Systemic Anti-Cancer Treatment Protocol

Cisplatin/ Etoposide
(Oral and IV regimens)

PROTOCOL REF: MPHACISET
(Version No: 1.1)

1.0 Approved for use in

Small cell lung cancer

Good performance status (PS 0 and 1)

Can be given with concurrent radiotherapy

Limited stage disease.

2.0 Dosage:

Drug	Dose	Route	Frequency
Cisplatin	**70mg/m^2**	IV infusion	Day 1 only
Etoposide	**120mg/m^2**	IV	Day 1 only
Etoposide	**240mg/m^2**	PO in 2 divided doses	Days 2 and 3

Repeated every 3 weeks for 4 cycles

Supportive Treatments

Anti-emetic risk - High

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, three times a day when required.

3.0 Interactions

Aminoglycosides e.g. gentamicin, vancomycin and diuretics

Increased risk of nephrotoxicity and ototoxicity. Renal function should be well monitored and audiometric tests carried out as indicated.

Phenytoin

Cisplatin can cause a decrease in phenytoin serum levels. This may lead to reappearance of seizures and may require an increase of phenytoin dosages.

Warfarin

The effects of warfarin may be increased. Monitor INR closely.

4.0 Extravasation risk

Cisplatin: Irritant - 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. A specific treatment for extravasation reactions is unknown at this time

Etoposide: Non vesicant

Refer to the network guidance for the prevention and management of extravasation.

5.0 Administration

- **Review patient's fluid intake over the previous 24 hours**
- **Review common toxicity criteria and performance status**
- **Calculate creatinine clearance using Cockcroft and Gault equation (see investigation section)**

Day	Drug	Dose	Route	Diluent and rate
1	Aprepitant	125mg	PO	1 hour before chemotherapy (80mg to be taken as a single dose on day 2 and day 3)
	Ondansetron	24mg	PO	30 mins before chemotherapy
	Dexamethasone	12mg	PO	30 mins before chemotherapy

	Furosemide	20mg	PO	
	Sodium Chloride 0.9% 1000mL (+ 20mmol Potassium Chloride)		IV	Over 90 minutes
	Etoposide	**120mg/m^2**	IV	In 100mL sodium chloride 0.9% infusion over 15 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 medical team**			
	Cisplatin	**70mg/m^2**	IV	In 1000mL sodium chloride 0.9% infusion over 90 minutes
	Sodium Chloride 0.9% 1000mL (+ 20mmol Potassium Chloride)		IV	Over 90 minutes
2	**Etoposide**	**240mg/m^2**	PO	in 2 divided doses
3	**Etoposide**	**240mg/m^2**	PO	in 2 divided doses

OR

For patients who are unable to swallow etoposide capsules

Day	Drug	Dose	Route	Diluent and rate
2	**Etoposide phosphate**	**120mg/m^2**	IV	In 100ml sodium chloride 0.9% infusion over 15 minutes

3	**Etoposide phosphate**	**120mg/m^2**	IV	In 100ml sodium chloride 0.9% infusion over 15 minutes

If etoposide phosphate is unavailable then switch to standard etoposide intravenous preparation, administered in 1000mL of sodium chloride 0.9% over 60 minutes. If standard etoposide is administered then pre-hydration with Sodium Chloride 0.9% 1000ml (+20 mmol Potassium Chloride) is not required.

At the end of IV fluids:

- **Weigh the patient and review fluid balance chart**
- **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 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.**

Notes

Etoposide

Round oral etoposide doses to the nearest 50mg

Swallow whole on an empty stomach or one hour before food.

6.0 Main Toxicities

Nausea, vomiting, immunosuppression (thrombocytopenia, anaemia and neutropenia), alopecia, allergic reactions

Cisplatin: diarrhoea, anorexia, nephrotoxicity, neuropathy, ototoxicity

Etoposide: mucositis, oesophagitis and stomatitis occur infrequently. Hyper or hypotension – see below, fatigue, fever, bronchospasm, peripheral neuropathy.

7.0 Investigations and treatment plan

	Pre	Cycle 1	Cycle 2	Cycle 3	Cycle 4	Comments
Medical Assessment	X		X		X	Alternate cycles
Nursing Assessment	X	X	X	X	X	Every cycle
FBC	X	X	X	X	X	Every cycle
U&E & LFT	X	X	X	X	X	Every cycle
Mg2+ and Ca2+	X	X	X	X	X	Every cycle
CrCl	X	X	X	X	X	Every cycle Cockcroft and Gault
Respiratory rate and O_2 sats	X	X	X	X	X	Every cycle
CT scan	X				X	At the end of treatment
Informed Consent	X					
ECG	X					Repeat as clinically indicated
Blood pressure	X					Repeat if clinically indicated
PS recorded	X	X	X	X	X	Every cycle
Toxicities documented	X	X	X	X	X	Every cycle
Weight recorded	X	X	X	X	X	Every cycle
Blood Glucose	X					Repeat if clinically indicated

8.0 Dose Modifications and Toxicity Management

Haematological Toxicity

Proceed on day 1 if-

Plt ≥ 100 x 10^9/L	ANC ≥ 1.0 x 10^9/L

Delay 1 week on day 1 if-

Plt ≤ 99 x 10^9/L	ANC ≤ 0.9 x 10^9/L

Non Haematological Toxicity

Renal

Cisplatin

Recalculate CrCl using Cockroft and Gault every cycle and consider EDTA if serum creatinine varies by >30% from baseline.

GFR (mL/min)	Cisplatin dose
≥ 60	100% dose
45 to 59	75% dose
< 45	Consider Carboplatin

If serum creatinine has increased by 50% between cycles then 20% dose reduction is required at next cycle

Etoposide

CrCl (mL/min)	Etoposide Dose
Above 50	100%
15 to 50	75%
Below 15	50%

<table>
<tr><td>Hepatic</td><td>Cisplatin – no dose modifications needed

Etoposide – conflicting information exists for reductions with etoposide, use table below but discuss with oncologist if in doubt

<table>
<tr><th>Bilirubin (µmol/L)</th><th>AST/ALT (units/L)</th><th>Etoposide Dose</th></tr>
<tr><td>26-51 or</td><td>60 - 180</td><td>50%</td></tr>
<tr><td>>51 or</td><td>>180</td><td>Clinical decision</td></tr>
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</td></tr>
<tr><td>Performance status</td><td>Defer 1 week and refer to consultant if there is any deterioration in performance status from cycle1 or previous cycles.</td></tr>
<tr><td>Ototoxicity or Neurotoxicity</td><td><u>Ototoxicity</u> 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.
Neurotoxicity is common
Discuss any reported ototoxicity or neurotoxicity with consultant</td></tr>
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9.0 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.
- Etopophos 100mg Powder for Solution for Injection, Summary of Product Characteristics Bristol-Myers Squibb Pharmaceutical Limited.23/05/1996 Available from www.medicines.org.uk/emc/medicine. Last updated 17/02/2012.
- Dosage Adjustment for Cytotoxics in Hepatic Impairment. January 2009 UCLH - Dosage Adjustment for Cytotoxics in Hepatic Impairment (Version 3 - updated January 2009).
- Dosage Adjustment for Cytotoxics in Renal Impairment. January 2009 UCLH - Dosage Adjustment for Cytotoxics in Renal Impairment (Version 3 - updated January 2009).