

Systemic Anti Cancer Treatment Protocol

**CISPLATIN AND FLUOROURACIL
Penile Cancer**

**PROCTOCOL REF: MPHACISFL
(Version No: 1.0)**

Approved for use in:

Advanced penile cancer
Creatinine clearance at baseline >50ml/min

Dosage:

Drug	Dose	Route	Frequency
Cisplatin	80mg/m ²	IV infusion	Day 1 only of 21 day cycle
Fluorouracil	1000mg/m ² /day	IV infusion over 24hours	Day 1 to 4 of 21 day cycle

Starting dose may be adjusted to cisplatin 60mg/m² and fluorouracil 3000mg/m² over 96 hours

Repeat at 21 day intervals for 4 to 6 cycles,

Supportive Treatments:

Aprepitant 125mg to be taken on day 1, an hour before chemotherapy and 80mg to be taken as a single dose on day 2 and day 3
Dexamethasone tablets 4mg twice daily for 3 days
Domperidone 10mg tablets, to be taken up to three times a day when required

Extravasation risk:

Cisplatin: Injection site reactions may occur during the administration of cisplatin. Given the possibility of extravasation, it is recommended to closely monitor the infusion site for possible infiltration during drug administration.

Flourouracil: refer to local guidelines for management extravasation

Issue Date: May 2017	Page 1 of 7	Protocol reference: MPHACISFL
Author: Helen Flint	Authorised by: Drugs & Therapeutics Committee & Dr Kirkbride	Version No: 1.0

Cockroft and Gault formula

Male patients $\frac{1.23 \times (140 - \text{age}) \times \text{weight (kg)}}{\text{Serum Creatinine (micromol/L)}}$

Female patients $\frac{1.04 \times (140 - \text{age}) \times \text{weight (kg)}}{\text{Serum Creatinine (micromol/L)}}$

Administration:

- Review patient's fluid intake over the previous 24 hours
- Review common toxicity criteria and performance status
- Calculate creatinine clearance using Cockroft and Gault equation
- Weigh the patient prior to commencing intravenous fluids
- Commence strict fluid balance (input and output)

Inpatient regimen

Day	Drug	Dose	Route	Diluent and rate	
1	Aprepitant 60 minutes before chemotherapy	125mg	PO		
	Ondansetron tablets 30mins before chemotherapy	24mg	PO		
	Dexamethasone tablets 30mins before chemotherapy	12mg	PO		
	Furosemide tablets	20mg	PO		
	Sodium Chloride 0.9% 1000mL With 20mmol Potassium Chloride			IV infusion over 90 minutes	
	Measure urine output volume and record If urine output averages 100mL/hour over previous 3 hours then proceed with cisplatin infusion If urine output is less than 100mL/hour the patient should be assessed and further 500mL sodium chloride 0.9% given IV over 30 minutes If urine output still not adequate contact the oncologist				
	Cisplatin	80mg/m²	IV	Sodium Chloride 0.9% 1000mL over 90 minutes	
	Sodium Chloride 0.9% 1000mL With 20mmol Potassium Chloride			IV infusion over 90 minutes	
	Fluorouracil	1000mg/m²	IV	Sodium Chloride 0.9% 1000mL over 24hours	
2	Aprepitant	80mg	PO		
2	Fluorouracil	1000mg/m²	IV	Sodium Chloride 0.9% 1000mL over 24hours	

Issue Date: May 2017	Page 2 of 7	Protocol reference: MPHACISFL
Author: Helen Flint	Authorised by: Drugs & Therapeutics Committee & Dr Kirkbride	Version No: 1.0

3	Aprepitant	80mg	PO	
3	Fluorouracil	1000mg/m²	IV	Sodium Chloride 0.9% 1000mL over 24hours
4	Fluorouracil	1000mg/m²	IV	Sodium Chloride 0.9% 1000mL over 24hours

Outpatient regimen

Day	Drug	Dose	Route	Diluent and rate	
1	Aprepitant 60 minutes before chemotherapy	125mg	PO		
	Ondansetron tablets 30mins before chemotherapy	24mg	PO		
	Dexamethasone tablets 30mins before chemotherapy	12mg	PO		
	Furosemide tablets	20mg	PO		
	Sodium Chloride 0.9% 1000mL With 20mmol Potassium Chloride		IV infusion over 90 minutes		
	Measure urine output volume and record If urine output averages 100mL/hour over previous 3 hours then proceed with cisplatin infusion If urine output is less than 100mL/hour the patient should be assessed and further 500mL sodium chloride 0.9% given IV over 30 minutes If urine output still not adequate contact the head and neck team				
	Cisplatin	80mg/m²	IV	Sodium Chloride 0.9% 1000mL over 90 minutes	
	Sodium Chloride 0.9% 1000mL With 20mmol Potassium Chloride		IV over 90 minutes		
1 to 4	Fluorouracil	4000mg/m² (1000mg/m²/day for 4 days)	IV	Sodium Chloride 0.9% over 4 days (96 hours) via infusion device	
2	Aprepitant	80mg	PO		
3	Aprepitant	80mg	PO		

At the end of IV fluids:

- Weigh the patient and review fluid balance chart

Issue Date: May 2017	Page 3 of 7	Protocol reference: MPHACISFL
Author: Helen Flint	Authorised by: Drugs & Therapeutics Committee & Dr Kirkbride	Version No: 1.0

- If there is a positive balance of 1.5L or 1.5kg in weight gained then consider furosemide 20mg orally and review output after 30 minutes. Any concerns then discuss with medical team prior to discharging the patient.

Ensure good oral (or via PEG) fluid intake

- Confirm patient understanding of the importance of fluid intake
- Patient should ensure they have 2 litres of fluid in the 24 hours following chemotherapy

Main Toxicities:

Haematological: Myelosuppression (Onset: 7-10 days, Nadir: 9-14 days, Recovery: 21-28 days), neutropenia, thrombocytopenia, leucopenia, agranulocytosis, anaemia and pancytopenia

Gastrointestinal: Anorexia, nausea, vomiting and diarrhoea, loss of taste or a metallic taste, stomatitis

Alopecia, loss of fertility.

Cisplatin	
Neuropathies	May be irreversible and may manifest by paresthesia, loss of muscle reflex and a sensation of vibrations. A neurologic examination must be carried out at regular intervals.
Ototoxicity	Observed in up to 31% of patients can be unilateral or bilateral and tends to become more frequent and severe with repeated doses; It is unclear whether ototoxicity is reversible
Additional side effects	Anaphylactic-like reactions to cisplatin have been reported
Fluorouracil	
Ocular	Nystagmus, watery eyes from increased production of Tears, gritty, red, sore eyes and blurred vision
Hepatobiliary disorders	Liver cell damage, liver necrosis, biliary sclerosis, cholecystitis
Dermatological	Palmar – plantar syndrome (hand-foot syndrome), on the palms of the hands and soles of the feet Hyperpigmentation of the skin Alopecia (hair may thin unlikely to cause total hair loss) Brittle, chipped and ridged nails –blue tinge or darkening or

Issue Date: May 2017	Page 4 of 7	Protocol reference: MPHACISFL
Author: Helen Flint	Authorised by: Drugs & Therapeutics Committee & Dr Kirkbride	Version No: 1.0

	the nails, flaking of the nails, or pain and thickening of the nail bed. Sensitivity of the skin to sunlight
Cardiovascular	Cardiac disorders <u>Common</u> - Angina, Ischemic ECG abnormalities <u>Uncommon</u> - Arrhythmia, myocardial infarction, myocardial ishchemia myocarditis, dilative cardiomyopathy, cardiac shock.

Investigations and Treatment Plan:

	Pre	C1	C2	C3	C4	Ongoing
Medical Assessment	X		X		X	Alternate cycles
Nursing Assessment		X	X	X	X	Every cycle
FBC	X		X	X	X	Every cycle
U&E & LFT	X		X	X	X	Every Cycle
CT scan	X				X	After cycle 3
Informed Consent	X					
ECG	X					If clinically indicated
Blood pressure measurement	X					If clinically indicated
PS recorded	X	X	X	X	X	
Toxicities documented	X	X	X	X	X	
Weight recorded	X	X	X	X	X	Every cycle

Issue Date: May 2017	Page 5 of 7	Protocol reference: MPHACISFL
Author: Helen Flint	Authorised by: Drugs & Therapeutics Committee & Dr Kirkbride	Version No: 1.0

Dose Modifications and Toxicity Management:

Recommended dose reduction for toxicity management	Cisplatin	Fluorouracil
First dose reduction	60mg/m ²	750mg/m ²
Second dose reduction	40mg/m ²	500mg/m ²

Haematological Toxicity:

Proceed on day 1 if-

ANC ≥ 1.0 x 10 ⁹ /L	Plt ≥ 100 x 10 ⁹ /L
--------------------------------	--------------------------------

Delay 1 week and consider dose reduction on day 1 if-

ANC ≤ 0.9 x 10 ⁹ /L	Plt ≤ 99 x 10 ⁹ /L
--------------------------------	-------------------------------

Hepatic impairment:

Cisplatin: No dose reduction necessary.

Fluorouracil		
Bilirubin /μmol/L	AST/ALT /units	Dose
<85	<180	No dose modification
>85	or >180	Contra indicated

Renal impairment:

GFR (mL/min)	Cisplatin	Fluorouracil
Above 60	80mg/m ² (100% dose)	100% dose
45 to 59	60mg/m ² (75% dose)	100% dose
Below 45	Consider carboplatin	Consider reduction if CrCl below 30mL/min

Issue Date: May 2017	Page 6 of 7	Protocol reference: MPHACISFL
Author: Helen Flint	Authorised by: Drugs & Therapeutics Committee & Dr Kirkbride	Version No: 1.0

References:

Cisplatin 1 mg/ml Sterile Concentrate, Summary of Product Characteristics Hospira UK Ltd Warwickshire.06/09/1996. Available from www.medicines.org.uk/emc/medicine. Last updated 30/04/2013.

Fluorouracil 50 mg/ml Solution for Injection or Infusion, Summary of Product Characteristics, Hospira, Warwickshire. 19/07/2004. Available from www.medicines.org.uk/emc/medicine. Last updated 24/07/14.

Dosage Adjustment for Cytotoxics in Hepatic Impairment. January 2009 UCLH (Version 3 - updated January 2009)

Dosage Adjustment for Cytotoxics in Renal Impairment. January 2009 UCLH (Version 3 - updated January 2009)

Penile cancer: current therapy and future directions
Sonpavde G et al
Annals of Oncology 2013 1-11

Cisplatin and 5-fluorouracil in inoperable, stage IV squamous cell carcinoma of the penis
Di Lorenzo G et al
BJUI 2012 E661-666

Issue Date: May 2017	Page 7 of 7	Protocol reference: MPHACISFL
Author: Helen Flint	Authorised by: Drugs & Therapeutics Committee & Dr Kirkbride	Version No: 1.0