Methotrexate in the Management of Immune-Related Adverse Effects (irAEs)

A guide for members on the prescribing and monitoring of methotrexate when used in the management of irAEs caused by treatment with immune-checkpoint inhibitors.

It should be noted that this use is considered off-label use; relevant governance processes within each organisation should be followed to ensure the risks associated with this are mitigated

British Oncology Pharmacy Association in Collaboration with The Immuno-oncology Clinical Network

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Contents

1. Introduction

- Methotrexate is a conventional synthetic disease-modifying anti-rheumatic drug (csDMARD). It is a folic acid antagonist, and its major site of action is the enzyme dihydrofolate reductase.

- Methotrexate is also classed as an antimetabolite cytotoxic agent.

- Within its licence, methotrexate is used in the treatment of adults with severe rheumatoid arthritis who are unresponsive or intolerant to conventional therapy. Other licenced indications include the treatment of neoplastic disease covering a wide range of tumour sites as well as the treatment of severe cases of uncontrolled psoriasis unresponsive to conventional therapy.

- Off-license it can be used as a steroid sparing agent to treat rheumatological toxicities induced by immune checkpoint therapy, including inflammatory arthritis, polymyalgia, myositis, as well as uveitis and iritis as per guidance from both ESMO and ASCO.

- This document is intended to be used as a monograph to provide prescribing and monitoring advice once the decision has been made to initiate methotrexate. It is not a clinical guideline, but a consensus view of current use of methotrexate when used for irAEs. It should be used in conjunction with any local policies/procedures/guidelines and should be approved for use according to the trust clinical governance processes.

2. Prescribing and Monitoring Advice

2.1 Contraindications

- Hypersensitivity to any of the excipients within the product formulation
- Hypersensitivity to methotrexate
- Active infectious disease
- Alcohol dependency
- Methotrexate should not be used concomitantly with other antifolate medications (e.g. co-trimoxazole)
- Liver disease including fibrosis, cirrhosis, recent or active hepatitis
- Significant hepatic impairment
- Avoid in patients with significant ascites or pleural effusion as methotrexate is extensively hydrophilic and accumulates in these fluids, then subsequently returns to the circulation causing myelosuppression
- Pre-existing blood dyscrasias, such as bone marrow hypoplasia, significant anaemia, leukopenia, or thrombocytopenia
- Severe acute or chronic infections and immunodeficiency syndrome
- Severe/significantly impaired renal function – see **section 2.9** for more information on dosing in renal impairment
- Stomatitis, ulcers of the oral cavity and known active gastrointestinal ulcer disease
  Pregnancy and breastfeeding (see section 2.3)

2.2 Precautions

- Immunisations - Avoid live immunisations. Contact specialist team for advice.
- Methotrexate should be used with extreme caution in elderly patients, a dose reduction should be considered due to reduced liver and kidney function as well as lower folate reserves which occurs with increased age.

2.3 Pregnancy Advice

- Women must not get pregnant during methotrexate therapy, and effective contraception must be used during treatment with methotrexate and at least 6 months thereafter.
- Female patients of reproductive potential must be counselled regarding pregnancy prevention and planning.
- It is recommended that prior to initiating therapy, women of childbearing potential must be informed of the risk of malformations associated with methotrexate and any existing pregnancy must be excluded with certainty via a pregnancy test.
- It is not known if methotrexate is present in semen.
- As precautionary measures, sexually active male patients or their female partners are recommended to use reliable contraception during treatment of the male patient and for at least 3 months after cessation of methotrexate.

2.4 Pre-treatment assessment

- FBC, U&Es and LFTs
- Albumin
- Virology: HIV, Hepatitis B and Hepatitis C
- Blood pressure
- Chest Xray unless the patient has had a CT scan within the past 8 weeks
- Weight
- Capillary blood glucose

If history and examination raise suspicion of parenchymal lung disease:
- Lung function testing
- Chest x-ray/CT chest
- Referral to respiratory medicine

Consider TB screening if suspected infection or patient at risk.

2.5 Pharmaceutical form

- **Oral tablet**
  2.5mg and 10mg strengths are available; however, always use **2.5mg** tablets as per NPSA guidance to reduce any dispensing errors with different strengths.

- **Oral solution**
  Methotrexate is available as a 2mg/ml solution. Pack sizes are 35ml, 60ml and 65ml.

- **Subcutaneous injection**

Injectable methotrexate must be prescribed as pre-filled syringes or pens only:

	Pre-filled pens for subcutaneous injection *		Pre-filled syringe for subcutaneous injection *	
Brand	**Nordimet®**	**Metoject®**	**Zlatal®**	**Methofill®**
Strengths available	7.5mg in 0.3ml	7.5mg in 0.15ml	7.5mg in 0.3ml	7.5mg in 0.15ml
	10mg in 0.4ml	10mg in 0.20ml	10mg in 0.4ml	10mg in 0.2ml
	12.5mg in 0.5ml	12.5mg in 0.25ml	12.5mg in 0.5ml	12.5mg in 0.25ml
	15ml in 0.6ml	15mg in 0.30ml	15ml in 0.6ml	15ml in 0.3ml
	17.5mg in 0.7ml	17.5mg in 0.35ml	17.5mg in 0.7ml	17.5mg in 0.35ml
	20mg in 0.8ml	20mg in 0.40ml	20mg in 0.8ml	20mg in 0.4ml
	22.5mg in 0.9ml	22.5mg in 0.45ml	22.5mg in 0.9ml	22.5mg in 0.45ml
	25mg in 1ml	25mg in 0.50ml	25mg in 1ml	25mg in 0.5ml
		27.5mg in 0.55ml		
		30mg in 0.60ml		

2.6 Dosage

General dosing as per Clatterbridge guidance for Methotrexate in Immune checkpoint inhibitor (ICI) Mediated Conditions:

Methotrexate 15mg PO once weekly on the same day each week for 2 weeks, then 20mg PO Once weekly on the same day each week after initial 2-week treatment.

Condition specific doses:

- ICI induced uveitis
  7.5-25 mg orally once weekly dose. Start at therapeutic doses rather than more traditional incremental increases i.e. a normal starting dose is between 12.5 and 15mg once weekly.

- ICI induced arthritis
  Initial dose 7.5-15 mg weekly, adjusted to 7.5 to 25 mg weekly depending on response and lowest effective dose. For doses of >20mg/week, there is an increased risk of toxicity including bone marrow suppression.

Note: Doses to be adjusted in increments of 2.5mg until therapeutic response.

Oral and subcutaneous doses are usually the same. For some patients, subcutaneous injections may be better absorbed and tolerated via this route.

* Subcutaneous methotrexate must be prescribed by brand and include the generic name where prescribing systems allow. If switching between subcutaneous methotrexate products is necessary, patients should be informed in advance. For patients who are self-administrating, training must be provided to ensure that new brand is administered correctly.

Folic acid must be prescribed alongside methotrexate.

The dose of folic acid is 5-10mg once weekly taken on a different day to Methotrexate. This should be co-prescribed to reduce the risk of minor side effects. Most patients are controlled on 5mg of folic acid once weekly and if blood tests are monitored there are very few patients who require 10mg once weekly.

Alternatively, folic acid can be prescribed at 5mg OD for 6 days per week but not to be taken on the same day as methotrexate.

2.7 Method of administration

Subcutaneous injection:

- Administration is brand specific – further information can be found in the product literature Home - electronic medicines compendium (emc)
- Patients must be educated on the proper injection technique and the first administration must be under direct medical supervision.
- If patients are switching between brands, those who self-administer must be given new training to ensure that the new brand is administered correctly.

Oral tablet:

- Advise patients to take methotrexate with food if they experience nausea if it's currently being taken on an empty stomach.
  NB. Absorption can be impaired by milk and dairy products.

2.8 Is there therapeutic Drug Monitoring?

Serum methotrexate levels are not needed in this scenario. They are needed when high dose methotrexate infusions are used in SACT protocols.

2.9 Other monitoring

FBC, U&Es and LFTs should be monitored every week for the first 8 weeks after which, if bloods stable, monitoring can be undertaken monthly until cessation. If the treatment is long term (i.e. 6 months or longer) the medical team may decide to perform monitoring tests at longer intervals (i.e. every 2-3 months).

Hepatic impairment:

- Bilirubin > 86 µmol/L – avoid (as per The Lancet, 2023)
- Increase in ALT/AST >2x ULN – withhold and monitor LFTs until improved.

Renal function:

Methotrexate is predominantly excreted by the kidneys; therefore, renal impairment will affect the clearance of methotrexate. Patients who develop dehydration, pre-renal or acute renal failure while on methotrexate should stop treatment and have regular monitoring of their FBC.

Note: Any changes in medication, particularly ACEIs and ARBs, should be reviewed.

Dose reductions depending on creatinine clearance (CrCl) as per The Lancet, 2023:

Creatinine clearance (ml/min)	Dose
≥ 50 ml	No dose adjustment is needed
20-50	50% of the original dose
<20ml	Avoid

2.10 Adverse effects

- These are the most common adverse effects.
- This is not an exhaustive list. See SmPC for further details.

System	Adverse Effects

WBC < $4x10^9$/L	Perform a differential and increase frequency of monitoring.
WBC < $3.5x10^9$ /L	Withhold and discuss with a specialist. Bone marrow suppression can occur abruptly.
Neutrophils < $2.0x10^9$/L	Withhold and discuss with a specialist. Bone marrow suppression can occur abruptly.
Platelets < $150x10^9$/L	Withhold and discuss with a specialist. Bone marrow suppression can occur abruptly.
Eosinophilia >0.5x 10^9/L	If eosinophilia unexplained, consider stopping treatment and contacting a specialist.
MCV > 105 -110 fl	Check folate, B12 and TFTs, and treat if appropriate. If WBC normal repeat in 4 weeks.
MCV > 110 fl	Stop methotrexate and seek advice.
Serum albumin less than 30g/L	If unexplained, consider stopping treatment and contacting a specialist.
AST and/or ALT >2xULN	Withold treatment and contacting a specialist. Persistent elevation and/or decrease in serum albumin (see above) may indicate severe hepatotoxicity
Renal impairment	An increase in creatinine of greater than 30% above baseline over 12 months – discuss with a specialist. If calculated GFR less than 60ml/min/1.73m^2 repeat in 1 week. If still more than 30% from baseline, withhold and discuss with specialist team.
Nausea and/or vomiting	Usually improves over time. If troublesome consider: - Continue folic acid 6 days a week. Omit on the day methotrexate is taken. - Split methotrexate dose over one evening and next morning - A short-term anti-emetic. Refer to local anti-emetic guidance.
Hair loss	Usually mild, rarely significant. Reversible on stopping methotrexate.
Rash	Withhold treatment and discuss with a specialist.
Mouth ulcers, mucositis	Mouth ulcers may respond to folic acid. If severe despite extra folic acid, stop methotrexate and refer to a specialist for advice.
Menstrual dysfunction/amenorrhoea	May occur during treatment and for a short while after cessation.
Otherwise, unexplained dyspnoea or cough	Methotrexate pneumonitis may occur. Withhold treatment, arrange chest CT (HRCT) and CXR and discuss urgently with consultant.
Abnormal bruising	Withhold until FBC result is available.

Sore throat or other unusual infection	Urgent FBC and withhold until FBC result is available. Susceptible to opportunistic infections such as viral wart, TB and pneumocystis.
Cervical dysplasia	Regular cervical smears.
Diarrhoea	Consider reducing dose.
Fever, chills	Withhold until FBC result is available.
Stomatitis	Withdraw treatment.

2.11 Drug interactions

- Methotrexate is partly metabolised in the liver.
- Methotrexate is extensively protein bound and may displace, or be displaced by other acidic drugs.
- Methotrexate and its metabolites are mainly excreted in urine by glomerular filtration and active tubular secretion (80- 90% unchanged).
- Excretion in faeces is minimal (10% or less).

The table below lists the most common interactions and is not exhaustive. The SmPC and other drug interactions resources should be consulted in addition to this list.

Drug	**Interaction**
NSAIDs	Increased risk of renal toxicity – avoid.
Alcohol	Should be avoided or reduced as much as possible.
Proton pump inhibitors e.g. omeprazole, lansoprazole.	PPIs may reduce high dose methotrexate elimination; consider temporarily stopping PPI. Consider H2 antagonist if needed.
Trimethoprim/Co-trimoxazole	Antifolate effect increased – avoid.
Penicillins	Reduce excretion of methotrexate (increased risk of toxicity).
Ciprofloxacin	Reduce excretion of methotrexate (increased risk of toxicity).
Other antibiotics: Doxycycline, sulphonamides and tetracycline.	Increased haematological toxicity.
Levetiracetam	Methotrexate concentration may possibly be increased.
Anti-convulsants: carbamazepine, phenobarbital, phenytoin, valproic acid and primidone.	Subtherapeutic anti-epileptic concentrations have been seen in the presence of cytotoxic regimens containing methotrexate. Avoid concurrent use. If this is not possible, antiepileptic concentrations should be closely monitored, making dose adjustments as necessary. Anti-convulsants appear to increase the clearance of methotrexate (although this is dose dependent and seen mainly in 24-hour infusions of MTX as SACT) however it may potentially be associated with lower methotrexate efficacy. Serum antiepileptic levels should be closely monitored during treatment, making dosage adjustments as necessary.
Theophylline	May reduce theophylline concentration.

Ciclosporin	Methotrexate may inhibit the clearance of ciclosporin or its metabolites. Ciclosporin may inhibit methotrexate elimination.
Probenecid	Excretion of methotrexate reduced.
Live vaccines	Increased risk of generalised infections – avoid.
Anaesthetics	Antifolate effect increased by nitrous oxide – avoid.
Retinoids	Methotrexate concentration increased by acitretin, also increased hepatotoxicity – avoid.
Leflunomide	Concurrent use might increase the risk of drug-induced toxicity (including blood dyscrasias, increased liver enzymes, and interstitial lung disease).
Anti-cancer medication	Effects of methotrexate antagonised by asparaginase, crisantaspase and pegasparagase –these medications should be given at least 24 hours after methotrexate; increased pulmonary toxicity with cisplatin.
Antimalarials	Antifolate effect enhanced by pyrimethamine.
Loop diuretics	Weak organic acids may potentially reduce the excretion of methotrexate
Oral contraceptives	Weak organic acids may potentially reduce the excretion of methotrexate

2.12 Advice to patients

- Methotrexate is taken once **WEEKLY** on the same day each week.
- If folic acid is also prescribed, advise patients NOT to take folic acid on the same day as methotrexate.
- Advise patients to take methotrexate with food if they experience nausea if it's currently being taken on an empty stomach.
- Advise patients on the frequency of monitoring e.g. blood tests every 1-2 weeks until told otherwise.
- Advise patients on missed doses
- Advise patients to avoid self-medication with over-the-counter NSAID's (e.g. aspirin or ibuprofen)
- Do not take vitamin and mineral supplements or any other products that contain folic acid (folate) if you're already taking folic acid prescribed by your doctor. Check the ingredients on the labels of any supplements.
- There's not enough information to say whether it's safe to take other herbal remedies or supplements together with methotrexate. They're not tested in the same way as pharmacy and prescription medicines. They're generally not tested for the effect they have on other medicines so it is usually best to avoid these for the duration of methotrexate treatment.

Advise patients to speak to their doctor, pharmacist or nurse if they experience:

- Nausea, upset stomach or diarrhoea
- Mouth ulcers, sore throat or sore mouth
- Infections
- Rashes
- Thinning of hair

- Photosensitivity

Advise patients to stop methotrexate and seek urgent medical advice if signs suggestive of:

- Blood disorders (e.g. severe sore throat, bruising, bleeding and severe
- mouth ulcers)
- Liver toxicity (e.g. nausea, vomiting, abdominal discomfort and dark urine,
- jaundice)
- Respiratory effects (e.g. shortness of breath)
- Severe and continuing diarrhoea or vomiting
- Pregnancy
- Chickenpox and shingles

3. Appendix 1 Example Patient Information Leaflet

What is Methotrexate?

Methotrexate is a type of medicine called an immunosuppressant. It is also sometimes called a disease modifying anti-rheumatic drug (DMARD). It slows down your body's immune system and helps reduce swelling (inflammation).

It's used to treat inflammatory conditions including immune related adverse events. It can also sometimes be used to treat other conditions, like cancer, but the dose used for cancer is usually much higher than when it's used to treat inflammatory conditions.

Methotrexate is available only on prescription.

How do I take Methotrexate?

Methotrexate comes as tablets and a liquid that you swallow, and pre-filled injection pens or syringes that you inject into your skin.

To treat immune related adverse events, you'll take methotrexate once a week. It's important to take it on the same day once a week. You'll be given a starting dose of methotrexate while your oncology team tries to bring your side effects under control, but this may be increased if it isn't helping your symptoms.

You'll get a patient card to record the details of your weekly dose and the day you take it. Keep this with you and show it to any healthcare staff involved in your care. You'll also usually get a booklet to record how much you take and your blood test results.

Swallow methotrexate tablets whole with a drink of water. You can take your tablets before or after food. Wash your hands after touching the tablets to remove any traces of methotrexate powder. Your oncology team will tell you how many tablets to take each time. You may have to take several tablets to make up your dose.

Methotrexate tablets come in two strengths: 2.5 mg and 10 mg. To avoid confusion, it's recommended that you only be given one strength, usually 2.5 mg. If you are prescribed both tablet strengths, be very careful not to confuse them, as they can look quite similar.

Always use the oral syringe that comes with your methotrexate liquid to measure your dose. It's important to use this syringe so that you get the right amount. If you do not have one, ask a pharmacist for one. Do not use a kitchen teaspoon as it will not measure the right amount.

It's a good idea to have a drink of water after taking your medicine.

If you are having methotrexate injections, you'll usually go to your GP surgery or a hospital outpatient clinic once a week to have your injection. Alternatively, you may get a pre-filled injection pen or syringe for you to use at home. Your nurse will show you how to use this.

If you forget to take a dose, take it as soon as you remember the next day or the day after. If your dose is more than 2 days late, contact your oncology team for advice about what to do. Never take 2 doses together to make up for a missed dose.

You must always wash your hands before and after handling methotrexate.

You may be prescribed folic acid tablets (one of the B vitamins) while you're taking methotrexate. Folic acid helps protect the healthy cells in your body and reduces some of the side effects of methotrexate. It can make you less likely to be sick (vomit) or get diarrhoea. Your oncology team will usually start you on one 5mg folic acid tablet, taken once a week. Take it the day after your methotrexate; do not take it the same day as your methotrexate. If you're still bothered by side effects, your doctor may increase the dose of folic acid. You may need to take 1 tablet 6 times a week, starting the day after you take your methotrexate.

It is important to not take folic acid on the same day as your methotrexate. It can stop your methotrexate from working properly.

Drug monitoring

Before starting treatment, you may have a chest x-ray and breathing tests to check your lung function. Depending on your general health, your oncology team may want to run some other tests to make sure you can take methotrexate.

When you first start treatment, you'll have a check-up and blood tests to check your blood, liver and kidneys every 1 to 2 weeks.

These tests are to check if the methotrexate is working and if it's causing any side effects.

Your doctor may increase or decrease your methotrexate dose, depending on the results of your tests.

It's important to record how much methotrexate you take and the results of your blood tests. You'll usually get a booklet for this.

Once you and your oncology team have found the right dose and your treatment is working well, you'll have a check-up and blood tests every 2 to 3 months.

Your oncology team will monitor you very closely and any concerns or problems will be found during routine check-ups.

How long will I need to take Methotrexate for?

If methotrexate works for you, you may need to take it for several years to control your symptoms. Your oncology team will review you to decide when methotrexate can be stopped.

Does Methotrexate have any side-effects?

There are several possible side effects that you may notice, although many people do not experience any of these.

Side effects include:

- Loss of appetite
- Feeling or being sick

- Stomach pain or indigestion
- Diarrhoea
- Headaches
- Feeling tired or drowsy
- Minor hair loss and hair thinning
- Skin that is more sensitive to sunlight (photosensitivity)
- Mouth ulcers, skin rashes
- Fever, signs of infection, bruising, bleeding
- Shortness of breath

Serious side effects are rare and happen in less than 1 in 10,000 people. It is important to tell your oncology team of any side effects or unusual symptoms that you are experiencing.

Your skin may become very sensitive to sunlight while you're taking methotrexate. This can cause a reaction that looks and feels like sunburn. To reduce the chance of this side effect, stay out of bright sun, use a high factor sunscreen (SPF 30 or above) and wear clothes that protect you from the sun, even on a cloudy day. Do not use a sun lamp or sun beds.
Tell your oncology team or call 111 immediately if you get:

- yellowing of the whites of your eyes, or yellowing of your skin (although this may be less obvious on brown or black skin) – these may be signs of liver problems
- a persistent cough, chest pain, difficulty breathing, or you become breathless – these may be signs of inflammation of your lungs
- swollen hands, ankles or feet, changes to how often you pee or not peeing at all – these may be signs of kidney problems
- a high temperature, chills, muscle aches, sore throat – these may be signs of an infection
- bleeding gums, blood in your pee, vomiting blood or unexplained bruising – these may be signs of a blood disorder

Can I still be vaccinated?

It's important to have any vaccinations that you're invited for. Tell the person giving the vaccine that you take methotrexate, as some types of vaccine may not be suitable for you. You may need to avoid live vaccines.

Other treatments that affect your immune system, such as steroids, may prevent you from having vaccines. Check with your oncology team if you're unsure.

The pneumonia vaccine and yearly flu vaccines, usually given to adults, are not live vaccines and don't affect methotrexate, so it's recommended that you have these.

People who live with you can reduce the risk of passing on an infection by also having vaccinations.

Methotrexate may lower the number of white cells in your blood. This can make you more likely to get an infection.

It's important to reduce your risk of getting an infection. When possible, avoid close contact with people who you know are unwell.

Tell your oncology team if you think you're getting a sore throat, if you have a high temperature or if you have symptoms or test positive for coronavirus (COVID-19).

You should also contact your oncology team urgently if you develop chickenpox or shingles, or come into contact with someone who has chickenpox or shingles. These infections can sometimes be very serious in people who are taking methotrexate. You might need treatment against chickenpox or shingles, and you might be told to stop taking methotrexate until you're better.

Is it safe to become pregnant while I am taking Methotrexate?

You may have already had these conversations with your oncology team before starting immunotherapy. It is important that you do not plan a pregnancy if you are on methotrexate and should use effective contraception if sexually active.

Methotrexate is not recommended in pregnancy, as it can cause birth defects.

If you're taking methotrexate and want to get pregnant, speak to your oncology team. They'll discuss whether you need to switch to a different medicine before stopping your contraception.

If you become pregnant while taking methotrexate, do not stop taking your medicine but speak to your oncology team as soon as possible. They'll review your treatment and help you decide what to do next.

Your oncology team will only prescribe methotrexate for you while you're pregnant if the benefits of the medicine outweigh the chances of it being harmful.

Can I take other medicines whilst I am taking Methotrexate?

You should always check with your oncology team or pharmacist if you are started on any new medicines, including anything you may buy over the counter. You can usually carry on taking painkillers like paracetamol if needed, unless your oncology team advises otherwise.

Tell your oncology team or pharmacist if you're taking any of these medicines before you start taking methotrexate:

- non-steroidal anti-inflammatory drugs (NSAIDs) like ibuprofen, or cough and cold remedies containing NSAIDs
- co-trimoxazole, trimethoprim or other antibiotics for bacterial infections
- medicines that make you pee more (diuretics), such as indapamide or bendroflumethiazide
- epilepsy medicines such as phenytoin or levetiracetam
- theophylline, a medicine used to treat asthma
- medicines used to treat indigestion, known as proton pump inhibitors (PPI), such as omeprazole
- folic acid or vitamin supplements that contain folic acid (or folate) – this is because your oncology team may prescribe folic acid to take with your methotrexate

These are not all the medicines that may affect methotrexate. Check the leaflet that comes with your medicine.

There are no specific foods that you need to avoid while taking methotrexate. However, methotrexate may reduce your ability to fight infection, so it's best to avoid unpasteurised milk and soft cheeses.

It's also best to avoid having too much caffeine, contained in coffee, tea, cola, energy drinks and chocolate. This is because caffeine can stop methotrexate from working as well as it should.

Alcohol and methotrexate can both affect your liver, so it's important you don't drink more alcohol than the government's recommended limits. The government guidelines say both men and women should have no

more than 14 units of alcohol a week, and that you should spread these through the week rather than having them all in one go.

Supply of Methotrexate

You must not stop taking methotrexate unless advised to do so by your oncology team. It will be prescribed from the hospital, and it is important you make sure you don’t run out of methotrexate.

Once the dose is right and your condition is stable, the oncology team in the hospital may ask your GP to continue your treatment. Your GP will also decide where you'll go for blood tests and how often.

Once this is agreed, and if your blood results are OK, your GP will usually give you 1 month's supply of methotrexate at a time (or 4 doses).

Who can I contact for further information?

If you have any queries about your methotrexate the best people to speak to are the oncology team who you are under, team of specialists who have prescribed the methotrexate for you or an oncology pharmacist.

4. References

- British National Formulary, 2024. Methotrexate. Accessed online: **Methotrexate | Drugs | BNF | NICE**
- Dobsen, L. 2019. THE CLATTERBRIDGE CANCER CENTRE NHS FOUNDATION TRUST. PHARMACY TREATMENT PROTOCOL Oral Methotrexate for Use in Immune Mediated Conditions. Accessed Online: Oral_Methotrexate_for_Use_in_Immune_Mediated_Conditions_Protocol_V1.0.docx.pdf
- Electronic Medicines Compendium, 2023. Methotrexate 2.5 mg Tablets. *Advanz Pharma*. Accessed online: Methotrexate 2.5 mg Tablets - Summary of Product Characteristics (SmPC) - (emc)
- Epps, S. 2023. A Clinical Handbook of Adult Immunosuppressive Therapy for Ocular Inflammatory Disease. UHBW Clinical Guideline. Accessed via trust intranet.
- H. Taylor, 2021. UHBW guidance Clinical Guideline. IMMUNE MEDIATED TOXICITY OF IMMUNE CHECKPOINT INHIBITORS. Accessed via trust intranet.
- Haanen, J. et al, 2022. Management of toxicities from immunotherapy: ESMO Clinical Practice Guideline for diagnosis, treatment and follow-up. ESMO Management of toxicities from immunotherapy: ESMO Clinical Practice. Management of toxicities from immunotherapy: ESMO Clinical Practice Guideline for diagnosis, treatment and follow-up☆ - Annals of Oncology
- Krens S et al, 2019. Dose recommendations for anticancer drugs in patients with renal or hepatic impairment. Lancet Oncol 2019;20: e201–08.
- Methotrexate monitoring, 2024. Specialist Pharmacist Service. Accessed online: Methotrexate monitoring – SPS - Specialist Pharmacy Service – The first stop for professional medicines advice
- NHS, 2023. Taking methotrexate with other medicines and herbal supplements. Accessed online: **Taking methotrexate with other medicines and herbal supplements - NHS**
- Pan Mersey Area Prescribing Committee, 2021. METHOTREXATE: safe prescribing and dispensing. Accessed online: METHOTREXATE: safe prescribing and dispensing
- Renal Drug Database. Accessed online: https://www.renaldrugdatabase.com/s/
- Schneider, B. et al, 2021. Management of Immune-Related Adverse Events in Patients Treated with Immune Checkpoint Inhibitor Therapy: ASCO Guideline Update. ASCO J Clin Oncol 39:4073-4126. 2021 by American Society of Clinical Oncology. Accessed online: Management of Immune-Related Adverse Events in Patients Treated With Immune Checkpoint Inhibitor Therapy: ASCO Guideline Update | Journal of Clinical Oncology.

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6. Document control

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Authors / Editors version 1.0	Sarah Freeburn – Lead Immunotherapy Pharmacist. University Hospitals Bristol and Weston. Kavita Kantilal – Consultant Pharmacist, University Hospitals Sussex NHS Foundation Trust. Bethan Mortley, Advanced Cancer Pharmacist, Swansea Bay University Health board		
Owner	BOPA.		
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