Intrathecal Methotrexate for CNS prophylaxis in GTN

INDICATIONS FOR USE:

INDICATION	ICD10	Regimen Code	Reimbursement Status
Central nervous system (CNS) prophylaxis in patients with high risk gestational trophoblastic neoplasia (GTN).	D39	00249a	Hospital
Central nervous system (CNS) prophylaxis in patients with low risk gestational trophoblastic neoplasia (GTN) with lung metastases.	D39	00249b	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.

Intrathecal methotrexate is administered on **Day 1** and repeated every **14 days** for a total of 3 doses.

Low risk GTN with lung metastases: Administration of intrathecal methotrexate occurs during the first 3 methotrexate courses (see regimen 00246).

High risk GTN (all patients): Administration of intrathecal methotrexate usually coincides with the EMA (etoposide, methotrexate and DACTINomycin) treatment for the high risk patients (see regimen 00248).

Day	Drug	Dose	Route	Diluent & Rate	Cycle
1	Methotrexate	12.5mg	**Intrathecal**	n/a	Every 14 days for 3 doses
2	Folinic acid	15mg	PO	24 hrs after start of methotrexate	Every 14 days for 3 doses
Refer to NCCP Guidance on the Safe Use of Intrathecal Chemotherapy in the Treatment of Cancer https://www.hse.ie/eng/services/list/5/cancer/profinfo/medonc/safetyreview/itcguidance.pdf					

ELIGIBILITY:

- Indications as above

EXCLUSIONS:

- Hypersensitivity to methotrexate or any of the excipients

PRESCRIPTIVE AUTHORITY:

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

TESTS:

Baseline tests:

- FBC, renal and liver profile
- Serum human chorionic gonadotropin (hCG) using a validated test method

Regular tests:

- FBC renal and liver profile prior to each cycle
- Serum hCG/blood levels (using a validated test method) should be done on day one of each cycle or more frequently if required.

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.

SUPPORTIVE CARE:

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

PREMEDICATIONS: Not usually required.

OTHER SUPPORTIVE CARE: No specific recommendations.

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**: There is some systemic absorption of intrathecal chemotherapy. This may be further complicated by systemic therapy if given concurrently or by poor marrow tolerance due to previous therapy. Fever or other evidence of infection must be assessed promptly and treated aggressively.
- **Renal Dysfunction**: Methotrexate, given by any route, should be given with special caution if the creatinine clearance is less than 30 mL/minute with all subsequent doses determined based on hematologic and mucosal tolerance for the first dose given.
- **Precautions for Intrathecal Administration**: Refer to local policy on Intrathecal Therapy.

DRUG INTERACTIONS:

- Current drug interaction databases should be consulted for more information.

REFERENCES:

1. Newlands ES, Holden L, Seckl MJ, McNeish I, Strickland S, Rustin GJ. Management of brain metastases in patients with high-risk gestational trophoblastic tumors J Reprod Med. 2002 Jun;47(6):465-71
2. NCCP National Clinical Guideline (Draft) - Diagnosis, staging and treatment of patients with Gestational Trophoblastic Disease. July 2021.
3. Dosage Adjustment for Cytotoxics in Renal Impairment January 2009; North London Cancer Network.
4. Dosage Adjustment for Cytotoxics in Hepatic Impairment January 2009; North London Cancer Network.
5. NCCP Classification Document for Systemic Anti-Cancer Therapy (SACT) Induced Nausea and Vomiting. V3 2021. 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
6. Methotrexate 50mg/2ml Summary of Product Characteristics. Accessed Oct 2021. Available at: https://www.hpra.ie/img/uploaded/swedocuments/Licence_PA0822-206-002_19052021104201.pdf

Version	Date	Amendment	Approved By
1	01/02/2016		Prof Maccon Keane
2	22/02/2018	Updated with new NCCP Regimen Template	Prof Maccon Keane
3	22/10/2021	Reviewed. Updated treatment section (clarification of GTN risk). Updated hCG testing (baseline and regular tests).	Prof Maccon Keane

Comments and feedback welcome at oncologydrugs@cancercontrol.ie.