**Systemic Anti Cancer Treatment Protocol**

# CAPECITABINE

**PROTOCOL REF: MPHACOLCAP**
**(Version No: 3.2)**

**Please see the Oral SACT Operational Changes during Covid-19. Amendments may include less frequent blood monitoring, telephone SACT assessments and longer durations of treatment being dispensed**

**This protocol has also been temporarily amended for lower GI cancer - please see the SRG Guidelines during COVID-19 Lower GI cancer regarding duration of therapy**

## Approved for use in:

**Colorectal:** Adjuvant and advanced colorectal cancer

Adjuvant – completely resected biliary tract cancers

ECOG PS 0 - 1

## Dosage:

| Disease site | Dosage | Frequency |
|---|---|---|
| **Colorectal - Adjuvant** | 1250mg/m$^2$ oral twice daily for 14 days<br>Caution in elderly patients | Repeat at 21 day intervals for a maximum of 8 cycles |
| **Advanced Colorectal Cancer** | 1250mg/m$^2$ oral twice daily for 14 days<br>Or<br>1000mg/m$^2$ for patients over 70yrs | Repeat at 21 day intervals until disease progression |
| **Biliary Tract - Adjuvant** | 1250mg/m2 oral twice daily for 14 days | Repeat at 21 day intervals for a maximum of 8 cycles |

Round doses to nearest whole dose using 150mg and 500mg tablets

**Supportive treatments:**

Emetic Risk: Low – follow antiemetic policy

Loperamide 4mg immediately after first liquid stool followed by 2mg every 2 hours for at least 12 hours

Domperidone 10mg oral tablets, up to 3 times a day or as required

Caution in patients with pre-existing coronary heart disease, angina pectoris, arrhythmias or those on high dose aspirin or coumarin anticoagulants.

## Administration:

Counselling points:

Tablets should be taken 12 hours apart, morning and evening.

Swallow whole with water within 30 minutes of a meal.

Do not add doses missed due to toxicity onto the end of the cycle. Continue according to the treatment plan and stop taking on the originally scheduled day.

Take missed doses if remembered within 2 hours of the normal scheduled time. Otherwise continue with the next scheduled dose. Do not double up missed doses

In case of swallowing difficulties the tablets may be dissolved in 200ml warm water. Once dissolved stir the contents with a spoon and drink immediately. Wash well and reserve the glass and spoon for chemotherapy administration only

**Drug Interactions**

Allopurinol – reduced efficacy of capecitabine – avoid

Clozapine – additive risk of agranulocytotis

Folic acid – increased risk of side effects of capecitabine, avoid if possible – discuss with pharmacy

Phenytoin – potentially toxic levels of phenytoin have been reported- monitor carefully

Warfarin and other coumarin anticoagulants – increased bleeding risk, monitor INR carefully, consider switch to LMWH.

## Main Toxicities:

Myelosuppression, diarrhoea, Palmar Plantar Erythema (PPE or hand- foot syndrome), stomatitis, fatigue, asthenia, anorexia, cardiotoxicity (uncommon), ovarian failure/infertility, increased renal dysfunction on those with preexisting compromised renal function, and thrombosis/embolism

DPD deficiency – leads to severe early fluorouracil toxicity, affects approximately 3% of population, may be life threatening

## Investigations:

| | Pre | Cycle 1 | Cycle 2 | Cycle 3 | Cycle 4 | Ongoing | Last cycle |
|---|---|---|---|---|---|---|---|
| Clinical assessment | X | | X | | X | Alternate cycles | |
| SACT Assessment | X | X | X | X | X | Every cycle | Check has OPD |
| FBC | X | X | X | X | X | Every cycle | X |
| U&E & LFT | X | X | X | X | X | Every cycle | X |
| CrCl | X | X | X | X | X | Every cycle | X |
| Dihydropyrimidine dehydrogenase (DPD) deficiency test | X | | | | | This test is normally only required if a patient has not had capecitabine, or fluorouracil in the past. However a consultant may still request this test if capecitabine or fluorouracil was not tolerated previously. The result must be available before administration of chemotherapy unless clear documentation from the consultant is available to the contrary. Treatment with capecitabine and fluorouracil is contraindicated in patients with known complete DPD deficiency. | |
| CT scan | X | | | | | As required if palliative | Check has date for CT |
| Informed Consent | X | | | | | Verbal each cycle | |
| Weight recorded | X | X | X | X | X | Every cycle | X |

## Dose Modifications:

### Haematological toxicity

Proceed on day 1 if all apply:-

| | |
|---|---|
| ANC ≥ 1.0 x $10^9$/L | Platelets ≥ 100 x $10^9$/L |

### Non-haematological toxicity

**Renal**

Calculate CrCl using Cockroft and Gault formula at baseline and before each cycle and adjust dose according to table.

| Creatinine Clearance (mL/min) | Capecitabine Dose |
|---|---|
| >50 | Give 100% |
| 30 to 50 | Give 75% |
| <30 | Omit |

**Cockroft and Gault formula**

Male patients $\frac{1.23 \times (140 - \text{age}) \times \text{weight (kg)}}{\text{Serum Creatinine (micromol/L)}}$

Female patients $\frac{1.04 \times (140 - \text{age}) \times \text{weight (kg)}}{\text{Serum Creatinine (micromol/L)}}$

**Hepatic**

| Liver function | Capecitabine dose |
|---|---|
| Bilirubin > 3 x ULN or ALT/AST > 2.5 x xULN | Omit capecitabine |

Note that significantly impaired hepatic function might be a sign of disease progression and require cessation or change of treatment.
**Always discuss deteriorating organ function with consultant**

| | |
|---|---|
| Diarrhoea | Loperamide at standard doses – ensure maximum dose reached, codeine may be added – see table below for dose reductions |
| Stomatitis | Regular mouthwashes (water, saline or non alcoholic proprietary brand), brush gently with a soft brush, adequate pain relief, nutritional support in severe cases – see below for dose reductions. |

| | |
|---|---|
| Palmar plantar erythema (PPE) or hand foot syndrome | Manage as per trust policy, withhold treatment until resolved to grade 1, dose reductions as per table below. |
| Sore eyes / Conjunctivitis | Eye drops for symptomatic treatment such as hypromellose 0.3% – avoid antimicrobial eye drops unless indicated for infective conjunctivitis |
| Chest Pain / coronary artery spasm | Stop capecitabine, standard angina investigations, refer to consultant, if symptoms persist stop capecitabine permanently |

**Capecitabine Dose adjustment guidelines according to Common Toxicity Criteria**

including diarrhoea, vomiting, stomatitis, and PPE

| Common Toxicity Criteria | Dose changes within a treatment cycle | Dose adjustment for next cycle/dose(% of starting dose) |
|---|---|---|
| Grade 1 | Maintain dose level | Maintain dose level |
| Grade 2 | | |
| -1st appearance | Interrupt until resolved to grade 0-1* | 100% |
| -2nd appearance | | 75% |
| -3rd appearance | | 50% |
| -4th appearance | Discontinue treatment permanently | Not applicable |
| Grade 3 | | |
| -1st appearance | Interrupt until resolved to grade 0-1* | 75% |
| -2nd appearance | | 50% |
| -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% (consultant approval only) |
| -2nd appearance | Discontinue permanently | Not applicable |

## References:

Electronic Medicines Compendium, Xeloda 150mg and 500mg film-coated tablets, https://www.medicines.org.uk/emc/medicine/4619

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Colorectal Cancer: Results of a Randomized Phase III Study. *Journal of Clinical Oncology* 19, no. 8 (April 15 2001) 2282-2292

Van Cutsem E, Twelves C, Cassidy J. Oral Capecitabine Compared With Intravenous Fluorouracil Plus Leucovorin in Patients with Metastatic Colorectal Cancer: Results of a Large Phase III Study *Journal of Clinical Oncology* 19, no. 21 (November 1 2001) 4097-4106

Twelves C, Wong A, Nowacki MP et al. Capecitabine as Adjuvant Treatment for Stage III Colon Cancer. N Engl J Med 2005; 352:2696-2704

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