High Dose Cytarabine Consolidation Therapy (post R-MPV) - 28 day Therapy

INDICATIONS FOR USE:

INDICATION	ICD10	Regimen Code	HSE approved reimbursement status*
Consolidation chemotherapy for the treatment of patients with newly diagnosed primary CNS lymphoma (PCNSL)	C85	00666a	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 is administered after five to seven cycles of induction chemotherapy with R-MPV (Reference NCCP regimen 00664 riTUXimab, methotrexate, procarbazine and vinCRIStine (R-MPV) – 14 Days Induction Therapy) and whole brain radiotherapy.
- Treatment is administered on Days 1 and 2 of a 28 day cycle for two cycles.
    - Treatment with Cycle 2 may proceed on count recovery.

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

Day	Drug	Dose	Route	Diluent & Rate	Cycle
1 and 2	Cytarabine	3000mg/m^2	IV infusion	500mL NaCl 0.9% over 4 hours	Every 28 days for 2 cycles

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

ELIGIBILITY:

- Indication as above
- ECOG status 0-2

CAUTION:

- May not be suitable for immunodeficient patients

EXCLUSIONS:

- Hypersensitivity to cytarabine or any of the excipients
- Breastfeeding
- Pregnancy

PRESCRIPTIVE AUTHORITY:

The treatment plan must be initiated by a Consultant Medical Oncologist or Consultant Haematologist working in the area of haematological malignancies.

TESTS:

Baseline tests:

- FBC, renal and liver profile
- Blood glucose
- Virology screen* - Hepatitis B (HBsAg, HBcoreAb) & Hepatitis C, HIV
  *(Reference Regimen Specific Complications for information on Hepatitis B reactivation)

Regular tests:

- FBC, renal and liver profile prior to each cycle
- Blood glucose

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.
- Note: Dose modification required in renal impairment (Ref Table 1). Increased neurotoxicity may be seen with CrCl of <60mL/minute.
- Consideration should be given to reducing doses of cytarabine in older patients and those with reduced renal or hepatic function. Elevations in liver function tests occur with both standard and high dose cytarabine. Significant liver function abnormalities may require discontinuation or a dose reduction. However doses of cytarabine less than 2 g/m^2 may be associated with inferior outcomes.

Renal and Hepatic Impairment:

Table 1: Dose modification of cytarabine in renal and hepatic impairment

Drug	Renal Impairment		Hepatic Impairment
Cytarabine	**CrCl (mL/min)**	**Dose**	Mild and moderate: no need for dose adjustment is expected Severe: consider 25-50% of the original dose and increase if tolerated
	≥ 60	No dose adjustment is needed	
	31-59	50% of the original dose	
	< 30	Not recommended	
	Haemodialysis:	50% of the original dose, start haemodialysis 4-5 hours after administration	
Cytarabine: Renal and hepatic – Giraud et al 2023			

SUPPORTIVE CARE:

EMETOGENIC POTENTIAL:

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

Cytarabine: Moderate (**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 NCCP website
- NCCP Supportive Care Antiemetic Medicines for **Inclusion in NCIS** (Haemato-oncology) - Available on NCCP website

PREMEDICATIONS:

To prevent a chemical induced conjunctivitis developing with cytarabine, prednisoLONE eye drops (e.g. Pred Mild®) 1-2 drops per eye 4 hourly during waking hours prior to cytarabine and continued 5 days post treatment should be administered.

OTHER SUPPORTIVE CARE:

- G-CSF prophylaxis required after each cycle, please discuss with consultant **(Refer to local policy)**
- Proton pump Inhibitor**(Refer to local policy)**
- Anti-viral prophylaxis **(Refer to local policy)**
- Anti-fungal prophylaxis **(Refer to local policy)**
- PJP prophylaxis **(Refer to local policy)**

ADVERSE EFFECTS:

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

REGIMEN SPECIFIC COMPLICATIONS:

- **Cytarabine syndrome:** Treatment with cytarabine may cause a 'Cytarabine Syndrome' characterised by flu-like symptoms, skin rash and occasionally chest pain.
- **Hand-foot syndrome (HFS):** HFS, also known as palmar-plantar erythrodysaesthesia (PPE), may involve bilateral erythema, tenderness, pain, swelling, tingling, numbness, pruritus, dry rash, or moist desquamation and ulceration of the palms and soles. Symptoms appear to be dose dependent and palms are affected more than soles.
- **Skin Rash:** Anti-cancer drugs can cause a number of changes in the skin with maculo-papular rash the most common type of drug-induced skin reaction. Consider prednisolone prophylaxis on subsequent cytarabine cycles.

DRUG INTERACTIONS:

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

REFERENCES:

1. Morris PG, Correa DD, Yahalom J, Raizer JJ, Schiff D, Grant B, Grimm S, Lai RK, Reiner AS, Panageas K, Karimi S, Curry R, Shah G, Abrey LE, DeAngelis LM, Omuro A. Rituximab, methotrexate, procarbazine, and vincristine followed by consolidation reduced-dose whole-brain radiotherapy and cytarabine in newly diagnosed primary CNS lymphoma: final results and long-term outcome. J Clin Oncol. 2013 Nov 1; 31(31):3971-9. doi: 10.1200/JCO.2013.50.4910. Epub 2013 Oct 7. PMID: 24101038; PMCID: PMC5569679
2. 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/
3. 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
4. Cytarabine Summary of Product Characteristics. Last updated: 18/08/2021. Accessed 12/03/2024. Available at: https://www.hpra.ie/img/uploaded/swedocuments/Licence_PA0822-200-002_18082021114137.pdf

Version	Date	Amendment	Approved By
1	01/12/2022		Prof Patrick G Morris, Dr Liam Smyth
2	15/11/2024	Regimen reviewed. Amended Baseline and Regular tests. Renal and Hepatic dose modifications updated to align with Giraud et al (2023). Emetogenic potential amended as per NCCP standard wording. Minor amendment to Premedications section. Adverse effects removed and regimen specific complications amended as per NCCP standard wording.	Prof Patrick G Morris, Dr Liam Smyth

Comments and feedback welcome at oncologydrugs@cancercontrol.ie.