CAPECITABINE SINGLE-AGENT (Breast & Colorectal)

NHS Northern Cancer Alliance

DRUG ADMINISTRATION SCHEDULE

Day	Drug	Daily Dose	Route	Diluent	Rate
Days 1 to 14	**Capecitabine**	**1250mg/m^2 Twice Daily**	Oral	N/A	N/A

DOSE FORM
Capecitabine is supplied as 150mg and 500mg tablets, therefore calculated doses must be rounded to the nearest 150mg.

CYCLE LENGTH AND NUMBER OF DAYS
21-day cycle. Capecitabine taken from Day 1 to 14 then 1 week off treatment.
8 cycles given for adjuvant & advanced disease.

APPROVED INDICATIONS
- Adjuvant Dukes C colon cancer
- Advanced/ metastatic colorectal cancer – for patients unsuitable for FOLOX/FOLFIRI
- Advanced/ metastatic breast cancer for patients not tolerating intravenous therapy.

ELIGIABILITY CRITERIA
Colorectal and breast cancer patients with adequate renal function (CrCl>30ml/min)

EXCLUSION CRITERIA
Patients with baseline renal function less than 30 ml/min.
Patients incapable of managing oral chemotherapy themselves or with the assistance of a carer and or patients with swallowing difficulties

PREMEDICATION: As above

RECOMMENDED TAKE HOME MEDICATION
Metoclopramide 10mg three times daily as required
Suggested antiemetic regimen - may vary with local practice. See CINV policy for more details

INVESTIGATIONS / MONITORING REQUIRED
Pre-treatment: Assessment of renal function, FBC, Cardiac history
Prior to each cycle - FBC, U&E's, LFT's & tumour markers as appropriate
FBC on the day of treatment
Where CEA is elevated this should be measured before each cycle.

ASSESSMENT OF RESPONSE
Assessed radiologically after 4th cycle.
Metastatic: Tumour size and patient symptomatic response
Adjuvant There will be no visible disease to monitor for adjuvant treatment.

REVIEW BY CLINICIAN
To be reviewed by either a Nurse, Pharmacist or Clinician before every cycle.

NURSE / PHARMACIST LED REVIEW
On cycles where not seen by clinician.

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ADMINISTRATION NOTES

Counselling Points for Oral Capecitabine

How to take: Take tablets 12 hours apart, within 30 minutes after the end of meal (i.e. breakfast & evening meal.) Swallow whole with water

Side effects Common side effects to discuss with patient include; diarrhoea, nausea & vomiting, stomatitis (mouth ulcers), Hand-foot syndrome (painful red swelling in hands and feet), fever or infection. If patients notice any of these advise them to stop taking treatment, contact doctor/chemotherapy day unit who will take steps to manage side effects and advise on continuing treatment.

Missed dose: If remember half an hour after they should have taken their tablets, then take the missed dose, otherwise only take the regular dose at next scheduled time. Do not double-up doses to make up for the missed doses or take extra doses at the end of the treatment cycle.

Post dose vomiting: In the case of vomiting within a few hours after drug intake, never repeat the administration of the dose.

Storage/ Disposal Tablets should be stored in cool dry place less than 30°C. Unused medicines must be returned to hospital pharmacy for disposal

Diarrhoea is common, and may require intervention with fluids and electrolytes if severe. If diarrhoea is a problem give loperamide 2 to 4 mg four times daily as required or codeine phosphate 30mg four times daily and stop taking Capecitabine if diarrhoea moderate/severe.

TOXICITIES

- Palmar/Plantar Erythrodysesthesia - Can be severe, patients must be forewarned
- Diarrhoea
- Abdominal pain
- Nausea and vomiting
- Pyrexia, fatigue, asthenia, anorexia
- Myelosuppression
- Hyperbilirubinemia
- Stomatitis
- Contra-indicated in patients with severe hepatic impairment, a history of severe and unexpected reactions to fluoropyrimidine therapy, DPD deficiency,
- Hypersensitivity. Avoid concomitant use with allopurinol
- Cardiotoxicity Occasionally patients may experience coronary artery spasm

DPD Deficiency and Severe Toxicity Risk

Dihydropyrimidine dehydrogenase (DPD) plays an important role in the metabolism of fluoropyrimidine drugs 5-fluorouracil (5FU) and capecitabine. Patients with DPD deficiency may be predisposed to experience increased or severe toxicity when receiving 5-FU or capecitabine, and in some cases these events can be fatal.

For all patients having capecitabine or fluorouracil, the risk of severe side effects from capecitabine or 5FU if patients have a deficiency of DPD must be mentioned and patient given a copy of the DPD toxicity information leaflet from cancer research UK.

Available at http://www.cancerresearchuk.org/about-cancer/cancer-in-general/treatment/chemotherapy/side-effects/dpd-deficiency-and-fluorouracil

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DOSE MODIFICATION / TREATMENT DELAYS

Haematological toxicity:

- Delay 1 week if ANC < 1.0 and/ or Platelets < 75. No dose reduction for CTC grade I/II ANC
- Grade III/IV ANC → delay chemotherapy until recovered, then proceed at 25% dose reduction
- If further delay(s) for bone marrow suppression occur despite a 25% dose reduction, consider a further 25% dose reduction or stopping/changing treatment.

Non-haematological toxicity: Diarrhoea

- Grade 2 during course of treatment → delay until recovered and give full dose
- Diarrhoea grade 3/ 4 during a course of treatment, delay until recovered and resume treatment at 25% reduced dose of capecitabine
- Note CTC grading for Diarrhoea toxicity grading for capecitabine only
  - CTC Grade 1 = Diarrhoea (watery stool 2-3 times/day) ***OR*** mild increase in ostomy output compared to baseline
  - CTC Grade 2 = Diarrhoea (watery stool 4-6 times/day) ***OR*** moderate increase in ostomy output compared to baseline
  - CTC Grade 3/4 = Diarrhoea (watery stool >7 times/day ***OR*** severe increase in ostomy output compared to baseline

Renal function:

- Capecitabine is renally excreted; therefore, patients with moderate renal impairment (< 50ml/min) require a 25% dose reduction.
- Contra-indicated in severe renal failure (CrCl < 30ml/min) (Wright equation or measured GFR)

Table of dose adjustments according to CTC toxicity (Not PPE/hand/foot))

	Grade 2	Grade3	Grade 4
1st appearance	Interrupt treatment until resolved to grade 0/1, then continue at 100% of original dose with prophylaxis where possible	Interrupt treatment until resolved to grade 0/1, then continue at 75% of original dose with prophylaxis where possible	**Discontinue treatment**
2nd appearance	Interrupt treatment until resolved to grade 0/1, then continue at 75% of original dose	Interrupt treatment until resolved to grade 0/1, then continue at 50% of original dose	
3rd appearance	Interrupt treatment until resolved to grade 0/1, then continue at 50% of original dose	**Discontinue treatment**	
4th appearance	**Discontinue treatment**		

Table of hand/ foot toxicity grading for capecitabine only

Grade	Clinical	Functional
1	Numbness, dysesthesia/parathesia, tingling, painless swelling or erythema	Discomfort but no interruption Of normal activities
2	Painful erythema with swelling	Discomfort which affects activities of daily living
3	Moist desquamation, ulceration, Blistering, severe pain	Severe discomfort, unable to work or perform activities of daily living

Once the capecitabine dose has been reduced, it should **not** be increased at a later time. Omitted doses are **not replaced or restored**, instead the patient should resume the planned treatment cycle.

TREATMENT LOCATION

Can be given at Cancer Centre or Cancer Unit

REFERENCES:

- Twelves, C. et al. N Capecitabine as Adjuvant Treatment for Stage III Colon Cancer Eng J Med 2005;352:2696-2704
- Hoff PM *et al*. (2001) Comparison of oral capecitabine versus intravenous 5FU plus leucovorin as first-line treatment in 605 patients with metastatic colorectal cancer: results of a randomized phase III study. *J Clin Oncol*. **19**: 2282-92
- Blum JL, et al. Multicenter phase II study of capecitabine in paclitaxel-refractory metastatic breast cancer. J Clin Oncol 1999;17:485-93.

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Summary of Changes	1.1	Reformatted from old NCN/CCA versions
	1.2	Updated capecitabine dose/ toxicity modification advice
	1.3	Protocol reviewed.
	1.4	Protocol reviewed and reissued, Antiemetic advice updated
	1.5	Protocol reviewed, parameters updated from Chemocare.