Two Day Etoposide CISplatin (EP) Therapy

INDICATIONS FOR USE:

INDICATION	ICD10	Regimen Code	Reimbursement Status
Emergency treatment of women with Gestational Trophoblastic Neoplasia (GTN) who are acutely unwell from liver or CNS disease and particularly those at risk of respiratory failure.	D39	00267a	Hospital
Hepatic Metastases. Women with GTN who are acutely unwell from liver disease.	D39	00267b	Hospital
Cerebral Metastases. Women with GTN who are acutely unwell from cerebral metastases.	D39	00267c	Hospital

TREATMENT:

The starting dose of the drugs detailed below may be adjusted downward by the prescribing clinician, using their independent medical judgement, to consider each patients individual clinical circumstances.

Emergency treatment
Patients are treated with etoposide and CISplatin for two consecutive days. This can be repeated weekly for 1-3 weeks and then altered to EMA/CO (NCCP Regimen 00248) or EP/EMA (NCCP Regimen 00264).

Hepatic Metastases
Patients are treated with etoposide and CISplatin for two consecutive days. This can be repeated weekly for 1-3 weeks and then altered to EP/EMA (NCCP Regimen 00264)

Cerebral Metastases
Patients are treated with etoposide and CISplatin for two consecutive days. This can be repeated weekly for 1-3 weeks and then altered to high dose EMA/CO (NCCP Regimen 00268)

Admin. Order	Day	Drug	Dose	Route	Diluent & Rate
1	1, 2	Etoposide[a]	100mg/m^2	IV	1000ml 0.9% NaCl over 60 mins
2	1, 2	CISplatin[b]	20mg/m^2	IV	1000ml 0.9% NaCl over 2 hours

[a]Hypotension following rapid IV administration has been reported.
Longer infusion times may be required based on the patient's tolerance

[b]**Pre hydration therapy required for CISplatin**
See local hospital policy recommendations.
Suggested prehydration for CISplatin therapy:
1. Administer 10mmol magnesium sulphate ($MgSO_4$) ((+/-KCl 20mmol/L if indicated) in 1000 mL sodium chloride 0.9% over 60 minutes.

Administer CISplatin as described above.

ELIGIBILTY:

- Indications as above

EXCLUSIONS:

- Hypersensitivity to etoposide, CISplatin or any of the excipients
- Severe hepatic impairment

PRESCRIPTIVE AUTHORITY:

The treatment plan must be initiated by a Consultant Medical Oncologist.

TESTS:

Baseline tests:

- FBC, renal and liver profile
- human chorionic gonadotropin (hCG)

Regular tests:

- FBC, renal and liver profile
- 24hr creatinine clearance prior to cycle 3
- hCG
- Patient should have hCG levels monitored twice weekly during treatment.
    - After remission is achieved, serum hCG should be measured fortnightly until monitoring has shown one year of normal hCG levels.
    - Follow-up for at least 5 years may be considered for those at highest risk**.**

Disease monitoring:

Disease monitoring should be in line with the patient's treatment plan and any other test/s as directed by the supervising Consultant.

DOSE MODIFICATIONS:

- Any dose modification should be discussed with a Consultant.
- In general treatment may proceed if neutrophils ≥ 1 x10^9/L and platelets > 75 x10^9/L.
- The use of G-CSF support may be considered.

Renal and Hepatic Impairment:

Table 1: Dose modifications in renal and hepatic impairment

Drug	**Renal Impairment**		**Hepatic Impairment**			
Etoposide	**Cr Cl (ml/min)**	**Dose**	**Bilirubin (micromol/L**		**AST**	**Dose**
	>50	100%	26-51	or	60-180	50%
	15-50	75%	>51	or	>180	Clinical decision
	<15	50%				
	Subsequent doses should be based on clinical responses					
CISplatin	**Cr Cl (ml/min)**	**Dose**	No dose reduction necessary			
	>60	100%				
	45-59	75%				
	<45	Consider CARBOplatin				

SUPPORTIVE CARE:

EMETOGENIC POTENTIAL: High (**Refer to local policy).**

PREMEDICATIONS:

Hydration prior and post CISplatin administration **(Reference local policy or see recommendations above).**

OTHER SUPPORTIVE CARE:

G-CSF may be used to mitigate the risk of haematological toxicities.

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS

The adverse effects listed are not exhaustive. Please refer to the relevant Summary of Product Characteristics for full details.

- **Neutropenia**: Fever or other evidence of infection must be assessed promptly and treated appropriately. G-CSF will likely be needed to maintain white blood cell count.
- **Hypersensitivity**: There is a high risk of hypersensitivity reactions with etoposide.
- **Renal Toxicity:** Nephrotoxicity is common with CISplatin. Encourage oral hydration. Avoid nephrotoxic drugs such as aminoglycoside antibiotics.
- **Ototoxicity and sensory neural damage** should be assessed by history prior to each cycle of CISplatin.

DRUG INTERACTIONS:

- CISplatin may potentiate the nephrotoxic and ototoxic effects of loop diuretics and aminoglycosides so concurrent use should be avoided.
- Current drug interaction databases should be consulted for more information.

ATC CODE:

Etoposide	L01CB01
CISplatin	L01XA01

REFERENCES:

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2. Newlands ES, Holden L, Seckl MJ et al. Management of brain metastases in patients with high-risk gestational trophoblastic tumors. J Reprod Med 2002; 47: 465–471.
3. NCCP Clinical Guidelines Diagnosis, staging and treatment of patients with gestational trophoblastic disease 2015. Available at http://www.hse.ie/eng/services/list/5/cancer/profinfo/guidelines/gtd/gtdguideline.pdf
4. Nephrotoxicity Associated with CISplatin EviQ ID: 184 v.3 https://www.eviq.org.au/clinical-resources/side-effect-and-toxicity-management/prophylaxis-and-prevention/184-nephrotoxicity-associated-with-CISplatin
5. Portilla D et al. CISplatin nephrotoxicity. UptoDate Accessed Oct 2017 https://www.uptodate.com/contents/CISplatin-nephrotoxicity?source=search_result&search=CISplatin%20hydration&selectedTitle=1~150

Version	Date	Amendment	Approved By
1	1/02/2016		Prof Maccon Keane
2	22/02/2018	Clarified dosing in renal and hepatic impairment. Applied new NCCP regimen template	Prof Maccon Keane
3	21/08/2019	Standardisation of administration fluid volume of CISplatin	Prof Maccon Keane

Comments and feedback welcome at oncologydrugs@cancercontrol.ie.