Methotrexate busting the myths

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Outreach Service Longreach

President Australian Rheumatology Association (ARA)

Conflict of interest – none relating to today's presentation

- Outreach Clinics
  - Check up QLD
  - ARA
- National Prescribing Service
- Pharmaceutical companies
  - ARA monthly meetings sponsored by industry

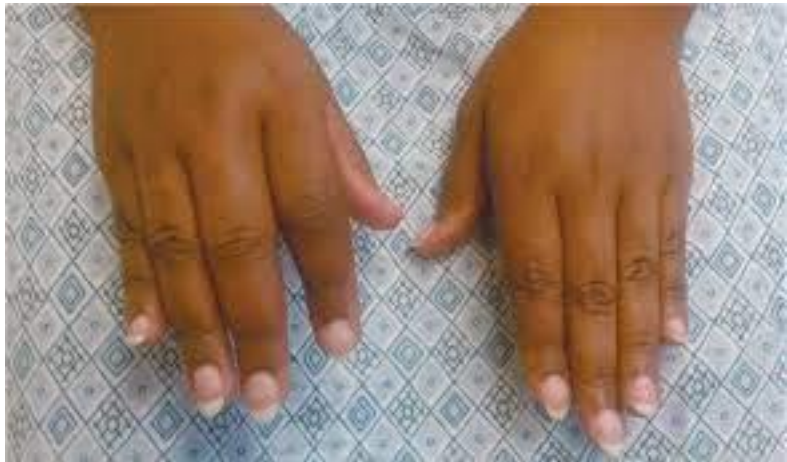
Methotrexate – busting myths what you need to know

- What is it?
- What do we use it for?
- How does it work?
- How do we use it?
- What are the possible adverse effects?
- How can you mitigate them?
- Myth busters

Case study

35 female
3 months postnatal
2 months swollen tender feet and hands
Tried OTC NSAIDs
GP appt
Ex tender swollen MCP and MTP joints

- Investigations
  - RF 300
  - CCP > 350
  - ESR 50
  - CRP 37
  - ELFT/FBC normal



American College of Rheumatology
Empowering Rheumatology Professionals

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Case study

- "Barn door RA"
- Needs Disease Modifying Antirheumatic Drug (DMARD)
  - **Methotrexate**

Australian Living Guidelines

Consider using methotrexate in combination with other DMARDs as initial therapy in people with rheumatoid arthritis

2021 American College of Rheumatology Guideline for the Treatment of Rheumatoid Arthritis

Methotrexate is strongly recommended over hydroxychloroquine or sulfasalazine for DMARD-naive patients with moderate-to-high disease activity

Recommendation

EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2019 update

	Recommendations			
1.	Therapy with DMARDs should be started as soon as the diagnosis of RA is made.	1a	A	9.8
2.	Treatment should be aimed at reaching a target of sustained remission or low disease activity in every patient.*	1a	A	9.7
3.	Monitoring should be frequent in active disease (every 1–3 months); if there is no improvement by at most 3 months after the start of treatment or the target has not been reached by 6 months, therapy should be adjusted.	2b	B	9.3
4.	MTX should be part of the first treatment strategy.	1a	A	9.4
5.	In patients with a contraindication to MTX (or early intolerance), leflunomide or sulfasalazine should be considered as part of the (first) treatment strategy.	1a	A	9.0
6.	Short-term glucocorticoids should be considered when initiating or changing csDMARDs, in different dose regimens and routes of administration, but should be tapered as rapidly as clinically feasible.	1a	A	8.9
7.	If the treatment target is not achieved with the first csDMARD strategy, in the absence of poor prognostic factors*, other csDMARDs should be considered.	5	D	8.4
8.	If the treatment target is not achieved with the first csDMARD strategy, when and poor prognostic factors* are present, a bDMARD† or a tsDMARD‡ should be added.	1a	A	9.3
9.	bDMARDs and tsDMARDs should be combined with a csDMARD; in patients who cannot use csDMARDs as comedication, IL-6 pathway inhibitors and tsDMARDs may have some advantages compared with other bDMARDs.	1a	A	8.9
10.	If a bDMARD[#] or tsDMARD[##] has failed, treatment with another bDMARD† or a tsDMARD‡ should be considered; if one TNF inhibitor therapy has failed, patients may receive an agent with another mode of action or a second TNF inhibitor.	[#]1b [##]5	A D	8.9
11.	If a patient is in persistent remission after having tapered glucocorticoids, one can consider tapering bDMARDs or tsDMARDs, especially if this treatment is combined with a csDMARD.	1b	A	9.2

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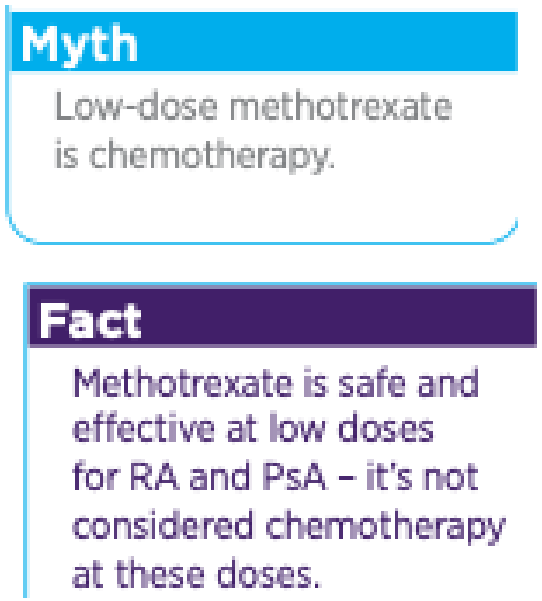
Myth – Low dose methotrexate is chemotherapy



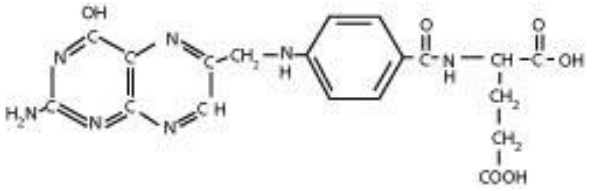
In my hands, Methotrexate is NOT chemotherapy

- MTX chemotherapy is much higher doses
  - But still "reputation"
  - A little knowledge is dangerous
- Friends, family members, well-wishing community members, health professionals scaremonger through ignorance of current best evidence
- In autoimmune disease MTX is much lower doses
  - "homeopathy"
  - once weekly

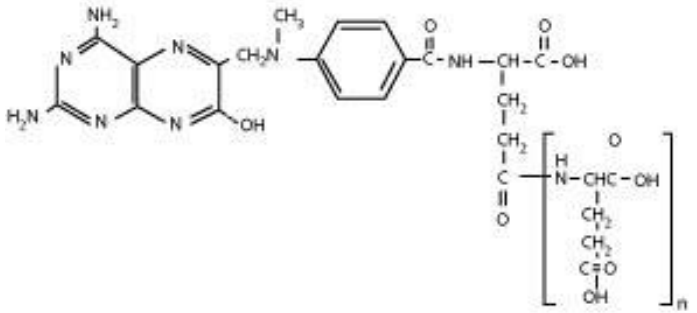
MTX
What is it?

- High doses
  - folic acid antagonist
  - antimetabolite cytotoxic drug
- Low doses
  - Disease Modifying Anti-Rheumatic Drug
    - DMARD
  - steroid-sparing agent
  - immunomodulator/immunosuppressive

Dihydrofolic Acid



Methotrexate



MTX
What is it?

- Most common DMARD
- Been used for RA for 40 yrs
  - 1985 1st systematic report on use of low dose in RA
  - 1988 FDA approved
- In all treatment guidelines

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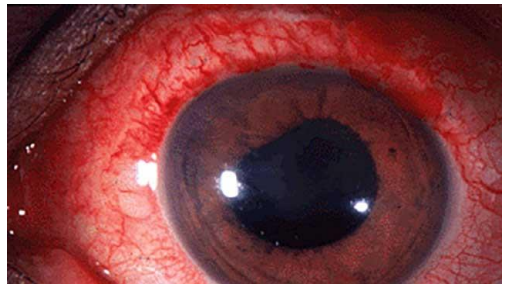
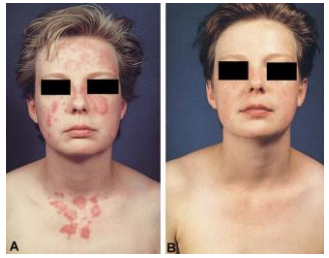
Methotrexate- MTX
What do we use it for ?

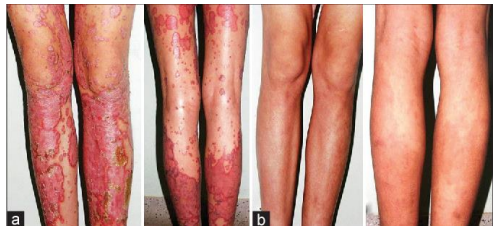


- Inflammatory arthritis
  - Rheumatoid Arthritis
  - Psoriatic Arthritis
  - Juvenile Idiopathic Arthritis (JIA)
  - Spondylarthritis
- Connective Tissue Diseases
  - Systemic Lupus Erythematosus
  - Other CTD eg scleroderma



- Vasculitis
- Myositis
- PMR

- Inflammatory eye disease
  - scleritis, either idiopathic or in RA, vasculitis or CTD
  - commonest indication children with persistent sight-threatening uveitis
- Severe psoriasis



- Neurological disease
  - myasthenia gravis, inflammatory myopathies and neuropathies, vasculitis, other immune-mediated central & peripheral nervous system diseases
- Inflammatory Bowel Disease
- Respiratory disease
  - Interstitial lung diseases, sarcoidosis, pulmonary vasculitis

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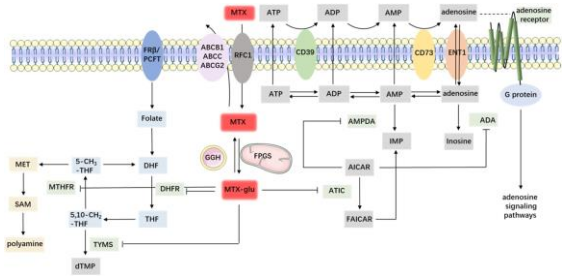
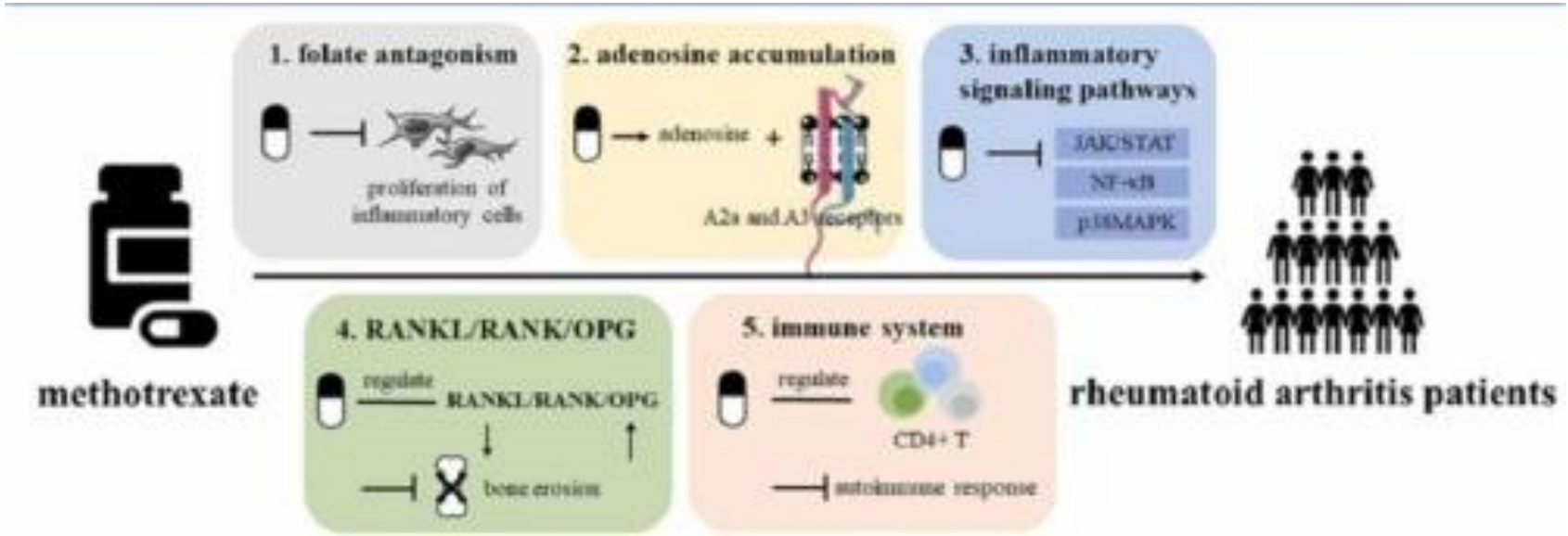
Methotrexate- MTX
How does it work ?

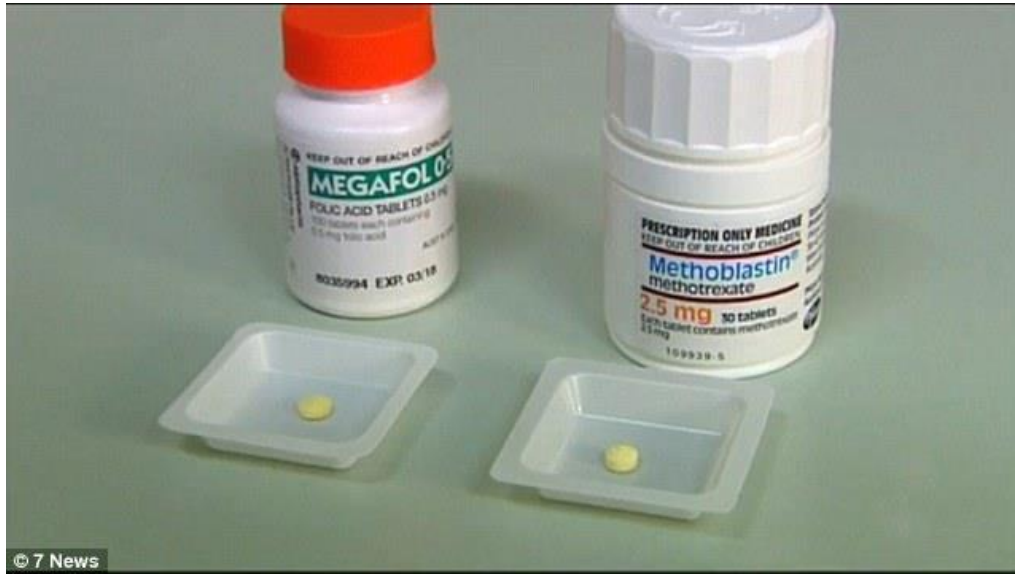
- folate antagonism
- adenosine accumulation
- inflammatory signalling
  - NF-κB
  - JAK/STAT
  - p38MAPK

- regulates balance of RANKL/RANK/OPG
- regulates CD4 + Th1/Th2, Th17/Treg & CD73





Low dose once weekly MTX is NOT cytotoxic



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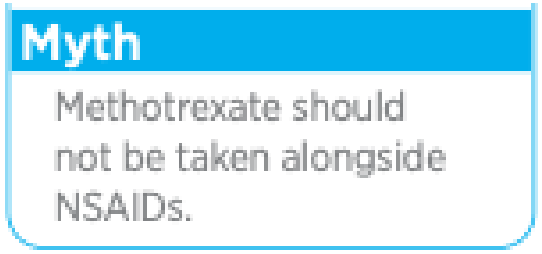
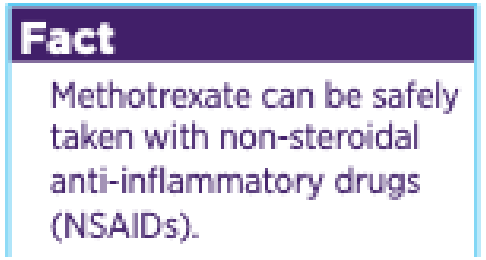
Methotrexate- MTX
How do we use it?

- We use it a lot
- Low dose
- Once weekly
- Oral
- SC

- Dose 10-30mg once a week

Myth –NSAIDs should not be taken with MTX





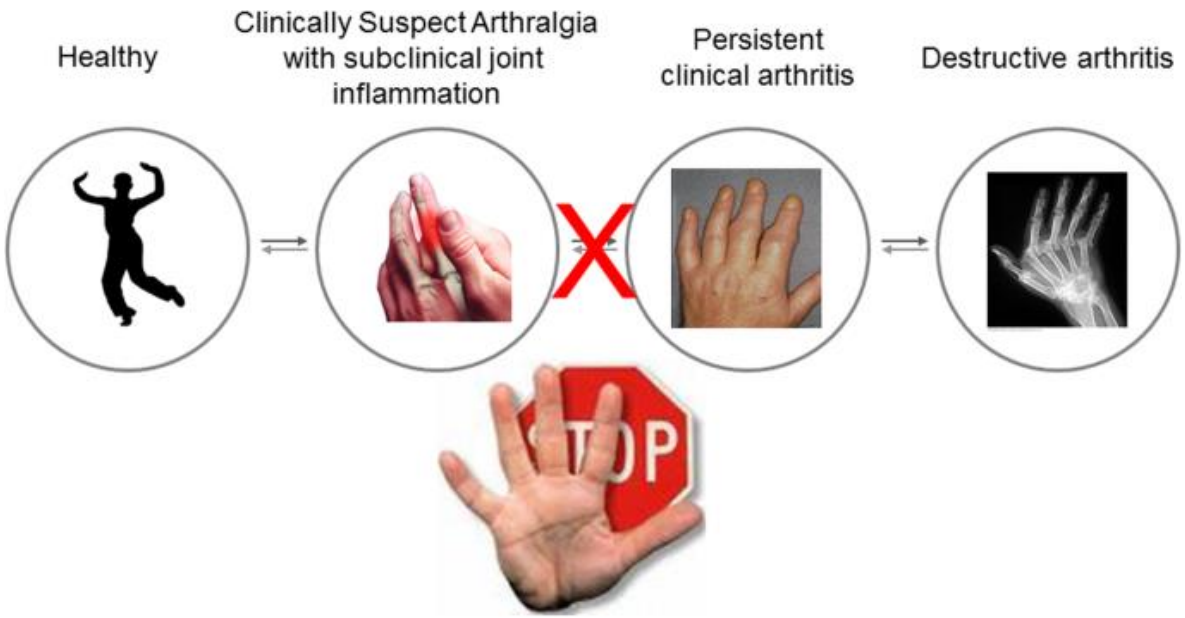
- **Can other medication be taken with methotrexate?**
  Methotrexate is often taken in combination with other arthritis medicines, including:
  - other DMARDs
  - biological DMARDs
  - steroid medicines such as prednisolone or cortisone injections into the joint
  - **anti-inflammatory medicines (NSAIDs) such as naproxen (Naprosyn) or ibuprofen (Brufen/Nurofen)**
  - simple pain medicines such as paracetamol

MTX – how do we use it safely?

- Needs monitoring
  - **FBC, E/LFT, ESR/CRP**
- Monthly until MTX dose stable for 3 months & no other relevant changes (e.g impaired renal function)
- Then **minimum 3 monthly**
- If **co-prescribed leflunomide minimum interval 2 monthly**
  - increased potential toxicity
- **Do not check MTX levels**
- Annual CV risk review, including lipids

Methotrexate- MTX
Why do we use it?

- Because it works



- Early stage & adequate doses remission 40%
  - highest rate of continued long-term treatment
  - maintains efficacy without excessive toxicity
  - generally well-tolerated

Methotrexate- MTX
Why do we use it?

- Convenient once a week
- Inexpensive
  - $52.46 for 50 x 10mg ($42.50)
  - $24.24 for 15 x 10mg ($40.09)
  - $17.97 for 30 x 2.5mg ($23.82)
  - $39.56 for 5 x 50mg/2ml ($42.50)
  - $89.54 for prefilled syringes ($42.50)

Methotrexate- MTX
Why do we use it?

- Oral or SC
- SC better bioavailability
- Doses > 20 mg

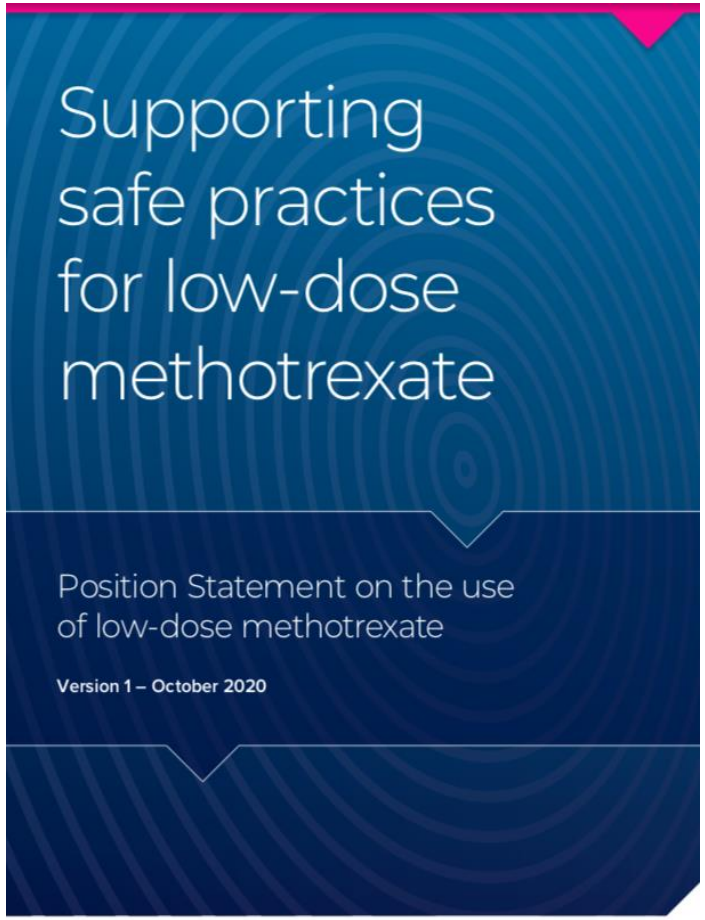
Myth –self administration of MTX injections is unsafe

Myth

Self-administration of methotrexate injections is unsafe.

Fact

Methotrexate injections can be safely self-administered.



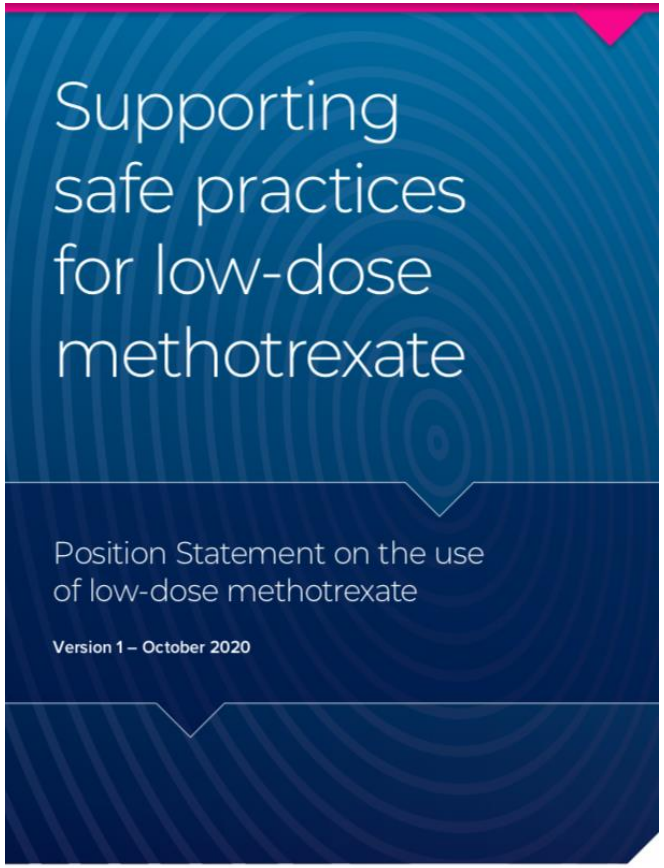
MTX- how to write the script

- “20 mg once a week on Monday”
- If injections say “20 mg once a week on Monday instead of MTX tablets”
- Co-prescribe Folic Acid
- Can get over the counter but 2 strengths
  - 0.5 mg & 5 mg

MTX- how to write the script

- Careful with the number of repeats
- Computers generate repeats
  - 10mg x 50 tablets =2
    - ie you are giving the patient access to 60 weeks at a dose of 25 mg/week without any need to be compliant with monitoring
  - 10mg x 15 tablets = 3
    - ie you are giving the patient access to 30 weeks at a dose of 20 mg/week
  - 2.5 mg x 30 tablets =5
    - ie you are giving the patient access to 60 weeks at a dose of 7.5 mg/week

Myth –those on low-dose MTX need to use special precautions when disposing of bodily fluids



- Precautions recommended for people receiving antineoplastic doses of MTX **are not necessary in those receiving low-dose MTX**
- *Therapeutic Guidelines: Rheumatology* **: 'at doses typically used in rheumatology, there is no risk of toxicity to close contacts of patients taking methotrexate and special precautions in handling bodily fluids are not required'.**

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Possible ADVERSE EFFECTS

Nuisance

- GIT -10-40 % F 2x> M
  - nausea (30%) vomiting, diarrhoea
- headache 5-19%
- hair loss 3-10%
- skin dryness, rashes, photosensitivity
- fatigue, mental clouding
- dizziness, tinnitus

Nasty

- Liver
  - 17% slight
  - 0.9% 3 xULN
- Haematology
- Lung <1%
  - Early
  - NOT LATE

Managing abnormal tests: Liver function

- ALT/AST levels >2x upper limit of normal but <3x
  - reduce dose 50%, repeat in 1 month
  - once normalized reintroduce MTX monthly monitoring until dose stable 3 months
- ALT/AST >3x ULN
  - withhold MTX, continue folic acid, contact rheumatologist/registrar
  - check compliance/dose of folic acid
  - reinstitute at lower dose following normalisation
- Consider screening for other causes if ALT/AST >3x ULN 4 weeks after discontinuation

Managing abnormal tests: Renal Function

- eGFR 20-40 max. dose MTX 10mg/wk
- eGFR <20 **STOP** MTX

Managing abnormal tests: Haematology

- Hb < 20 g/l below baseline, WBC <2 , neuts <0.5, platelets <50
  - withhold MTX
  - continue folic acid
  - discuss with rheumatologist/registrar
- less severe abnormalities
  - check folic acid compliance
  - consider increasing folic acid
  - reduce MTX dose by 50% and repeat tests in 2 weeks
- myelosuppression
  - more common at start
  - can occur any time during treatment – hence need for monitoring
- risk factors >70 yrs, low albumin, folate deficiency, renal impairment

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How can you mitigate risk of adverse effects?

- Check the patient has monitoring
- Take time to consider the number of repeats you are writing
- Only patients taking >20mg/week eligible for 50-tablet packs – carefully consider safety before prescribing

How can you mitigate risk of adverse effects?

- Review **vaccination status**
- COVID, pneumococcal and yearly flu vaccinations recommended
  - Patients on MTX receiving a first flu vaccine should probably get 2 doses, 4 weeks apart
- Live vaccines (e.g. varicella) not contraindicated with low dose MTX (<0.4mg/kg/wk.)
- **Biological and targeted synthetic DMARDs are a contraindication to live vaccines**

Mandatory co-prescription of Folic Acid

- Minimum 5mg a week
  - Maximum 3 x dose MTX (Therapeutic Guidelines 2017)
- ?Not the same time as MTX
- 400 rheumatologist = 400 regimes

To improve tolerance consider

- Dose reduction/splitting
- Increasing Folic Acid
- Changing to Folinic Acid
  - 15 mg once weekly 8-12 hours post MTX
- Taking with food
- Taking at night
- Stopping caffeine
- Stopping alcohol

Special Considerations

- Pregnancy
- Breastfeeding
- Chronic liver disease
- COPD
- Renal Disease
- Cytopaenias
- Immunodeficiency
- Infection
- Surgery

MTX myths- you can’t get pregnant on low dose MTX

- You can
  - But we don’t want that to happen
- Ensure contraception
- In case of accidental pregnancy
  - stop MTX
  - start folic acid 5mg daily
  - contact rheumatologist/registrar

Special Considerations

- Pregnancy
- Breastfeeding
- Chronic liver disease
- COPD
- Renal Disease
- Cytopaenias
- Immunodeficiency
- Infection
- Surgery

MTX myths- you can’t drink alcohol

- 2017 study
  - risk of liver damage in patients with RA taking MTX increases with high alcohol consumption
  - risk in those consuming 14 units or less per week is no greater than those who do not drink

Special Considerations

- Pregnancy
- Breastfeeding
- Chronic liver disease
- COPD
- Renal Disease
- Cytopaenias
- Immunodeficiency
- Infection
- Surgery

Therapeutic Guidelines

methotrexate

Before starting therapy:

- follow the recommendations in considerations before starting immunomodulatory therapy
- **assess the patient's alcohol intake**

Throughout therapy :

- implement the recommendations in considerations throughout immunomodulatory therapy
- **promptly investigate patients reporting new or worsening pulmonary symptoms**

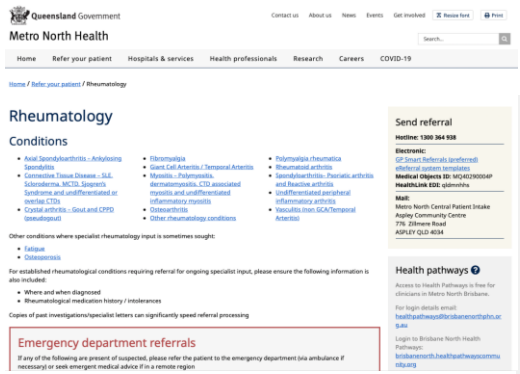
Other considerations:

- methotrexate is **given weekly rather than daily**, and serious toxicity can occur if taken more frequently. The **clinician and patient should agree** on which day of the week the patient will take their methotrexate and this should be specified on the prescription
- **folic acid and/or calcium folinate supplementation decreases the risk of adverse effects**, including gastrointestinal adverse effects, liver transaminitis and mouth ulcers. It should not be taken on the same day as the weekly methotrexate dose
- **adverse effects can be limited** by administering the methotrexate dose at night, splitting the weekly dose over 2 consecutive days (usually 12 hours apart) or administering the dose subcutaneously
- **leflunomide and methotrexate have synergistic bone marrow, liver and pulmonary toxicity**
- **at the doses typically used in rheumatology, there is no risk of toxicity to close contacts of patients taking methotrexate and special precautions in handling bodily fluids are not required**

Why bother to encourage MTX use

- It works – it prolongs life
- It is safe
- It is effective
- It is required for access to some other treatments on the PBS

Methotrexate- MTX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Rheumatology

Conditions

- Axial Spondyloarthritis – Ankylosing Spondylitis
- Connective Tissue Disease – SLE, Scleroderma, MCTD, Sjogren's Syndrome and undifferentiated or overlap CTDs
- Crystal arthritis – Gout and CPPD (pseudogout)
- Fibromyalgia
- Giant Cell Arteritis / Temporal Arteritis
- Myositis – Polymyositis, dermatomyositis, CTD associated myositis and undifferentiated inflammatory myositis
- Osteoarthritis
- Other rheumatology conditions
- Polymyalgia rheumatica
- Rheumatoid arthritis
- Spondyloarthritis- Psoriatic arthritis and Reactive arthritis
- Undifferentiated peripheral inflammatory arthritis
- Vasculitis (non GCA/Temporal Arteritis)

Other conditions where specialist rheumatology input is sometimes sought:

- Fatigue
- Osteoporosis

For established rheumatological conditions requiring referral for ongoing specialist input, please ensure the following information is also included:

- Where and when diagnosed
- Rheumatological medication history / intolerances

Copies of past investigations/specialist letters can significantly speed referral processing

Emergency department referrals

If any of the following are present of suspected, please refer the patient to the emergency department (via ambulance if necessary) or seek emergent medical advice if in a remote region

Send referral

Hotline: 1300 364 938

Electronic:
GP Smart Referrals (preferred)
eReferral system templates
Medical Objects ID: MQ4029000I4P
HealthLink EDI: qldmnhhs

Mail:
Metro North Central Patient Intake
Aspley Community Centre
77b Zillmere Road
ASPLEY QLD 4034

Health pathways

Access to Health Pathways is free for clinicians in Metro North Brisbane.

For login details email: healthpathways@brisbanenorthphn.org.au

Login to Brisbane North Health Pathways: brisbanenorth.healthpathwayscommunity.org

Resources

Guideline for the Management of Knee and Hip Osteoarthritis Second Edition (PDF)

Specialists list

Osteoarthritis of the Knee Clinical Care Standard

General referral criteria

Methotrexate

Shared Care Fact Sheet – Low Dose Methotrexate. (PDF)

Notes for prescribers of low dose once weekly methotrexate (PDF)

Handling Low Dose Methotrexate (PDF)

Self injection of low dose MTX (PDF)

Other medications

Shared Care Fact Sheet – Biologic and Targeted Synthetic DMARDs V3.1 (PDF)

Shared Care Fact Sheet - Leflunomide (PDF)

Shared Care Fact Sheet – Sulfasalazine (PDF)

Shared Care Fact Sheet - Hydroxychloroquine (PDF)

ARA Position Statement Medical Cannabis (PDF)

Prescribing Medications for Rheumatic Diseases in Pregnancy (PDF)

Healthcare Excellence and Innovation

Shared Care of Patient on low dose Methotrexate for Rheumatological Disease

Rheumatology Sub-Stream

This document is available under "Resources" at https://metronorth.health.qld.gov.au/specialist_service/refer-your-patient/rheumatology

Many rheumatology patients are suitable for rheumatologist/GP **shared care** methotrexate (MTX) management. MNHHS rheumatologists advocate this where appropriate (including for this patient if this document accompanies a clinic letter). Sharing care can improve specialist access and enhance patient compliance and satisfaction.

Please do the following for your patient:

- ☐ **Review vaccination status** – COVID, pneumococcal and yearly flu vaccinations recommended. Patients on MTX receiving a first flu vaccine should probably get 2 doses, 4 weeks apart. Live vaccines (e.g. varicella) are not contraindicated with low dose MTX (<0.4mg/kg/wk.). Biological and targeted synthetic DMARDs are a contraindication to live vaccines. Rheumatology - Table of Vaccinations
- ☐ **Arrange a skin check if** not done within previous 6m and ensure repeated annually
- ☐ **Discuss the critical importance of ongoing, effective contraception in women**
- ☐ **Ensure pathology tests are done** and action results appropriately - *see Tab A: below*
- ☐ **Arrange clinical reviews** as appropriate and consider software reminders for regular tasks
- ☐ **Please contact the rheumatology team if you have any concerns (Registrar via switch)**

A: Pathology testing

- Regular **FBC, E/LFT, ESR/CRP** are required with **results to GP and rheumatologist**
- Please review the patient in the context of the clinic letter to assess symptoms, possible side effects and to action abnormal results. If the protocol below recommends a treatment change please alert rheumatologist.
- When the dose of MTX is stable for 3 months and there are no other relevant changes (e.g. development of impaired renal function) the above tests should be performed at **minimum 3 monthly**
- If **co-prescribed leflunomide** the **minimum interval is 2 monthly** due to increased potential toxicity
- Regular cardiovascular risk review, including lipids, is advisable for all patients with autoimmune disease

If your patient has elected to use Queensland Health pathology, they have been provided with a form.
If your patient wishes to use a private pathology provider, their GP will need to issue pathology forms.
The rheumatologist may have given them a form for their first test. Ensure your details are in the cc field.

Managing abnormal tests:

- **Liver function**
  - If ALT/AST levels >2x upper limit of normal (ULN) but <3x ULN, MTX dose should be reduced by 50% and tests repeated in 1 month. Once normalized any MTX titration should be monitored with monthly blood tests until the dose has been stable for 3 months
  - If ALT/AST >3x ULN, withhold MTX, continue folic acid and discuss with rheumatology registrar
  - Compliance and dose of folic acid should be confirmed
  - Lower dose MTX may be reinstituted following ALT/AST normalisation
  - Consider screening for other causes of LFT derangement if ALT/AST >3x ULN 4 weeks after discontinuation
- **Renal Function**
  - In cases of acute kidney injury: eGFR 20-40 max. dose MTX 10mg/wk, if eGFR <20 **STOP** MTX. Please inform treating team if changes are made
- **Haematology**
  - If Hb drops 20 g/l below baseline, WBC <2 x 10^9/L, neutrophils <0.5 x 10^9/L or platelets <50 x 10^9/L withhold MTX, continue folic acid and discuss with rheumatology registrar
  - If less severe abnormalities check compliance with folic acid treatment and consider increasing folic acid as outlined in C below. Reduce MTX dose by 50% and repeat tests in 2 weeks
  - Myelosuppression is more common in initial months but can occur any time during treatment. Risk factors include age >70, low albumin, folate deficiency and renal impairment

V03: Effective: September 2021 Review: September 2024

Metro North Health | Queensland Government

B: Possible side effects

- The most common side effects are mouth ulcers, nausea, vomiting and diarrhoea. Using folic/folinic acid, taking MTX with food/in the evening or changing to SC administration may reduce these
- Skin dryness, rashes and increased sensitivity to the sun may also occur
- Fatigue, headache, mental clouding, fever, dizziness, tinnitus, blurred vision, and alopecia are reported
- Serious side effects of myelosuppression, hepatotoxicity and pneumonitis are much less common

C: Folic acid

- Folic acid minimises adverse effects and must be co-prescribed (not funded by the PBS unless ATSI/DVA)
- At least 5mg/wk should be taken, but not on the day of MTX due to potential GI absorption competition
- Folic acid dose can be increased to 5mg/day if needed but not on the day of MTX
- Therapeutic Guidelines recommend the total weekly dose of folic acid ≤3x the total weekly dose of MTX
- Folinic Acid (Calcium Folinate/Leucovorin) may be considered if the patient is unable to tolerate MTX. It is given 7.5-15mg once a week, 8-12 hours after MTX

Further Information

MTX is CONTRAINDICATED with trimethoprim (including co-trimoxazole) in most clinical situations:

- It may be indicated in PJP prophylaxis (which is usually a lower/less frequent dosing)
- This interaction can be life threatening; seek expert input before co-prescribing

MTX and infections

- Patients can usually continue MTX while being treated with oral antibiotics (except as above)

MTX can be taken with other medications including:

- Other DMARDs including biological and targeted synthetic DMARDs
- Steroids such as prednisolone
- NSAIDs / low dose aspirin / paracetamol / PPIs

MTX and alcohol:

- MTX usage in heavy drinkers has been associated with liver cirrhosis
- It is not known precisely what level of drinking is safe when on MTX
- Maximum intake should remain within NHMRC alcohol consumption guidelines
- Drinking >4 std drinks on one occasion, even infrequently, is strongly discouraged

Dose titration will be directed by the rheumatologist

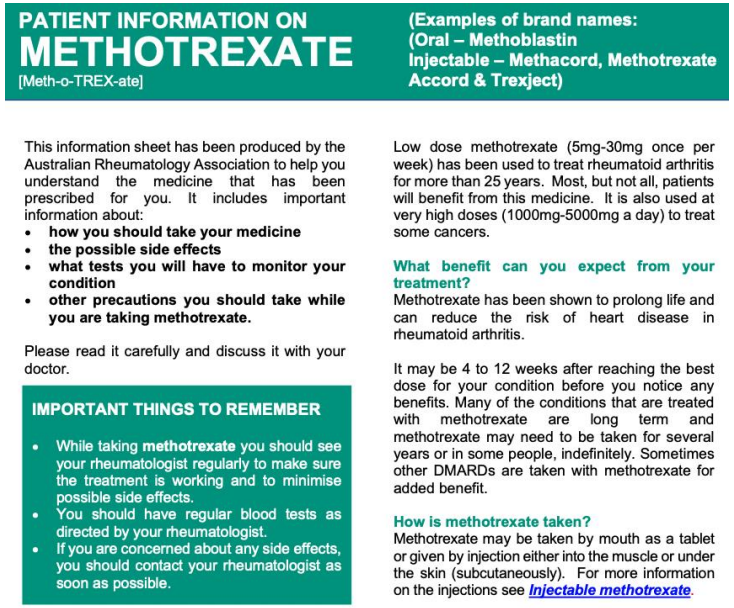
- Standard dose is 20-30mg/wk., it may be lower if elderly / mild renal impairment / low BMI
- MTX is usually taken as a single dose on the same day each week. The oral dose may be divided over 24h to improve tolerance without compromising efficacy
- Dose escalations range from 5mg to 15mg/week every 1-4 weeks to a maximum of 30mg once a week
- Response is assessed after 4-8 weeks at a specific dose
- At doses of 20mg a week or above the parenteral (SC) route is often used to improve absorption

Ongoing prescribing

- MTX tablets are available in 2.5mg or 10mg strengths. It is recommended to only prescribe the 10mg tablets
- Please carefully consider the number of repeats you provide to ensure recommended monitoring is adhered to
- Only patients taking >25mg/week eligible for 50-tablet packs – carefully consider safety before prescribing
- Be precise with prescriptions e.g. "20mg once a week on Monday"
- SC administration is encouraged if patient unable to tolerate a sufficient oral dose for disease control
- Prefilled syringes are now available on the PBS for RA and psoriasis
- In case of accidental pregnancy: stop MTX, start folic acid 5mg daily and contact the treating rheumatologist
- MTX is undetectable in serum 24h after administration. Patients on low dose weekly MTX are NOT "HOT" and pose no risk to others. It is not absorbed through the skin so tablets and injections can be handled safely

The ARA website has more information including up-to-date COVID advice and vaccine information and a Methotrexate SC injection demonstration video:
Medications: https://rheumatology.org.au/patients/medication-information.asp
Pregnancy: Rheumatology Medications for Autoimmune Rheumatic Diseases in Pregnancy
For more information on MTX shared care from NPS: Shared care approaches to rheumatoid arthritis: supporting early and sustained methotrexate - NPS MedicineWise
HealthPathways is a valuable GP decision-support tool which includes sections on all major rheumatology conditions: https://brisbanenorth.healthpathwayscommunity.org/18668.htm Username: Brisbane Password: North

Methotrexate resources



PATIENT INFORMATION ON
METHOTREXATE
[Meth-o-TREX-ate]

(Examples of brand names: (Oral – Methoblastin Injectable – Methacord, Methotrexate Accord & Trexject)

This information sheet has been produced by the Australian Rheumatology Association to help you understand the medicine that has been prescribed for you. It includes important information about:

- **how you should take your medicine**
- **the possible side effects**
- **what tests you will have to monitor your condition**
- **other precautions you should take while you are taking methotrexate.**

Please read it carefully and discuss it with your doctor.

IMPORTANT THINGS TO REMEMBER

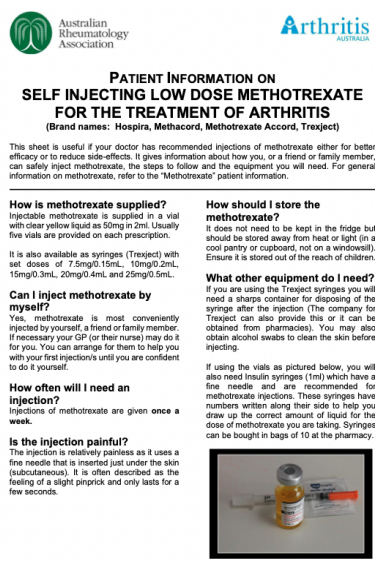
- While taking **methotrexate** you should see your rheumatologist regularly to make sure the treatment is working and to minimise possible side effects.
- You should have regular blood tests as directed by your rheumatologist.
- If you are concerned about any side effects, you should contact your rheumatologist as soon as possible.

Low dose methotrexate (5mg-30mg once per week) has been used to treat rheumatoid arthritis for more than 25 years. Most, but not all, patients will benefit from this medicine. It is also used at very high doses (1000mg-5000mg a day) to treat some cancers.

What benefit can you expect from your treatment?
Methotrexate has been shown to prolong life and can reduce the risk of heart disease in rheumatoid arthritis.

It may be 4 to 12 weeks after reaching the best dose for your condition before you notice any benefits. Many of the conditions that are treated with methotrexate are long term and methotrexate may need to be taken for several years or in some people, indefinitely. Sometimes other DMARDs are taken with methotrexate for added benefit.

How is methotrexate taken?
Methotrexate may be taken by mouth as a tablet or given by injection either into the muscle or under the skin (subcutaneously). For more information on the injections see ***Injectable methotrexate***.



Australian Rheumatology Association

Arthritis AUSTRALIA

PATIENT INFORMATION ON
SELF INJECTING LOW DOSE METHOTREXATE FOR THE TREATMENT OF ARTHRITIS
(Brand names: Hospira, Methacord, Methotrexate Accord, Trexject)

This sheet is useful if your doctor has recommended injections of methotrexate either for better efficacy or to reduce side-effects. It gives information about how you, or a friend or family member, can safely inject methotrexate, the steps to follow and the equipment you will need. For general information on methotrexate, refer to the "Methotrexate" patient information.

How is methotrexate supplied?
Injectable methotrexate is supplied in a vial with clear yellow liquid as 50mg in 2ml. Usually five vials are provided on each prescription.

It is also available as syringes (Trexject) with set doses of 7.5mg/0.15mL, 10mg/0.2mL, 15mg/0.3mL, 20mg/0.4mL and 25mg/0.5mL.

Can I inject methotrexate by myself?
Yes, methotrexate is most conveniently injected by yourself, a friend or family member. If necessary your GP (or their nurse) may do it for you. You can arrange for them to help you with your first injection/s until you are confident to do it yourself.

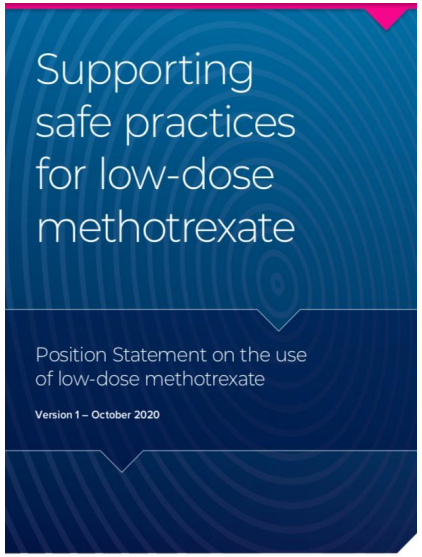
How often will I need an injection?
Injections of methotrexate are given **once a week.**

Is the injection painful?
The injection is relatively painless as it uses a fine needle that is inserted just under the skin (subcutaneous). It is often described as the feeling of a slight pinprick and only lasts for a few seconds.

How should I store the methotrexate?
It does not need to be kept in the fridge but should be stored away from heat or light (in a cool pantry or cupboard, not on a windowsill). Ensure it is stored out of the reach of children.

What other equipment do I need?
If you are using the Trexject syringes you will need a sharps container for disposing of the syringe after the injection (The company for Trexject can also provide this or it can be obtained from pharmacies). You may also obtain alcohol swabs to clean the skin before injecting.

If using the vials as pictured below, you will also need Insulin syringes (1ml) which have a fine needle and are recommended for methotrexate injections. These syringes have numbers written along their side to help you draw up the correct amount of liquid for the dose of methotrexate you are taking. Syringes can be bought in bags of 10 at the pharmacy.



Supporting safe practices for low-dose methotrexate

Position Statement on the use of low-dose methotrexate

Version 1 – October 2020

LOW-DOSE METHOTREXATE FOR RHEUMATOID ARTHRITIS AND PSORIATIC ARTHRITIS

Rheumatoid arthritis (RA) and psoriatic arthritis (PsA) are long-term conditions where the body's immune system mistakenly attacks healthy tissues such as the joints and skin. This causes inflammation, leading to symptoms such as joint pain and swelling.

Use this action plan to discuss methotrexate with your rheumatologist and plan the best way to take your medicine.

Methotrexate acts to control the disease
Methotrexate doesn't just block pain and other symptoms of RA and PsA. It interrupts the activity of the immune system, slowing the disease and reducing inflammation.

Early treatment with methotrexate (within 3 months of symptoms appearing) can:
- stop the disease from getting worse
- reduce the chance of long-term joint damage caused by uncontrolled inflammation
- improve symptoms such as joint pain, swelling and stiffness.

Methotrexate is a recommended disease-modifying medicine for RA and PsA

Methotrexate
- is called a **disease-modifying antirheumatic drug**. You might hear it called a DMARD for short.
- is usually taken as a **tablet**, but can also be an **injection**.
- takes **time** to work – you might not feel better for **6–12 weeks**.
- is also used for the skin condition **psoriasis**, which is associated with PsA.

Focus on facts
Myths about methotrexate can be barriers to treatment. Knowing the facts helps people stick to their treatment and improves results.

Fact	Fact	Fact	Fact
Methotrexate is safe and effective at low doses for RA and PsA – it's not considered chemotherapy at these doses.	Methotrexate can be safely taken with non-steroidal anti-inflammatory drugs (NSAIDs).	Methotrexate injections can be safely self-administered.	People taking methotrexate for RA or PsA can safely make physical contact with pregnant women.
Myth	**Myth**	**Myth**	**Myth**
Low-dose methotrexate is chemotherapy.	Methotrexate should not be taken alongside NSAIDs.	Self-administration of methotrexate injections is unsafe.	People taking methotrexate cannot be near pregnant women.

Ongoing care

Blood tests
Regular blood tests are used to check treatment is working and monitor for side effects, measuring kidney and liver function, and doing full blood count. Over time, these tests are needed less often.

Clinical review
Joint pain and physical function are reviewed regularly. How often depends on how active the disease is.

Vaccinations
Keep your pneumococcal and influenza vaccinations up to date.

Other conditions
You will be monitored for heart disease, osteoporosis and skin cancer, as the risk of these increases with RA and PsA. Annual skin checks are recommended.

Reproductive health
You should seek specialist advice if you plan to have children. Women should use birth control while taking methotrexate, stop methotrexate 3 months before planning a pregnancy, and avoid breastfeeding while on methotrexate.

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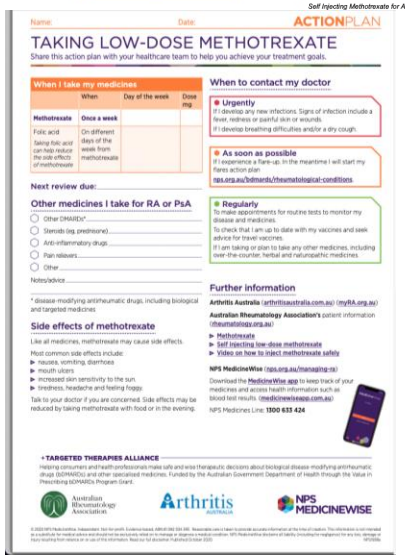

Name: Date: **ACTIONPLAN**

TAKING LOW-DOSE METHOTREXATE
Share this action plan with your healthcare team to help you achieve your treatment goals.

When I take my medicines

	When	Day of the week	Dose mg
Methotrexate	Once a week		
Folic acid Taking folic acid can help reduce the side effects of methotrexate	On different days of the week from methotrexate		

Next review due:

Other medicines I take for RA or PsA
- Other DMARDs*
- Steroids (eg, prednisone)
- Anti-inflammatory drugs
- Pain relievers
- Other

Notes/advice

* disease-modifying antirheumatic drugs, including biological and targeted medicines

Side effects of methotrexate
Like all medicines, methotrexate may cause side effects.
Most common side effects include:
- nausea, vomiting, diarrhoea
- mouth ulcers
- increased skin sensitivity to the sun
- tiredness, headache and feeling foggy.

Talk to your doctor if you are concerned. Side effects may be reduced by taking methotrexate with food or in the evening.

When to contact my doctor
- **Urgently** If I develop any new infections. Signs of infection include a fever, redness or painful skin or wounds. If I develop breathing difficulties and/or a dry cough.
- **As soon as possible** If I experience a flare-up. In the meantime I will start my flares action plan rps.org.au/bdmards/rheumatological-conditions
- **Regularly** To make appointments for routine tests to monitor my disease and medicines. To check that I am up to date with my vaccines and seek advice for travel vaccines. If I am taking or plan to take any other medicines, including over-the-counter, herbal and naturopathic medicines.

Further information
Arthritis Australia (arthritisaustralia.com.au) (myRA.org.au)
Australian Rheumatology Association's patient information (rheumatology.org.au)
- Methotrexate
- Self injecting low-dose methotrexate
- Video on how to inject methotrexate safely

NPS MedicineWise (nps.org.au/managing-ra)
Download the MedicineWise app to keep track of your medicines and access health information such as blood test results (medicinewiseapp.com.au)
NPS Medicines Line: **1300 633 424**

TARGETED THERAPIES ALLIANCE
Helping consumers and health professionals make safe and wise therapeutic decisions about biological disease-modifying antirheumatic drugs (bDMARDs) and other specialised medicines. Funded by the Australian Government Department of Health through the Value in Prescribing bDMARDs Program Grant.

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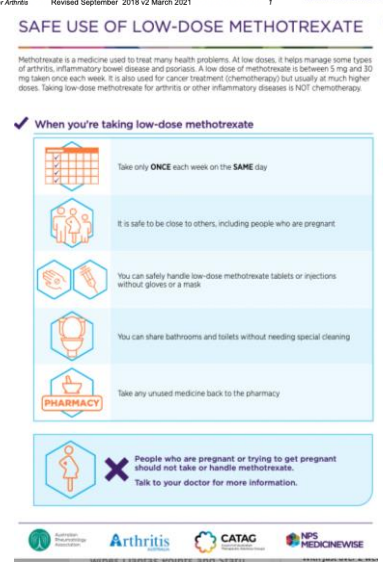

SAFE USE OF LOW-DOSE METHOTREXATE

Methotrexate is a medicine used to treat many health problems. At low doses, it helps manage some types of arthritis, inflammatory bowel disease and psoriasis. A low dose of methotrexate is between 5 mg and 30 mg taken once each week. It is also used for cancer treatment (chemotherapy) but usually at much higher doses. Taking low-dose methotrexate for arthritis or other inflammatory diseases is NOT chemotherapy.

When you're taking low-dose methotrexate

- Take only **ONCE** each week on the **SAME** day
- It is safe to be close to others, including people who are pregnant
- You can safely handle low-dose methotrexate tablets or injections without gloves or a mask
- You can share bathrooms and toilets without needing special cleaning
- PHARMACY Take any unused medicine back to the pharmacy

People who are pregnant or trying to get pregnant should not take or handle methotrexate.
Talk to your doctor for more information.

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CATAG
Council of Australian Therapeutic Advisory Groups

What about low-dose methotrexate in hospital?
Sometimes hospital staff take extra precautions when handling methotrexate. These include wearing gloves, masks or other protective equipment when:
- dispensing and giving methotrexate or
- handling body fluids (eg, double flushing the toilet).

These precautions are designed for cancer treatment and not low-dose methotrexate. Staff may take extra precautions because they may handle it many times in a day. When you're taking low-dose methotrexate at home, you do not need to follow these steps.

While you are in hospital, you may have a different number of tablets than you usually take at home. This is because the hospital keeps different strengths of methotrexate and may not break tablets. Check with the hospital staff if you are concerned about the medicines you are being given.

Where can I get more information?
- Ask your specialist
- Ask your pharmacist
- Arthritis Australia (arthritisaustralia.com.au, MyRA, MyPsA)
- Australian Rheumatology Association's patient information (rheumatology.org.au)
- Methotrexate
- NPS MedicineWise (nps.org.au)
- Low-dose methotrexate action plan
- Download the MedicineWise app to keep track of your medicines and access health information such as blood test results (medicinewiseapp.com.au)
- NPS Medicines Line: **1300 633 424**

CATAG This material has been adapted from the Council of Australian Therapeutic Advisory Groups Position Statement on the use of low-dose methotrexate. CATAG, 2020.

TARGETED THERAPIES ALLIANCE
Helping consumers and health professionals make safe and wise therapeutic decisions about biological disease-modifying antirheumatic drugs (bDMARDs) and other specialised medicines. Funded by the Australian Government Department of Health and Aged Care through the Value in Prescribing bDMARDs Program Grant.

Australian Rheumatology Association | Arthritis AUSTRALIA | CATAG | NPS MEDICINEWISE

References

- In my hands, Methotrexate is NOT chemotherapy
- https://tgldcdp.tg.org.au/guideLine?guidelinePage=Rheumatology&frompage=etgcomplete
- MTX FOR USE IN RHEUMATOLOGY (ADULT AND PAEDIATRIC), DERMATOLOGY, NEUROLOGY, GASTROENTEROLOGY, OPHTHALMOLOGY AND RESPIRATORY MEDICINE Shared care protocol
- CATAG Position Statement on the use of low dose MTX
- ARA Patient Medication Information MTX
- Shared Care of Patient on low dose Methotrexate for Rheumatological Disease