Chemotherapy Protocol

COLORECTAL CANCER

CAPECITABINE-MITOMYCIN

Regimen

- Colorectal Cancer – Capecitabine-Mitomycin

Indication

- Second / third line therapy of metastatic/advanced colorectal cancer
- WHO performance status 0, 1, 2

Adverse Effects

Drug	Adverse Effect
Capecitabine	Palmar-plantar erythrodysesthesia, diarrhoea, mucositis, chest pain
Mitomycin	Nephrotoxicity, myelosuppression (cumulative)

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 $1.5x10^9$/L
Platelets	equal to or more than $100x10^9$/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 1.5×10^9/L or the platelet count is less than 100×10^9/L, delay the mitomycin treatment until these levels are achieved. Re-start therapy at the full dose for a 7 day delay or with 75% of the original dose for a 14 day delay. There is little need to reduce capecitabine doses for haematological toxicity.

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.
Mitomycin	Dose reductions are probably not necessary. However, it is a clinical decision when the AST levels are greater than 2xULN.

Renal Impairment

Drug	Creatinine Clearance (ml/min)	Dose (% of original dose)
Capecitabine	51-80 30-50 less than 30	100% 75% C/I
Mitomycin	10 or greater 10 or less	100% 75%
	Consider a dose reduction for high doses of mitomycin when the GFR is between 10-60ml/min	

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.

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 NCI-CTC grade 0-1.

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

Regimen

Different variations of this regimen are used in conjunction with radiotherapy for the treatment of anal cancer. Always check the indication and apply the correct protocol.

42 day cycle for 2 cycles

Patients with metastatic disease should normally be assessed for response to treatment after 12 weeks. If the disease is stable or has responded a further 12 weeks of therapy may be given after which response should once again be determined.

Drug	Dose	Days	Administration
Capecitabine	1250mg/m^2 twice a day	1-14 incl. 22-35 incl.	Oral
Mitomycin	7mg/m^2	1	Intravenous bolus over 10 minutes

Dose Information

- Capecitabine will be dose banded in accordance with the national dose bands
- Mitomycin will be dose rounded to the nearest 1mg (up if halfway).
- The maximum dose of mitomycin is 14mg

Administration Information

Extravasation

- Mitomycin - vesicant

Other

- Capecitabine should start on the evening of day 1 and 22
- Capecitabine should be taken with or after food

Additional Therapy

- Antiemetics

  15-30 minutes prior to chemotherapy on **day one** only

  - dexamethasone 8mg once only dose oral or intravenous
  - metoclopramide 10mg once only dose oral or intravenous

  As take home medication on **day one** only

  - dexamethasone 4mg once a day for 3 days
  - 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).
- Consider mouthwashes according to local or national guidelines
- Gastric protection with a proton pump inhibitor or a H_2 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. Chong C, Dickson JLB, Cunningham D et al. Capecitabine and mitomycin C as third line therapy for patients with metastatic colorectal cancer resistant to fluorouracil and irinotecan. Br J Cancer 2005; 93: 510-514.

REGIMEN SUMMARY

Capecitabine-Mitomycin

Day One

1. Dexamethasone 8mg oral or intravenous

2. Metoclopramide 10mg oral or intravenous

3. Mitomycin 7mg/m^2 intravenous bolus over 10 minutes

Take Home Medicines Day One

4. Capecitabine 1250mg/m^2 twice a day on days 1-14 inclusive

5. Dexamethsone 4mg once a day for 3 days oral starting the day after mitomycin

6. Metoclopramide 10mg three times a day when required oral

Take Home Medicines Day Twenty-Two

4. Capecitabine 1250mg/m^2 twice a day on days 22-35 inclusive

DOCUMENT CONTROL

Version	Date	Amendment	Written By	Approved By
1.3	Nov 2020	Updated monitoring with DPD testing Dose banding statement updated Coding removed	Donna Kimber Pharmacy Technician	Dr Debbie Wright Pharmacist
1.2	May 2014	Header changed Tabulation throughout Hepatic and renal dose modifications updated Mitomycin administration changed to 10 minutes Metoclopramide dose changed to 10mg throughout Stat removed from summary Bolus removed from supportive treatments Dexamethasone TTO clarified Capecitabine TTO clarified	Dr Debbie Wright (Pharmacist)	Donna Kimber (Pharmacy Technician)
1.1	23rd March 2011	Mitomycin dose information altered to state that it will be dose rounded to the nearest 1mg Twice daily changed to twice a day Once daily changed to once a day Regimen name added to summary page Pyridoxine removed from supportive treatments Abbreviations changed to full wording for routes of administration Document control changed to tabular format	Dr Debbie Wright (Pharmacist)	Donna Kimber (Pharmacy Technician)
1	27th Aug 2010	None	Dr Debbie Wright (Pharmacist)	Dr Tim Iveson (Consultant 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 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.