Etoposide and CISplatin 20mg/m^2 (EP) 5 Day Therapy

INDICATIONS FOR USE:

INDICATION	ICD10	Regimen Code	HSE approved reimbursement status*
Treatment of good prognosis (IGCCCG criteria) metastatic germ cell tumours (both non-seminoma and seminoma)	C62	00301a	N/A

*This is for post 2012 indications only

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.

Treatment with etoposide and CISplatin is administered on 5 consecutive days (days 1-5), of a 21 day cycle and repeated for 4 cycles or until disease progression or unacceptable toxicity develops.

Facilities to treat anaphylaxis MUST be present when systemic anti-cancer therapy (SACT) is administered.

Admin Order	Day	Drug	Dose	Route	Diluent & Rate
1	1-5	Etoposide	100mg/m^2	IV infusion	1000mL NaCl 0.9% over 60 minutes[b]
2	1-5	CISplatin	20mg/m^2	IV infusion	1000mL NaCl 0.9% over 60 minutes (Pre hydration therapy required)[a]
[a]Prehydration therapy required for CISplatin See local hospital policy recommendations. Suggested prehydration for CISplatin therapy: Administer 10mmol magnesium sulphate ($MgSO_4$) ((+/-KCl 10-20mmol/L if indicated) in 1000 mL NaCl 0.9% over 60-120 minutes. (Refer to relevant local hospital policy for advice on administration of electrolyte infusions).Administer CISplatin as described above					
[b]Hypotension following rapid IV administration has been reported. Longer infusion times may be required based on the patient's tolerance					

Note: Administration volumes and fluids have been standardised to facilitate electronic prescribing system builds.

ELIGIBILITY:

- Indications as above
- ECOG status 0-3

CAUTIONS:

- Severe liver impairment

EXCLUSIONS:

- Hypersensitivity to etoposide, CISplatin or any of the excipients.
- Pre existing neuropathies ≥ grade 2
- Creatinine clearance <40mL/min
- Significant hearing impairment/tinnitus
- Pregnancy
- Breastfeeding

PRESCRIPTIVE AUTHORITY:

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

TESTS:

Baseline tests:

- FBC, renal, liver profile
- Consider sperm banking for appropriate patients prior to initiation of therapy
- Audiology if clinically indicated

Regular tests:

- FBC weekly during treatment
- Renal and liver profile prior to each treatment cycle
- Audiology if clinically indicated

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

Haematological:

- Delay and dose reductions are not recommended as the efficacy of this treatment may be greatly compromised.
- All delays to treatment must be approved by prescribing consultant.
- Prophylactic use of G-CSF is not recommended.
- G-CSF is indicated in patients receiving their second or subsequent cycle of EP who have had an episode of neutropenic fever or who have not recovered their neutrophil count by Day 5.

Renal and Hepatic Impairment:

Table 2: Dose modification in renal and hepatic impairment

Drug	Renal impairment		Hepatic Impairment			
Etoposide	**CrCl (mL/min)**	**Dose**	**Bilirubin (micromol/L)**			**Dose**
	>50	100%				
	10-50	75% of the original dose , increase if tolerated	< 50	and	Normal albumin and normal renal function	No need for dose adjustment is expected
	Haemodialysis	Not dialysed, consider 75% of the original dose	≥ 50	or	Decreased albumin levels	Consider 50% of the dose, increase if tolerated
CISplatin	**CrCl (mL/min)**	**Dose**	No need for dose adjustment is expected			
	50-59	75% of original dose				
	*40-49	50% of original dose				
	<40	Not recommended				
	Haemodialysis	50% of the original dose may be considered				
**Due to the curative intent of this chemotherapy regimen , in cases where CrCl falls between 40-59mL/min it may be appropriate to maintain dose of CISplatin but with extra hydration, longer infusion time and daily creatinine measurements at the discretion of the prescribing consultant.*						

SUPPORTIVE CARE:

EMETOGENIC POTENTIAL:

- As outlined in NCCP Classification Document for Systemic AntiCancer Therapy (SACT) Induced Nausea and Vomiting Available on the NCCP website

CISplatin High **(Refer to local policy).**
Etoposide Low **(Refer to local policy).**

For information:
Within NCIS regimens, antiemetics have been standardised by Medical Oncologists and Haemato-oncologists and information is available in the following documents:

- NCCP Supportive Care Antiemetic Medicines for **Inclusion in NCIS** (Medical Oncology) - Available on the NCCP website
- NCCP Supportive Care Antiemetic Medicines for **Inclusion in NCIS** (Haemato-oncology) - Available on the NCCP website

PREMEDICATIONS:

Hydration prior to CISplatin administration **(Refer to local policy or see recommendations above).**

OTHER SUPPORTIVE CARE:

No specific recommendations

ADVERSE EFFECTS

- Please refer to the relevant Summary of Product Characteristics (SmPC) for details.

DRUG INTERACTIONS:

- Current SmPC and drug interaction databases should be consulted for information.

REFERENCES:

1. Culine, S., P. Kerbrat, A. Kramar, et al. Refining the optimal chemotherapy regimen for good-risk metastatic nonseminomatous germ-cell tumors: a randomized trial of the Genito-Urinary Group of the French Federation of Cancer Centers (GETUG T93BP). Ann Oncol 2007;18(5):917-924.
2. Einhorn LH, Williams SD, Loehrer PJ, et al. Evaluation of optimal duration of chemotherapy in favorable-prognosis disseminated germ cell tumors: a Southeastern Cancer Study Group protocol. J Clin Oncol 1989; 7:387-91
3. Irish Medication Safety Network: Best Practice Guidelines For the Safe Use of Intravenous Potassium in Irish Hospitals Available at: https://imsn.ie/wp-content/uploads/2020/10/IMSN-Best-Practice-Guideline-on-IV-Potassium-Oct-2020-approved.pdf
4. Prevention and management of cisplatin induced nephrotoxicityEviQ ID: 184 v.4. Available at:https://www.eviq.org.au/clinical-resources/side-effect-and-toxicity-management/prophylaxis-and-treatment/184-prevention-and-management-of-cisplatin-induced
5. Perazella MA et al. CISplatin nephrotoxicity. UptoDate. Last updated April 2024. Available at: https://www.uptodate.com/contents/cisplatin-nephrotoxicity?search=portilla%20cisplatin&source=search_result&selectedTitle=4%7E150&usage_type=default&display_rank=4
6. Giraud E L, Lijster B D, et al. Dose recommendations for anticancer drugs in patients with renal or hepatic impairment: an update. Available at: https://pubmed.ncbi.nlm.nih.gov/37269847
7. NCCP Classification Document for Systemic Anti-Cancer Therapy (SACT) Induced Nausea and Vomiting. V5 2023. Available at: https://www.hse.ie/eng/services/list/5/cancer/profinfo/chemoprotocols/nccp-classification-document-for-systemic-anti-cancer-therapy-sact-induced-nausea-and-vomiting.pdf
8. CISplatin 1mg/mL SmPC Last updated: 06/09/2024 . Accessed September 2024 Available at: https://www.hpra.ie/img/uploaded/swedocuments/Licence_PA0822-199-001_06092024154018.pdf
9. Etoposide 20 mg/mL Concentrate for Solution for Infusion SmPC Last updated: 13/02/2024 Accessed September 2024 Available at: https://www.hpra.ie/img/uploaded/swedocuments/Licence_PA2059-036-001_13022024104803.pdf

Version	Date	Amendment	Approved By
1	08/04/2016		Dr Maccon Keane
2	20/09/2017	Updated with new NCCP regimen template	Prof Maccon Keane
3	06/12/2017	Updated with revised CISplatin hydration regimen recommendations	Prof Maccon Keane
4	20/11/2019	Reviewed. Standardised treatment table and renal dose modifications.	Prof Maccon Keane
5	09/12/2024	Reviewed. Updated pre hydration information for CISplatin in treatment table. Added cautions section. Updated exclusions section. Updated renal and hepatic dose modifications table to align with Giraud et al 2023. Regimen updated in line with NCCP standardisation.	Prof Maccon Keane

Comments and feedback welcome at oncologydrugs@cancercontrol.ie.