Chemotherapy Protocol

COLORECTAL CANCER

CAPECITABINE-CARBOPLATIN (AUC5)

Regimen

- Colorectal Cancer – Capecitabine-Carboplatin (AUC5)

Indication

- Treatment of recurrent squamous cell carcinoma of the anal canal
- WHO performance status 0, 1, 2

Toxicity

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

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
- EDTA or calculated creatinine clearance before the first 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 cycle one 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 less than 8g/dL

For subsequent cycles if the neutrophils are less than $1.5x10^9$/L and/or the platelets are less than $100x10^9$/L then delay treatment for 7 days and re-start treatment at the original dose provided the counts recover to above these levels. If a 14 day delay is required to allow counts to recover or there are two separate delays of 7 days during treatment the dose of the carboplatin should be reduced to 80% of the original dose. There is generally little need to reduce the dose of capecitabine 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.
Carboplatin	No dose reduction necessary

Renal Impairment

Drug	Creatinine Clearance (ml/min)	Dose (% of original dose)
Capecitabine	51-80 30-50 less than 30	100% 75% C/I
Carboplatin	Significant changes in GFR (of more than 10%) may require dose adjustment Do not administer if the CrCl is less than 20ml/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.

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 using 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

The starting dose of carboplatin is AUC 5 is used with calculated GFR. AUC 4 may be considered with EDTA clearance, seek advice from the appropriate consultant before prescribing. The recommended maximum dose when using a calculated creatinine clearance at AUC5 is 750mg (creatinine clearance 125ml/min). This is not a dose included in the national dose banding table. The maximum dose has been set at 790mg in ARIA. Please check if this dose is appropriate. If you have an obese patient or an individual with a calculated creatinine clearance above 125ml/min please seek advice from the relevant consultant

It should be noted that the dose of carboplatin may need to be altered if there is a change (improvement or reduction) in renal function of more than 10% from the previous cycle.

For those individuals with a performance status of 2 and above or who have had extensive prior treatment consider, for cycle one, prescribing only 10 days of capecitabine. This can be increased to 14 days depending on tolerability and response.

21 day cycle for 6 cycles

Drug	Dose	Days	Administration
Capecitabine	1000mg/m^2 twice a day	1-14 incl.	Oral
Carboplatin	AUC5 (max dose)	1	Intravenous infusion in 500ml glucose 5% over 60 minutes

Dose Information

- Capecitabine will be dose banded in accordance with the national dose bands
- Carboplatin will be dose banded in accordance with the national dose bands (10mg/ml)
- The maximum dose of carboplatin for AUC 5 is 750mg. This will be set as 790mg in ARIA to comply with national dose bands

Administration Information

Extravasation

- Carboplatin - irritant

Other

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

Additional Therapy

- Antiemetics

  15-30 minutes prior to chemotherapy;

  - ondansetron 8mg oral or intravenous
  - dexamethasone 8mg oral or intravenous

As take home medication;

- dexamethasone 4mg twice a day oral for 3 days
- metoclopramide 10mg three times a day when required oral

- 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 for the treatment of mucositis

- 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. National Institute for Health and Clinical Excellence (2003). Technology Appraisal 61. Capecitabine and tegafur uracil for the Treatment of Colorectal Cancer. DOH: London.

REGIMEN SUMMARY

Capecitabine-Carboplatin (AUC5)

Day One

1. Dexamethasone 8mg oral or intravenous
   Administration Instructions
   This may be given as 8mg intravenous stat if required

2. Ondansetron 8mg oral or intravenous
   Administration Instruction
   This may be given as 8mg intravenous stat if required

3. Warning - Carboplatin Maximum Dose
   Administration Instructions
   The dose of carboplatin is capped at a creatinine clearance of 125ml/min. The internationally recommended maximum dose of carboplatin for AUC 5 is 750mg. The national dose bands do not contain this dose so the cap has been set at 790mg in ARIA. Please check this dose is appropriate for your patient.

4. Carboplatin AUC 5 intravenous infusion in 500ml glucose 5% over 60 minutes
   Administration Instructions
   The dose of carboplatin is capped at a creatinine clearance of 125ml/min. The internationally recommended maximum dose of carboplatin for AUC 5 is 750mg. The national dose bands do not contain this dose so the cap has been set at 790mg in ARIA. Please check this dose is appropriate for your patient

Take Home Medicines

5. Capecitabine 1000mg/m^2 twice a day oral for 14 days

6. Dexamethasone 4mg twice a day oral for 3 days starting the day after carboplatin administration

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

DOCUMENT CONTROL

Version	Date	Amendment	Written By	Approved By
1.3	Aug 2022	Carboplatin changed to national dose bands Administration instructions changed in summary. Warning added in summary	Dr Deborah Wright Pharmacist	Donna Kimber Pharmacy Technician
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 Information tabulated throughout Renal impairment updated Maximum dose of carboplatin added Mouthwash statement changed Bolus removed from antiemetics Metoclopramide dose changed Dexamethasone TTO clarified Disclaimer added	Dr Debbie Wright Pharmacist	Donna Kimber Pharmacy Technician
1	Apr 2011	None	Dr Debbie Wright (Pharmacist)	Dr Chris Baughan (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.