast - the lower starting dose above (is not licensed) is used in breast patients it may be possible to consider 1250mg/m^2 in patients who tolerate the 1000mg/m^2 dose with minimal toxicity. However 50% of the patients in the main phase 3 trial required a reduction of capecitabine dose. This dose reduction was not associated with any increased risk of progression or resistance to treatment in fact there was slightly better controlled disease in those whose dose reduced by 25% in the oral capecitabine arm (the above dose)

CYCLE FREQUENCY AND NUMBER OF CYCLES

Breast - every 21 days until progression or unacceptable toxicity
Neuroendocrine, carcinoid - every 21 days for 8 cycles (review after 4 cycles)

ADMINISTRATION

Tablets should be taken 12 hours apart.
Swallow with water within 30 minutes after a meal.

ANTI-EMETICS

Low risk days 1 to 14

CONCURRENT MEDICATION REQUIRED

Capecitabine	Mouth and bowel support eg Loperamide, benzydamine mouthwash Consider prophylactic diclofenac gel 1% bd to the hands and feet for the first 12 weeks of treatment (use support regimen).

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 (carcinoid or neuroendocrine)
Neutrophils x 10^9/L ≥1.0 (breast)
Platelets x 10^9/L ≥100
Serum creatinine - GFR each cycle
DPYD 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

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
DPYD variant identified follow national or local DPD dose modification guidelines.

Haematological
Capecitabine
Neutrophils <1.5x10^9/l (<1.0x10^9/l in breast patients) or platelets <100x10^9/l delay treatment for 1 week.
Repeat FBC. If recovered, restart capecitabine, using dose adjustment guidelines below, according to worst grade of haematological toxicity recorded.

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.

Renal impairment

Capecitabine

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

REFERENCES

1. Reichardt P, von Minckwitz G, Thuss-Patience PC et al. Multicentre phase II study or oral capecitabine (“Xeloda”) in patients with metastatic breast cancer relapsing after treatment with a taxane-containing therapy. Ann Oncol 2003; 14 (8): 1227-33.
2. Akhil Santhosh et al. Randomized double-blind, placebo-controlled study of topical diclofenac in the prevention of hand-foot syndrome in patients receiving capecitabine (the D-TORCH study). 2022 May 19;23(1):420. doi: 10.1186/s13063-022-06353-2.