CARBOplatin (AUC7) and Etoposide- Autologous Conditioning Germ Cell Tumour Regimen

INDICATIONS FOR USE:

INDICATION	ICD10	Regimen Code	Reimbursement Status
Treatment of metastatic relapsed/refractory germ cell tumours	C62	00453a	Hospital

TREATMENT:

CARBOplatin and etoposide are administered for 3 consecutive days (days -5,-4 and -3) and stem cell transfusion is carried out on Day 0 according to treatment table below.
A second cycle may be given on recovery (minimum interval between cycles is 28 days), unless there was a grade 4 non-haematologic toxicity or no response to first cycle
A minimum of 1 million CD34+ cells per kilogram of body weight is required for each cycle of high-dose chemotherapy

Consideration should be given to the administration of a maintenance oral dose of 50mg/m^2 of etoposide for 21 consecutive days every 4 weeks for three cycles in patients who have a complete or partial remission after two cycles of high-dose CARBOplatin and etoposide chemotherapy and who have normal serum levels of human chorionic gonadotropin (hCG) and alpha-fetoprotein.

Facilities to treat anaphylaxis MUST be present when the chemotherapy is administered.

Admin Order	Day	Drug	Dose	Route	Diluent & Rate
1	-5, -4, -3	CARBOplatin	AUC 7	IV Infusion	500ml 5% glucose over 60mins
2	-5, -4, -3	Etoposide	[a]750mg/m^2	IV Infusion	*0.9% NaCl over 2 hours
	0	Stem cell infusion			
	Start day +1	G-CSF (Round to nearest whole syringe)	5mcg/kg	SC	Continue until ANC > 1 x 10^9/L for two consecutive days
*Consideration should be given to stability of etoposide when determining volume of fluid required for reconstitution (Refer to local policy)					
Maintain strict fluid balance during therapy, by (1) monitoring fluid balance and (2) daily weights. If fluid balance becomes positive by >1000mls or weight increases by >1 Kg, the patient should be reviewed and consideration given to diuresing with furosemide					

The dose in mg of CARBOplatin to be administered is calculated as follows:

Dose (mg) = target AUC (mg/ml x min) X (GFR ml/min +25)

Reference NCCP Protocol 00261 CARBOplatin Monotherapy for information on calculation of CARBOplatin dose.

ELIGIBILTY:

- Indication as above

EXCLUSIONS:

- Hypersensitivity to etoposide, CARBOplatin or any of the excipients.
- Severe liver impairment (etoposide)
- Pregnancy
- Breast Feeding

PRESCRIPTIVE AUTHORITY:

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

TESTS:

Baseline tests:

- FBC, renal and liver profile
- LDH, Urate
- Creatinine Clearance
- Pulmonary function tests
- Echocardiogram
- Audiology if clinically indicated
- Virology screen -Hepatitis B* (HBsAg, HBcoreAb), Hepatitis C, HIV I and II, CMV and HSV.
  *Hepatitis B reactivation: See Adverse events/ Regimen specific complications

Regular tests:

- FBC, renal and liver profile required daily during therapy

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

Renal and Hepatic Impairment:

Table 1: Dose modification in renal and hepatic impairment

Drug	Renal impairment		Hepatic Impairment			
Etoposide	**CrCl (ml/min)**	**Dose**	**Bilirubin (micromol/L)**		**AST (Units/L)**	**Dose Etoposide**
	>50	100%				
	15-50	75%	26-51	or	60-180	*50%
	<15	50%	>51	or	>180	Clinical decision
	Subsequent dosing should be based on patient tolerance and clinical effect.					
CARBOplatin	**CrCl (ml/min)**	**Dose**	No dose reduction necessary			
	<60	Greater risk of developing myelosuppression				
	<20	Contra-indicated				

SUPPORTIVE CARE:

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

PREMEDICATIONS: Prior to stem cell infusion administer premedications as per local policy.

OTHER SUPPORTIVE CARE:

- Anti-viral prophylaxis **(Refer to local policy)**
- Anti-fungal prophylaxis **(Refer to local policy)**
- Mouthcare **(Refer to local policy)**
- Proton Pump Inhibitor **(Refer to local policy)**
- PJP prophylaxis **(Refer to local policy)** *Do not give Co-trimoxazole until engraftment achieved* and continue until day 100 or CD4 count> 200/microlitre.
- All patients must receive irradiated cellular blood components starting one week prior to conditioning and until 12 months after stem cell infusion to prevent transfusion associated graft versus host disease.

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. Avoid aminoglycoside antibiotics.
- **Neurotoxicity and ototoxicity:** Neurological evaluation and an assessment of hearing should be performed in patients receiving high dose CARBOplatin. Neurotoxicity, such as parasthesia, decreased deep tendon reflexes, and ototoxicity are more likely seen in patients previously treated with cisplatin, other platinum treatments and other ototoxic agents. Frequency of neurologic toxicity is also increased in patients older than 65 years.

- **Hepatitis B Reactivation**: Patients should be tested for both HBsAg and HBcoreAb as per local policy. If either test is positive, such patients should be treated with anti-viral therapy. **(Refer to local infectious disease policy**). These patients should be considered for assessment by hepatology.

DRUG INTERACTIONS:

- Avoid concurrent use of CARBOplatin with nephrotoxic drugs (e.g. aminoglycosides, NSAIDS) due to additive nephrotoxicity. If necessary monitor renal function closely.
- Avoid concurrent use of CARBOplatin with ototoxic drugs (e.g. aminoglycosides, NSAIDS). When necessary perform regular audiometric testing.
- Current drug interaction databases should be consulted for more information e.g interaction potential with CYP3A4 inhibitors/ inducers.

ATC CODE:

CARBOplatin L01XA02
Etoposide L01CB01

REFERENCES:

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4. CARBOplatin Summary of Product Characteristics. Last updated: 10/11/2019. Accessed Dec 2019. Available at https://www.hpra.ie/img/uploaded/swedocuments/Licence_PA2059-032-001_10112019092721.pdf
5. Etoposide 20 mg/ml Concentrate for Solution for Infusion Summary of Product Characteristics. Last updated: 29/07/2019. Accessed Dec 2019. Available at https://www.hpra.ie/img/uploaded/swedocuments/Licence_PA2059-036-001_29072019103821.pdf
6. NCCP Classification Document for Systemic Anti-Cancer Therapy (SACT) Induced Nausea and Vomiting. V1 2018. Available at: https://www.hse.ie/eng/services/list/5/cancer/profinfo/chemoprotocols/nccp%20antiemetic%20classification%20document%20v1%202018.pdf

Version	Date	Amendment	Approved By
1	18/12/2017		Prof Maccon Keane
2	15/01/2020	Reviewed. Updated exclusions, etoposide renal dose modifications, hepatitis B reactivation recommendations.	Prof Maccon Keane

Comments and feedback welcome at oncologydrugs@cancercontrol.ie.