Methotrexate 40mg/m^2 Monotherapy -28 Day

INDICATIONS FOR USE:

INDICATION	ICD10	Regimen Code	HSE approved reimbursement status*
Recurrent, advanced or metastatic head and neck squamous cell carcinoma (SCC) in patients with comorbidities or as palliative treatment in patients unsuitable for combination chemotherapy	C76	00893a	N/A

* This applies to post 2012 indications

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.

Methotrexate is administered on Day 1, 8 and 15 of a 28 day cycle continuously until disease progression or unacceptable toxicity, whichever occurs first.

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

Day	Drug	Dose	Route	Diluent & Rate	Cycle
1, 8, 15	Methotrexate	[a]40mg/m^2	IV bolus	n/a	Every 28 days
[a] Dose may be escalated to 50mg/m^2 at the discretion of the treating clinician if the patient does not experience any mucositis.					

ELIGIBILITY:

- Indications as above

EXCLUSIONS:

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

PRESCRIPTIVE AUTHORITY:

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

TESTS:

Baseline tests:

- FBC, renal and liver profile
- Chest x-ray

Regular tests:

- FBC, Renal and Liver profile, urinalysis
- Examination of the mouth and throat for mucosal changes

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:

Table 2: Dose modification of Methotrexate in haematological toxicity

ANC ($x10^9$/L)	Dose
>1.0	100%
<1.0	Delay until counts return to normal. Consider dose reduction by 25%. Discuss with clinician.
Prolonged recovery greater than two weeks delay or 3rd delay for myelosuppression	Delay treatment until recovery and consider reducing methotrexate by 50% for subsequent cycles or discontinue

Platelets ($x10^9$/L)	Dose
>100	100%
75 – 100	Clinician Discretion: Continue or delay until recovery
50- 75	Delay until counts return to normal.
<50	Delay until recovery and consider dose reduction by 25%

Renal and Hepatic Impairment:

Table 3: Dose modification of methotrexate in renal and hepatic impairment

Renal Impairment		Hepatic Impairment
CrCl (mL/min)	**Dose**	No need for dose adjustment is expected Bilirubin > 86µmol/L: avoid use
≥50	No dose adjustment needed	
20-50	50% of the original dose	
< 20	Not recommended. If unavoidable consider Haemodialysis.	
Haemodialysis	Not recommended, if unavoidable 50% of the original dose, can be dialysed with daily high flux dialysis.	
Renal and hepatic dose modifications taken from Giraud et al 2023		

Management of adverse events

Table 4: Dose modification of methotrexate in Mucositis and Stomatitis

Mucositis and Stomatitis	Recommended dose modification
Grade 2	Delay treatment until toxicity has resolved to Grade 1 or less and reduce the dose for subsequent cycles as follows: 1st occurrence: No dose reduction 2nd occurrence: Reduce methotrexate by 25% 3rd occurrence: Reduce methotrexate by 50% 4th occurrence: Omit treatment
Grade 3	Delay treatment until toxicity has resolved to Grade 1 or less and reduce the dose for subsequent cycles as follows: 1st occurrence: Reduce methotrexate by 50% 2nd occurrence: Omit treatment

SUPPORTIVE CARE:

EMETOGENIC POTENTIAL:

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

Methotrexate: Low (**Refer to local policy)**

For information:
Within NCIS regimens, anti-emetics have been standardised by the 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 NCCP website

PREMEDICATIONS: None

OTHER SUPPORTIVE CARE:

- Mouth care (**Refer to local policy**).

ADVERSE EFFECTS:

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

REGIMEN SPECIFIC COMPLICATIONS

- Patients with significant third space accumulations should be appropriately managed and monitored prior to and during treatment

DRUG INTERACTIONS:

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

REFERENCES:

1. Banipal RPS and Mahajan MK. Methotrexate Revisited—in Recurrent Head and Neck Cancer. Palliative care: Research & Treatment 2011:5 9-13.
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. V6 2025. 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. Methotrexate (Pfizer®) Summary of Product Characteristics. Accessed January 2025 .Available here: Licence_PA0822-206-002_09012025154622.pdf

Version	Date	Amendment	Approved By
1	24/05/2025		Prof Seamus O Reilly

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