Wales Centre for Pharmacy Professional Education
Canolfan Addysg Fferylliaeth Broffesiynol Cymru

METHOTREXATE (LOW DOSE)

Top tips for MURs

- Check that patient understands the purpose of the medication
- Check that patient has had a full blood count, renal and liver function test within last 2 to 3 months (within last 2 weeks if dose has been changed (even if patient has been on methotrexate for a while) or if therapy not yet stabilised))*
- Check patient has a methotrexate record booklet & check that any dosage alterations have been annotated in the patient's record booklet by the prescriber making that change
- Ensure that only one strength of methotrexate tablet is supplied to patient (record on PMR - 2.5mg tablets)
- Patients should be reminded of the need to check the dose and strength of the tablets with each prescription
- Ensure that methotrexate tablets are taken once a week, on the same day each week. They should be swallowed whole, after food (Dose range 7.5mg – 25mg weekly). Lower doses often used in frail elderly patients due to poor renal function.
- Counsel patient on signs / symptoms that need referral (see red flags overleaf) and common side effects (**see overleaf**)
- Counsel female patients on importance of effective contraception during treatment and for three months after stopping (as teratogenic)
- Check that patient is also taking folic acid and counsel on how to take this correctly
- Counsel patient that if they vomit within a few hours of taking methotrexate not to take another dose
- Advise patient to avoid OTC preparations containing NSAIDS / aspirin as additional NSAIDs can increase methotrexate levels. Please note that prescribed NSAIDs are often used intentionally in rheumatology until the methotrexate effect is established and low dose aspirin for cardiovascular indications, which should be continued as prescribed
- Advise patient that beneficial effect from methotrexate may not occur for up to six - twelve weeks after initiation (reassure patient it is working in this period) and may take as long as 6 months for them to see the full effect.
- Patients on Methotrexate should be advised that annual flu vaccination is recommended, they must not receive immunisation with any live vaccines
- Advise patients who are to receive the Zostavax vaccination, to consult the specialist team in advance
- Check that patients taking methotrexate for rheumatic disease can open the bottle /pop the tablet out of blister pack
- Report any relevant adverse drug reactions to the Yellow Card Scheme

* The exact monitoring schedule depends on the combination of DMARDs and is guided by the local shared care protocol in place for every Health Board

What is methotrexate used for?

Methotrexate is licensed for use in the treatment of rheumatic diseases, severe psoriasis, bowel disorders and to treat cancer (high doses only).

How does methotrexate work?

Methotrexate works by slowing the production of new cells by the immune system, which causes a reduction in inflammation, therefore reducing swelling, joint stiffness, skin thickening and bowel damage. It reduces the permanent damage to joints caused by continuing inflammation.[1] It is *not* a pain killer.

Potential drug interactions? – See BNF Appendix 1: Interactions

- The plasma concentration of methotrexate may be increased by some antibacterials, ciclosporin, leflunomide, probenacid, retinoids and NSAIDs which may result in toxicity – more frequent monitoring may be needed if using these combinations
- An increased risk of haematological toxicity (marrow aplasia) with concomitant use of co-trimoxazole / trimethoprim due to increased anti-folate effect of methotrexate.
- The antifolate effect of methotrexate is increased by concomitant use of antimalarials and phenytoin (Note: methotrexate and hydroxychloroquine combination commonly used by rheumatology teams)

Lifestyle issues:

- Counsel patient on ensuring their alcohol intake is well within recommend limits (up to 14 units a week, spread evenly over 3 more days, with several alcohol free days) - dermatologists suggest their patients stay well within a lower limit of 4 – 6 units per week.
- Counsel patient on healthy eating, exercise & weight loss (if BMI > 25kg/m^2) – advise patients to complete 30 minutes of aerobic exercise three to five times a week, reduce caffeine intake to no more than 5 cups a day and recommend 5 portions of fruit and vegetables a day
- Advise patients who smoke the benefits of stopping smoking and how to access pharmacy smoking cessation services or Stop Smoking Wales

Compiled: D Roberts, WCPPE, November 2011
Expert review: Sarah Gage, C & V HB, December 2011
Updated: Melissa Siew, Cwm Taf UHB, February 2017

Wales Centre for Pharmacy Professional Education
Canolfan Addysg Fferylliaeth Broffesiynol Cymru

Red flags that need referral

- Severe sickness or diarrhoea for more than a few days as may need to consider increasing folate dose or switching to S/C route. In severe cases treatment may need to be stopped altogether
- Signs of liver toxicity or blood dyscrasias
    - Regularly catching infections
    - Severe sore throats
    - Whites of eyes becoming yellow
    - Dark urine
    - Bruising or bleeding easily
- Severe itching or rash
- Signs of pulmonary toxicity
    - Shortness of breath (when resting & no signs of chest infection)
    - Cough
    - Fever
- Pregnancy, as risk of teratogenicity
- Breastfeeding as present in milk and a risk of toxicity in the infant
- Close contact with someone with chickenpox or shingles if you have never had these infections

What are the common side effects to look out for?

Side effect	Advice
Gastro-intestinal disturbances particularly at initiation of therapy	Advise patient that GI symptoms normally settles after a few weeks, if persistent refer to prescriber for anti-emetic therapy, dose adjustment or for alteration to an alternative route, e.g. subcutaneous route. Patients who feel sick/GI disturbance with methotrexate most commonly suffer with these symptoms on the day they take the methotrexate or the day immediately afterwards. Taking folic acid reduces these effects and should preferably be taken the day after the methotrexate. Increasing the dose of folate also helps if symtoms persist. Some patient find taking folic acid every day (except the day they take methotrexate) alleviates these symptoms enabling them to continue treatment with this drug.
Thinning or hair loss	This is quite rare as low doses used (always reassure the patient that it is generally only associated with high dose treatment). Advise patient that usually slight and returns to normal on stopping treatment.
Mouth ulcers & sore throats	Advise patient to rinse mouth frequently & brush teeth two to three times a day with a soft brush – patients who suffer with mouth ulcers on MTX usually suffered with them before and good oral hygiene (mouthwashes etc.) help. Advise patient that most ulcers will heal within a few days but It is important that patients know to seek an urgent blood test if they have persistent or worsening mouth ulceration or a severe sore throat as often a good indicator that the immune system isn't coping as well as it normally would.
Infections; Rash / itching	Refer to prescriber if persistent and troublesome.

Where can you find more information?

- NPSA has issued a safety alert for safer methotrexate therapy and can be found on the NPSA website (**http://www.nrls.npsa.nhs.uk/resources/type/alerts/?entryid45=59800&p=4**)
- Methotrexate – BNF sub-section 10.1.3 Drugs that suppress the rheumatic disease process
- Musculoskeletal disorders (level 1 & 2) distance learning packs can be found on WCPPE website (**http://www.wcppe.org.uk**)
- NICE guidance on management of rheumatoid arthritis that can be found on NICE website (**http://www.nice.org.uk**)
- Arthritis research UK can be found on arthritis research website (**www.arthritisresearchuk.org**)

References

1. NPSA Oral methotrexate patient information leaflet & dosage record booklet

Compiled: D Roberts, WCPPE, November 2011
Expert review: Sarah Gage, C & V HB, December 2011
Updated: Melissa Siew, Cwm Taf UHB, February 2017