Chemotherapy Protocol

GASTROINTESTINAL (UPPER) CANCER

CISPLATIN and FLUOROURACIL

Regimen

- Gastrointestinal Cancer (upper) – Cisplatin and Fluorouracil

Indication

- First line therapy of advanced / metastatic eosophagogastric cancer
- WHO performance status 0, 1, 2

Toxicity

Drug	Adverse Effect
Cisplatin	Neuropathy, nephrotoxicity, ototoxicity
Fluorouracil	Palmar-plantar erythrodysesthesia, diarrhoea, 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 fluorouracil. 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

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. 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 both cisplatin and fluorouracil should be reduced to 80% of the original dose.

Hepatic Impairment

Drug	Dose (% of original dose)
Cisplatin	No dose reduction necessary
Fluorouracil	If the bilirubin is more than 85umol/L and / or the AST more than 180 fluorouracil is contra-indicated. In moderate hepatic impairment consider reducing the dose by 30% and for severe impairment by 50%

Renal Impairment

Drug	Creatinine Clearance (ml/min)	Dose (% of original dose)
Cisplatin	more than 60	100
	45-59	75
	less than 45	Consider carboplatin
Fluorouracil	A dose adjustment is only required in severe renal impairment	

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.

Regimen

21 day cycle for 8 cycles

Drug	Dose	Days	Route
Cisplatin	60mg/m^2	1	Intravenous infusion in 1000ml sodium chloride 0.9% with 20mmol potassium chloride at a maximum rate of 1mg cisplatin per minute (minimum 120 minutes)
Fluorouracil	300mg/m^2/24hours	1-21	Intravenous Infusion (continuous)

Dose Information

- Cisplatin will be dose banded in accordance with the national dose bands (1mg/ml)
- Fluorouracil will be dose banded in accordance with the national dose bands (50mg/ml)

Administration Information

Extravasation

- Cisplatin - exfoliant
- Fluorouracil – inflammitant

Other

- Fluorouracil is administered using a continuous ambulatory pump changed every 7 days. A central or PICC line is required for treatment to commence and continue.

Additional Therapy

- Antiemetics

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

  - dexamethasone 8mg oral or intravenous
  - ondansetron 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
  - ondansetron 8mg twice a day for 3 days

- Cisplatin pre and post hydration as follows;

  Pre

  Furosemide 40mg oral or intravenous

  1000ml sodium chloride 0.9% with 20mmol potassium chloride and 16mmol magnesium sulphate over 60 minutes

  Post

  1000ml sodium chloride 0.9% with 20mmol potassium chloride and 16mmol magnesium sulphate over 60 minutes

  Patients should be advised to drink at least 3 litres of fluid in the 24 hours after administration of cisplatin.

- 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 as per national or local guidelines for the prevention or 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

References
1. Cunningham D, Starling N, Rao S et al. Capecitabine and Oxaliplatin for Advanced Esophagogastric Cancer. N Engl J Med 2008: 358 (1): 36-46.

REGIMEN SUMMARY

Day One

1. Dexamethasone 8mg oral or intravenous

2. Ondansetron 8mg oral or intravenous

3. Furosemide 40mg oral or intravenous

4. 1000ml sodium chloride 0.9% with 20mmol potassium chloride and 16mmol magnesium sulphate over 60 minutes

5. Cisplatin 60mg/m^2 intravenous infusion in 1000ml sodium chloride 0.9% with 20mmol potassium chloride at a maximum rate of 1mg cisplatin/minute (minimum time 120 minutes)

6. 1000ml sodium chloride 0.9% with 20mmol potassium chloride and 16mmol magnesium sulphate over 60 minutes

7. Fluorouracil 300mg/m^2/24 hours continuous intravenous infusion for 21 days

Take Home Medicines

8. Dexamethasone 4mg twice a day oral for 3 days starting on day 2 of the cycle

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

10. Ondansetron 8mg twice a day oral for 3 days starting on the evening of day one of the cycle

DOCUMENT CONTROL

Version	Date	Amendment	Written By	Approved By
1.2	Nov 2020	Updated monitoring with DPD testing Dose banding updated Coding removed	Donna Kimber Pharmacy Technician	Rebecca Wills Pharmacist
1.1	June 2014	Header changed Tabulation throughout Toxicities removed Renal and hepatic function updated < and > written out in full Bolus and stat removed from supportive treatments Metoclopramide dose changed to 10mg Pyridoxine removed from supportive treatments Mouthwashes updated TTOs clarified Disclaimer added	Dr Debbie Wright Pharmacist	Donna Kimber Pharmacy Technician
1	Aug 2010	None	Dr Debbie Wright Pharmacist	Dr Tim 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 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.