

Chemotherapy Protocol

COLORECTAL CANCER

CAPECITABINE

(21 day)

Regimen

- Colorectal Cancer – Capecitabine (21 day)

Indication

- Metastatic / advanced colorectal cancer
- Adjuvant therapy of stage II or III colon cancer following surgery
- WHO performance status 0, 1, 2

Toxicity

Drug	Adverse Effect
Capecitabine	Palmar-plantar erythrodysesthesia, diarrhoea, mucositis, chest pain

The adverse effects listed are not exhaustive. Please refer to the relevant Summary of Product Characteristics for full details.

Monitoring

Regimen

- FBC, LFT's and U&E's prior to each cycle
- Patients with complete or partial dihydropyrimidine dehydrogenase (DPD) deficiency are at increased risk of severe and fatal toxicity during treatment with capecitabine. All patients should be tested for DPD deficiency before initiation (cycle 1) to minimise the risk of these reactions.

Dose Modifications

The dose modifications listed are for haematological, liver and renal function only. Dose adjustments may be necessary for other toxicities as well.

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

Please discuss all dose reductions / delays with the relevant consultant before prescribing, if appropriate. The approach may be different depending on the clinical circumstances. The following is a general guide only.

Haematological

Prior to prescribing the following criteria must be met;

Criteria	Eligible Level
Neutrophil	equal to or more than $1.5 \times 10^9/L$
Platelets	equal to or more than $100 \times 10^9/L$

Consider blood transfusion if patient symptomatic of anaemia or has a haemoglobin of less than 8g/dL

For haematological toxicity, if the neutrophil count is less than $1.5 \times 10^9/L$ or the platelet count is less than $100 \times 10^9/L$, delay treatment until these levels are achieved. Re-start therapy at the full dose for a 7 day delay or at 75% of the original dose for a 14 day delay.

Liver Impairment

Drug	Dose (% of original dose)
Capecitabine	There is a lack of information available. In patients with mild to moderate hepatic dysfunction due to liver metastases, 100% of the dose dose is probably acceptable.

Renal Impairment

Drug	Creatinine Clearance (ml/min)	Dose (% of original dose)
Capecitabine	51-80	100%
	30-50	75%
	less than 30	C/I

Other

Dose reductions or interruptions in therapy are not necessary for those toxicities that are considered unlikely to be serious or life threatening. For example, alopecia, altered taste or nail changes. Dose limiting toxicities include diarrhoea, abdominal pain, emesis, stomatitis and palmar-plantar erythrodysesthesia among others. If chest pain occurs consider stopping capecitabine.

NCI-CTC Grade 2

Interrupt treatment until the toxicity resolves to NCI-CTC grade 0-1 then continue at the same dose. If the toxicity recurs for a second time again interrupt treatment until it resolves to NCI-CTC grade 0-1 then resume therapy at 75% of the original dose. If the same adverse effect develops on a third occasion once more interrupt treatment until it resolves to NCI-CTC grade 0-1 then continue at 50% of the original dose. Stop treatment if the toxicity re-appears on a fourth instance.

NCI-CTC Grade 3

Interrupt treatment until the toxicity resolves to NCI-CTC grade 0-1 then continue treatment using 75% of the original dose with prophylaxis if appropriate. If the toxicity recurs for a second time again interrupt treatment until it resolves to NCI-CTC grade 0-1 and then resume therapy at 50% of the original dose. If the same adverse effect develops on a third occasion discontinue capecitabine.

NCI-CTC Grade 4

Discontinue treatment unless the responsible consultant considers it to be in the best interest of the patient to continue at 50% of the original dose once the toxicity has resolved to grade 0-1.

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

[Regimen](#)

21 day cycle for 8 cycles

Patients with metastatic disease should normally be assessed for response to treatment after 4 cycles. If the disease is stable or has responded a further 4 cycles of therapy may be given after which response should once again be determined.

Drug	Dose	Days	Administration
Capecitabine	830mg/m ² twice a day	1-21 incl.	Oral

[Dose Information](#)

- Capecitabine will be dose banded in accordance with the national dose bands

[Administration Information](#)

- The capecitabine should start on the evening of day 1.
- Capecitabine should be taken with or after food.

[Additional Therapy](#)

- Antiemetics

As take home medication

- metoclopramide 10mg three times a day when required

- Oral loperamide 4mg after the first loose stool then 2-4mg four times a day when required for the relief of diarrhoea (maximum 16mg/24 hours).
- Mouthwashes according to local or national policy on the treatment of mucositis

- Gastric protection with a proton pump inhibitor or H₂ antagonist may be considered in patients considered at high risk of GI ulceration or bleed.

Additional Information

- The National Patient Safety Agency alert NPSA/2008/RRR001 must be followed when prescribing, dispensing or administering oral chemotherapy.
- Ensure the total daily dose of capecitabine is divided into two doses given twelve hours apart (the first should be administered in the evening of day one of the cycle) Serious toxicity has occurred where the total daily dose has been given twice a day.
- It must be made clear to all staff, including those in the community, that this is a short course of oral chemotherapy that must not be continued.

References

1. Van Cutsem E, Twelves C, Cassidy J et al. Oral capecitabine compared with intravenous fluorouracil plus leucovorin in patients with metastatic colorectal cancer; results of a large phase III study. *J Clin Oncol* 2001; 19 (21): 4097-106
2. Hoff PM, Ansari R, Batist G et al. Comparison of oral capecitabine versus intravenous fluorouracil plus leucovorin as first line treatment in 605 patients with metastatic colorectal cancer: results of a randomised phase III study. *J Clin Oncol* 2001; 19 (8): 2282-92
3. National Institute of Clinical Excellence. Capecitabine and tegafur uracil for metastatic colorectal cancer. *Technology Appraisal* 61. May 2003.

REGIMEN SUMMARY

Capecitabine (21 day)

Day One

1. Capecitabine 830mg/m² twice daily for 21 days oral
2. Metoclopramide 10mg three times a day when required oral

DOCUMENT CONTROL

Version	Date	Amendment	Written By	Approved By
1.2	Nov 2020	Updated monitoring with DPD testing Dose banding statement updated Coding removed	Donna Kimber Pharmacy Technician	Rebecca Wills Pharmacist
1.1	May 2014	Header changed Toxicities removed < symbol removed and written in full Information tabulated throughout Hepatic and renal impairment updated NCI-CTC added Pyridoxine removed Twice daily changed to twice a day Metoclopramide dose changed to 10mg Mucositis recommendation changed Stat removed from loperamide Name added to summary Disclaimer added	Dr Deborah Wright Pharmacist	Donna Kimber Pharmacy Technician
1	August 2010	None	Dr Deborah Wright Pharmacist	Dr Timothy Iveson Consultant Medical Oncologist

This chemotherapy protocol has been developed as part of the chemotherapy electronic prescribing project. This was and remains a collaborative project that originated from the former CSCCN. 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 Hospital NHS Foundation Trust
 University Hospital Southampton NHS Foundation Trust
 Western Sussex Hospitals NHS Foundation Trust

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.