SACT PROTOCOL

The Clatterbridge Cancer Centre NHS Foundation Trust

Systemic Anti Cancer Therapy Protocol

Etoposide
CNS

PROTOCOL REF: MPHAECNS
(Version No. 1.0)

Approved for use in:

- Glioblastoma multiforme/ anaplastic astrocytoma/ glioma
- Failure on previous temozolomide
- PS 0-2
- Prior nitrosourea

Dosage:

Drug	Dose	Route	Frequency
Etoposide	**50mg TWICE a day for 7-14 days**	Oral	28 day cycles until disease progression or unacceptable toxicity

Administration:

- Swallow capsules whole with a glass of water on an empty stomach
- Take 1 hour before or two hours after a meal
- Do not make up missed doses or double up next dose
- If patients are unable to swallow then the injection may be given orally. 50mg capsule = 35mg oral injection. Syringes must be prepared by the aseptic pharmacy
- Mask the unpleasant taste of the oral injection by taking with juice, cola or similar

Emetogenic risk:

Mildly emetogenic.

Supportive treatments:

Metoclopramide 10mg up to three times a day or as required for nausea and vomiting. Maximum for 5 consecutive days.

Dosing in renal and hepatic impairment:

Renal

Calculated using the Cockcroft-Gault equation

Crcl mL/min	Etoposide dose
>50	100%
15-50	For discussion with consultant/parent team
<15	Contraindicated

Subsequent doses should be based on clinical response

Hepatic

Conflicting information exists for reductions with etoposide, use table below but discuss with oncologist if in doubt.

AST transaminase		Bilirubin	Etoposide dose
<60U/L	AND	<25	100%
60 – 180	OR	26-51	For discussion with consultant/parent team
>180	OR	>51	Contraindicated

Interactions:

Warfarin / coumarin anticoagulants – Co-administration of warfarin and etoposide may result in elevated international normalized ratio (INR). Close monitoring of INR is recommended. Considering switching to a low molecular weight heparin.

Ciclosporin – Possible reduction in etoposide clearance at high doses of ciclosporin
St Johns Wort – Increased metabolism of etoposide

Clozapine – Both clozapine and cytotoxic antineoplastics might cause blood dyscrasias. Clozapine- induced neutropenia is not dose-related or predictable. Concurrent use is contraindicated.

Antiepileptics (CYP 3A4 inducers) (Carbamazepine, phenytoin, valproate) Etoposide can cause a decrease in phenytoin serum levels. This may lead to reappearance of seizures and may require an increase of phenytoin dosages.

Main toxicities:

Note that this is a very low dose of etoposide and is usually well tolerated but adverse events may still occur.

Etoposide
Nausea, vomiting, myelosuppression (thrombocytopenia, anaemia and neutropenia), alopecia, mucositis, oesophagitis and stomatitis occur infrequently, hyper or hypotension, fatigue, fever, bronchospasm, peripheral neuropathy.

Investigations and treatment plan:

	Pre	Cycle 1	Cycle 2	Cycle 3	Cycle 4	Cycle 5	Cycle 6	Ongoing
Informed Consent	X							
Clinical Assessment	X	X		X		X		Alternate cycles
SACT Assessment (to include PS and toxicities)	X	X	X	X	X	X	X	Every cycle
On treatment review	X	X	X	X	X	X	X	Every cycle
FBC	X	X	X	X	X	X	X	Every cycle
U&E & LFTs & Magnesium	X	X	X	X	X	X	X	Every Cycle
CrCl (Cockcroft and Gault)	X	X						If reduced or borderline SrCr
MRI scan	X							As appropriate
Weight recorded	X	X	X	X	X	X	X	Every cycle
Blood glucose	X							Repeat if clinically indicated
Height	X							

Dose Modifications and Toxicity Management:

Haematological toxicity:

Proceed on day 1 if-

ANC ≥ 1.0 x 10^9/L	Plt ≥ 100 x 10^9/L

Delay 1 week on day 1 if-

ANC ≤ 0.9 x 10^9/L	Plt ≤ 99 x 10^9/L

For patients delayed more than two weeks due to haematological toxicity, arrange for a review appointment with the consultant as reduced course length may be considered.

These haematological guidelines assume that patients are well with good performance status, that other acute toxicities have resolved and the patient has not had a previous episode of neutropenic sepsis.

Dose Modifications and Toxicity Management:

Dose Level	**Dose**
Recommended dose	50mg BD for 14 days
First dose reduction	50mg BD for 10 days
Second dose reduction	50mg BD for 7 days

Initial dose indicated as 50mg BD for 14 days. In the event of non-haematological toxicities, consider reducing the course length of etoposide to 10 days. In the event of further non-haematological toxicities, consider reducing the course length of etoposide to 7 days. If 50mg BD is not tolerated for 7 days then treatment should be discontinued.

References:

1. Summary of Product Characteristics, Vespid, Etoposide 50mg soft capsules, Neon Healthcare, https://www.medicines.org.uk/emc/product/10533/smpc#gref [accessed on 04th April 2022]
2. Dosage Adjustment for Cytotoxics in Hepatic Impairment. January 2009 UCLH - Dosage Adjustment for Cytotoxics in Hepatic Impairment (Version 3 - updated January 2009)
3. Krens S D, Lassche, Jansman G F G A, et al. Dose recommendations for anticancer drugs in patients with renal or hepatic impairment. Lancet Oncol 2019; 20: e201–08.
4. Stockley's Drug Interactions. Ninth Edition. Edited K. Baxter, Pharmaceutical Press, London, 2010.

Circulation/Dissemination

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Version History

		Author name and designation	Summary of main changes
		Hugh O'Neill **CNS SRG Pharmacist**	New Regimen Protocol V1.0
