SACT PROTOCOL

The Clatterbridge Cancer Centre NHS Foundation Trust

Systemic Anti Cancer Therapy Protocol

Methotrexate - Oral
Langerhans Cell Histiocytosis (LCH)

PROTOCOL REF: MPHAMOLCH
(Version No. 1.0)

Approved for use in:

Langerhans' cell histiocytosis (LCH) is a very rare condition characterised by excessive production of Histiocyte cells.

LCH can affect bones or organs and the symptoms present in a number of different ways. These can range from a skin rash and lumps on the skull to a swollen tummy, breathing difficulties and diarrhoea.

LCH is not cancer but some patients require chemotherapy and therefore are managed by an onologist.

Dosage:

Drug	Dose	Route	Frequency
Methotrexate	**20mg**	Oral	Weekly on the same day each week

Continued until disease progression or unacceptable toxicity

Doses may be titrated to once every 2, 3 or 4 weeks.
Doses should not exceed 25mg weekly

Administration:

To be taken as a single dose once weekly
Supplied as 2.5mg tablets
Women of childbearing potential should avoid handling crushed or broken tablets.

Emetogenic risk:

Minimally emetogenic. Frequency of nausea and vomiting <10%.

Supportive treatments:

Folic acid 5mg ONCE weekly to be taken 4 days after methotrexate.

Pregnancy:

Methotrexate is known to be harmful to the development of an unborn child.
Effective contraception should be continued for 6 months after taking methotrexate.
Patients taking methotrexate should not breastfeed.

Dosing in renal and hepatic impairment:

Renal	CrCL ≥20ml/min (Cockcroft-Gault)	No adjustment required
	CrCL <20ml/min (Cockcroft-Gault)	Not recommended

Hepatic	Bilirubin >86micromoles/L	Avoid

Interactions:

For a full list of interactions please refer to summary of product characteristics.

- Immunomodulators including, ciclosporin, leflunomide, sulfasalazine.
- Alcohol - The consumption of alcohol might increase the risk of methotrexate-induced hepatic cirrhosis and fibrosis.
- Penicillin antibiotics – Amoxicillin / Benzyl-peniciilin / Flucloxacillin / Phenoxymethylpenicillin / Pipercillin (Tazocin) / Pivmecillinam reduced clearance of methotrexate.
- Ciprofloxacin – increased methotrexate toxicity – usually with high dose methotrexate.
- Antiepileptics including; phemobarbital, Carbamazepine valproate phenytoin
- Aspirin – increased methotrexate toxicity
- NSAIDs – Celecoxib / Diclofenac / Etodolac / Etoricoxib / Ibuprofen / Ketorolac / Mefanamic acid / Naproxen– increased methotrexate toxicity.
- PPIs – Omeprazole / Esomeprazole / Lansoprazole / Pantoprazole – reports of reduced methotrexate elimination – usually high dose methotrexate
- Trimethoprim – risk of severe bone marrow supression
- Cloazapine

- Digoxin
- Colestyramine
- Eltrombopag

Main toxicities:

Common side effects affecting between 1 in 10 and 1 in 100 patients include; infections, leucopenia, headaches, dizziness, fatigue, nausea, vomiting, diarrhoea, loss of appetite, stomatitis, elevated liver transaminases, Erythematous rash, alopecia.

Other **less common side effects** include; thrombocytopenia, neutropenia, anaemia, thromboembolism pneumonitis, interstitial fibrosis, Stevens-Johnson's syndrome, toxic epidermal necrolysis, nephropathy, vaginal ulceration.

Investigations and treatment plan:

	Pre	Cycle 1	Cycle 1 D15	Cycle 2	Cycle 3	Ongoing
Informed Consent	X					
Clinical Assessment	X				X**	As clinically indicated or every 3 months
SACT Assessment (to include PS and toxicities)	X	X	X	X	X	Every 3 months
FBC	X	X	X	X	X	Every 3 months
U&E & LFTs & Magnesium	X	X	X	X	X	Every 3 months
CrCl (Cockcroft and Gault)	X	X	X	X	X	Every 3 months
Weight recorded	X	X		X	X	Every 3 months
Height	X					
Pregnancy Test	X					

During treatment and for 6 months after, appropriate measures must be taken to avoid pregnancy; this applies to patients of both sexes.

Dose Modifications and Toxicity Management:

Haematological toxicity:

Proceed on day 1 if-

WCC ≥ 3.5 x 10^9/L	ANC ≥ 1.5 x 10^9/L	Plt ≥ 150 x 10^9/L

Delay 1 week on day 1 if-

WCC ≥ 3.4 x 10^9/L	ANC ≤ 1.4 x 10^9/L	Plt ≤ 149 x 10^9/L

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.

Non- Haematological toxicity:

GI toxicity can be common. Folic acid can be increased to 5mg OD (except for methotrexate days).

References:

Summary of Product Characteristics, Methotrexate 2.5 mg Tablets, Avanz Pharma. Available at www.medicines.org.uk Last updated 07/01/21 [accessed on 12th November 2021]

Steen et al. Successful treatment of cutaneous Langerhans cell histiocytosis with low-dose methotrexate. British Journal of Dermatology 2001; 145: 137-140.

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.

Circulation/Dissemination

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Version History

Date	Version	Author name and designation	Summary of main changes
12/11/21	1.0	**Rob Challoner** **Advanced Pharmacist NMP**	**New Regimen Protocol**