DORSET MEDICINES ADVISORY GROUP
SHARED CARE GUIDELINE FOR THE USE OF DISEASE MODIFYING ANTI-RHEUMATIC DRUGS (DMARDS)

INTRODUCTION

Disease Modifying Anti-Rheumatic drugs (DMARDs) are added at increasingly early stages in the treatment of rheumatoid arthritis (RA) to suppress inflammation; they may be used as monotherapy or more commonly in combination. DMARDs are also used for the treatment of other rheumatology conditions (e.g. connective tissue disease and vasculitis) and in other specialties, including dermatology, respiratory medicine, neurology, ophthalmology and gastroenterology. This shared care guideline is intended for use alongside the locally agreed pathway for transfer of patients and the drug monitoring local enhanced service for primary care.

A number of these drugs are recommended for prescribing in unlicensed indications. All recommendations are based on the practice of a responsible body of peers of similar professional standing (e.g. British Society for Rheumatology (BSR); see References for full details). Prescribers are advised to discuss with the patient if the medicine is used out of license and document this agreement in the patient's medical record.

Many of the drugs have the potential for significant harm as well as benefit. Appropriate screening prior to drug initiation and vigilant monitoring during therapy are required to minimise the risk from harm.

This shared care guideline is intended to be used alongside the local enhanced service for West Dorset GPs. It is not currently applicable to east Dorset.

AREAS OF RESPONSIBILITY FOR SHARED CARE

Patients should be at the centre of any shared care arrangements. Individual patient information and a record of their preferences should accompany shared care prescribing guidelines, where appropriate.

Transfer of clinical responsibility to primary care should only be considered where the person's clinical condition is stable or predictable, the patient is established on the drug and in accordance with the locally agreed clinical pathway. The point at which a patient may be considered stable is individual and will vary between patients. Communication between primary and secondary care when this point is deemed to have been reached is essential. Communication of the potential transfer to the GP should take place after 8-9 weeks of drug therapy and the hospital or specialist will continue to provide prescriptions and monitoring until at least week 12. The GP should contact the hospital or specialist if they are not willing to accept the shared care arrangement within two weeks of receiving the communication. In the absence of any communication from the GP refusing to accept the shared care arrangement the secondary/tertiary provider must supply an adequate amount of the medication to cover the transition period with the patient then informed to obtain further prescriptions and monitoring from the GP. Where a GP is unwilling to accept shared care the responsibility for prescribing and monitoring remains with the hospital or specialist.

When clinical responsibility for prescribing is transferred to general practice, it is important that the GP, or other primary care prescriber, is confident to prescribe the necessary medicines. Shared care agreements play a key role in enabling primary care prescribers to prescribe medicines with which they may not initially be familiar or have specialist knowledge.

Clinical responsibility for prescribing is held by the person signing the prescription, who must also ensure adequate monitoring. If the GP is not confident to undertake these roles, due to concerns on an individual

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patient basis, then they should inform the specialist as soon as possible and the total clinical responsibility for the patient for the diagnosed condition remains with the specialist.

These guidelines are not intended to be a comprehensive review of DMARD therapy. Clinicians should consider nationally published guidelines such as NICE or BSR/BHPR (British Society of Rheumatology/British Health Professional in Rheumatology). Please consult the manufacturer's Summary of Product Characteristics (SPC) and the current BNF for full prescribing information on contra-indications, side-effects and interactions. The guidelines do not cover the initiation of biological therapy or the use of drugs in pregnancy (discuss with specialist).

REFERRAL AND INITIATION

DMARDs should be initiated by hospital specialists only and should not be initiated in the Primary Care setting. The intention to share care should be explained to the patient by the doctor initiating treatment. It is important that patients are consulted about treatment and agree with it. The doctor who prescribes the medication legally assumes clinical responsibility for the drug and the consequences of its use.

	Specialist Responsibilities
1	Provide patient with information on disease /drug treatment options. Explain where drugs are used outside license. Ensure patient has signed any necessary engagement or consent forms.
2	Make the decision to initiate DMARDs in conjunction with the patient / carer.
3	Discuss the benefits and side effects of treatment with the patient / carer.
4	Provide drug information to the patient (where appropriate). This may be in written hard copy or an electronic format, depending on availability or the accessibility of the patient. For methotrexate issue purple book.
5	Explain the intention to share care for drug prescribing and monitoring to the patient. Explain the process and the potential timescales for this.
6	Where available and applicable for the individual patient provide access to an electronic or hard copy self-management device which may enable the reporting of patient related outcome measures and sets out which blood tests are required.
7	Carry out pre-treatment assessment, including any necessary blood tests not provided within the baseline screening from the GP on referral, and review the results.
8	Initiate treatment with the DMARD & prescribe at least the first 12 weeks' medication.
9	Arrange tests and review the results for the first 12 weeks monitoring.
10	Seek agreement from primary care to share care. This should be initiated on or after week 9 of the supply of medication, recognizing the need for continued supply, the primary care team should respond within two weeks if they do not wish to participate. Send primary care details of baseline assessments and results within a clinical management plan, which includes diagnosis, dosing plan for DMARD, monitoring requirements of practice on transfer and a summary of the information that has been given to the patient. Transfer of responsibility should only occur when the patient has a first appointment within primary care arranged.
11	Review monitoring results following initiation and assess response to treatment.
12	At each routine review appointment confirm the individual patient's monitoring schedule. Communicate promptly with primary care when treatment is changed and when any changes in monitoring are required.
13	Have a mechanism to receive rapid referral of a patient from primary care in the event of deteriorating clinical condition or in case of non-adherence to monitoring requirements.
14	Ensure that clear backup arrangements exist for primary care to obtain advice and support.

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	Primary Care Responsibilities
1	Respond to request for shared care if the GP does not wish to undertake shared care. Practices may wish to respond to confirm that they are willing to undertake shared care. The following wording within a template may be used where the response is positive. *Dear.....* *Thank you for your recent letter requesting transfer of shared care to primary care.* *I confirm that I am happy to accept care into primary care and thereby to undertake continued prescribing and appropriate monitoring as described in the shared care agreement.* *Your sincerely*
2	Using the established process within primary care (template or SOP) set up call and recall system for initial appointments and blood tests.
3	Prescribe the DMARD at the dose recommended after the first 12 weeks of treatment. Within the prescribing system ensure that irrespective of whether the medication is entered as an acute or repeat medication any drug interactions can be picked up with concomitant medicines. (NB if the medication is entered as an acute, care must be taken to include this in any patient communications as acute medications are not usually copied into letters by computer systems and may not be picked up to flag drug interactions.)
4	Carry out monitoring according to the guideline recommendation below. Requests to vary the monitoring schedule by secondary care should be considered by the practice but may be declined where this is not within the scope of the practice. In this instance the responsibility for monitoring should be explicitly returned to secondary care.
5	Report results outside the set parameters below to the hospital specialist for advice / further management as appropriate via appropriate communication methods e.g. eRS advice and guidance.
6	Ensure the patient is aware of any treatment change and any patient held management and monitoring information is up to date.
7	Seek advice from the specialist on any aspect of patient care that is of concern and may affect treatment.
8	Stop treatment on the advice of the specialist or immediately if an urgent need to stop treatment arises.
9	Report adverse events to the specialist team and through local or national mechanisms where appropriate.

	Community Pharmacist/Dispenser's role
1	Ensure appropriate dose prescribed with clear directions not 'as directed'.
2	Ensure oral methotrexate is only dispensed in the 2.5mg tablet strength. For methotrexate check patient-held record including a check of dose in case of changes.
3	Provide advice on adverse effects and any drug interactions with prescription and/or OTC medicines.
4	Issue patient information leaflets where appropriate.
5	Monitor frequency of prescription requests and contact GP if quantities in excess of the prescribed dose are ordered.

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Patient's role (or that of carer)	
1	Maintain engagement with secondary care team and Practice and keep patient held information up-to-date. Report to specialist or Primary Care clinician if he/ she does not have a clear understanding or has any concerns in relation to treatment
2	Ensure safe storage and handling of medicine
3	Request repeat prescriptions from Practice at least one week in advance of medication running out
4	Book and attend for blood tests at GP practice at the timings set out by the Primary Care clinician or specialist team.
5	Ensure the Primary Care clinician, community pharmacist/dispenser and specialist are aware of any over- the -counter medicines they may be taking. Provide the patient-held record for methotrexate when it is requested.
6	Attend all review appointments within primary and secondary care.
7	Report any adverse effects to the Primary Care clinician or specialist

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PRE-TREATMENT ASSESSMENT (SECONDARY CARE)

PRE-TREATMENT ASSESSMENT FOR ALL DMARDS – TO BE UNDERTAKEN IN SECONDARY CARE

N.B some of the information may be provided as part of the referral.

1. Height, Weight, Blood pressure & Urinalysis
2. FBC, U&Es / eGFR / Creatinine, LFT's including Albumin, ESR and CRP
3. HIV, Hepatitis B and C serology (Before first DMARD for all patients and consider for at risk populations* with any DMARD change)
4. Respiratory history and examination (Rheumatology patients) (If abnormal consider imaging / lung function testing)
5. Vaccinations against pneumococcus and influenza should be recommended
6. Consideration of co-morbidities / pregnancy status that would influence DMARD choice, including lung disease

**People born or brought up in a country with an intermediate or high prevalence (2% or greater) of chronic hepatitis B. This includes: all countries in Africa, Asia, the Caribbean, Central and South America, Eastern and Southern Europe, the Middle East and the Pacific islands: People who have ever injected drugs: Men who have sex with men: People who may have been exposed to sexually acquired infection: Prisoners, including young offenders.*

DRUG	Additional Pre-treatment assessment	Notes
AZATHIOPRINE	TPMT (Thiopurine methyltransferase)	TPMT assay- *Homozygous deficiency* -serious and fatal toxicity- can occur within 6 weeks of starting. *Heterozygous deficiency* - linked to serious adverse events, symptoms may not be evident until 6 months after starting treatment daily
CICLOSPORIN	CVD screening/risk assessment, including non-fasting lipids	If BP >140/90mmHg or elevated lipid levels treat according to NICE guidelines before commencing.
HYDROXYCHLOROQUINE	Optical coherence tomography (OCT) scan within 1 year of starting	
LEFLUNOMIDE		If BP >140/90mmHg treat according to NICE guidelines before commencing
METHOTREXATE (ORAL & SUBCUTANEOUS)	CXR within 6 months (secondary care to arrange and review) P3NP in dermatology patients	Co-prescribe folic acid orally at a minimum dose of 5mg once a week. dose to be taken on a different day to methotrexate dose
MYCOPHENOLATE MOFETIL	Pregnancy test in pre-menopausal women	

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MONITORING SCHEDULES

DMARD INITIATION

ALL DMARDS THAT REQUIRE MONITORING

FORTNIGHTLY FOR 6 WEEKS (assuming dose is stable) then MONTHLY IN SECONDARY CARE
up to week 12 FBC / LFT'S / CREATININE / eGFR/ CRP/ ESR

MONTHLY FOR 2 FURTHER MONTHS IN PRIMARY CARE
FBC / LFT'S / CREATININE / eGFR/ CRP/ ESR

EXTENDED MONITORING SCHEDULE

FBC / LFT'S / CREATININE / eGFR

CRP/ESR

MONTHLY IN PRIMARY CARE

(Default until advised otherwise by specialist or if uncertainty.)

STANDARD MONITORING SCHEDULE

FBC / LFT'S / CREATININE / eGFR/ CRP/ ESR **QUARTERLY** IN PRIMARY CARE

- For patient at low risk of toxicity, e.g. normal range blood test parameters, no co-morbidities such as renal impairment / fatty liver
- As specified in secondary care review (at least annually) and communicated to GP by clinical letter

DOSE INCREASE OF DMARD

FORTNIGHTLY FOR 6 WEEKS IN PRIMARY CARE

FBC / LFT'S / CREATININE / eGFR / CRP / ESR

RESUME USUAL PATIENT MONITORING SCHEDULE IN PRIMARY CARE

(e.g. monthly / quarterly)

FBC / LFT's / CREATININE / eGFR / CRP / ESR

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ADDITIONAL MONITORING REQUIREMENTS

To be undertaken with blood tests at frequency set in dose increase of DMARD above

DRUG	OTHER MONITORING WITH EACH BLOOD TEST
LEFLUNOMIDE	BLOOD PRESSURE & WEIGHT
CICLOSPORIN (NEORAL)	BLOOD PRESSURE & BLOOD GLUCOSE
HYDROXYCHLOROQUINE	ANNUAL OCT ASSESSMENT AFTER 5 YEARS USE (TO BE REQUESTED BY SPECIALIST)

SUGGESTED DMARD MONITORING SCHEDULES

To be decided by specialist in Secondary Care and communicated to GP by clinical letter

DRUG	LABORATORY MONITORING
AZATHIOPRINE	STANDARD MONITORING
SULPHASALAZINE	STANDARD MONITORING for 1 year only in rheumatology patients
LEFLUNOMIDE	STANDARD MONITORING
METHOTREXATE (ORAL or SUBCUTANEOUS)	STANDARD MONITORING
MERCAPTOPURINE	STANDARD MONITORING
LEFLUNOMIDE & METHOTREXATE / HIGHER RISK COMBINATIONS	EXTENDED MONTHLY
MYCOPHENOLATE MOFETIL	EXTENDED MONTHLY
CICLOSPORIN (NEORAL)	EXTENDED MONTHLY
HYDROXYCHLOROQUINE	NO ROUTINE MONITORING

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MONITORING - actions for abnormal monitoring parameters

The prescriber has responsibility for ensuring patients are adhering to monitoring guidance and respond to abnormalities of the results included in the monitoring schedule.

As well as responding to absolute values in laboratory tests, it is also relevant to observe trends in results (e.g. gradual decreases in WBC or albumin, or climbing liver enzyme).

These parameters are suitable for the majority of patients. For some patient's individual parameters may be set by the specialist and communicated to Primary Care where results outside these set limits are medically acceptable (for example a persistently raised stable MCV due to drug therapy where no alternative cause has been identified).

Abnormality Detected	Recommended Action to include
WCC <3.5 x 10^9/L	With-hold and discuss with specialist team
Unexplained eosinophilia >0.5 x 10^9/L	With-hold and discuss with specialist team
Neutrophils <1.6 x 10^9/L	With-hold and discuss with specialist team
Platelet count <140 x 10^9/L	With-hold and discuss with specialist team
MCV >105 f/L	Check B12, Folate, TSH – if abnormal treat If normal discuss with specialist team
ALT and/or AST >100 units/L	With-hold and discuss with specialist team
Creatinine >30% above baseline and/or e GFR <35ml/min	Repeat in 1 week, if still >30% from baseline With-hold and discuss with specialist team
Unexplained fall in serum albumin <30 g/L	With-hold and discuss with specialist team
Urine dipstick protein 2+ or greater	Send MSU. If infection confirmed, treat appropriately. If sterile proteinuria seek advice from specialist team
BP > 140/90mmHg	Manage hypertension according to NICE guidance If on ciclosporin with-hold and discuss with specialist team
Abnormal Bruising / Sore Throat	With-hold until FBC result available
Unexplained widespread rash / hair loss	With-hold and seek urgent (preferably dermatological) advice
Unexplained oral ulceration	With-hold and discuss with specialist team
Unexplained new increasing dyspnoea or cough *	With-hold and discuss urgently with specialist team

* AZATHIOPRINE, CICLOSPORIN, LEFLUNOMIDE, METHOTREXATE, SULPHASALAZINE have pneumonitis listed on SPC. Cases reports of MYCOPHENOLATE pneumonitis exist.

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Sources of specialist advice and support

Rheumatology email = dch-ft.rheumatology@nhs.net
Rheumatology Advice line number = 01305 255864
Rheumatology Secretary = 01305 253753
Rheumatology Nurses = 01305 254814 & 01305 255990

Gastroenterology Help- line Number = 01305 255102
Gastroenterology email = IBDNurses@dchft.nhs.uk

6. Additional Information

6.1 Biologics monotherapy monitoring statement

Patients receiving biological therapy require clinical review in secondary care at least every 12 months to allow on-going prescribing of their treatment.

Monitoring blood tests will be undertaken at this appointment in secondary care where indicated.

Therefore, patients on biologics monotherapy DO NOT require drug monitoring in primary care.

6.2 Vaccinations and DMARDS

Vaccinations against pneumococcus (one off) and influenza (annually) are recommended and should be offered in primary care. Ideally these should be commenced before treatment, but can be given at any time.

Shingles vaccine (Zostavax®) is not routinely given to all individuals on DMARDS but where indicated may be used in individuals on less than 20mg of Prednisolone or standard doses of DMARD medications. (NB Doses of DMARDs for rheumatic indications are considered 'standard')

Other live vaccines are NOT recommended.

6.3 Inter-current infection and DMARDS

During infection requiring antimicrobial therapy or hospital admission, the following DMARDS should be discontinued temporarily until the patient has recovered from the infection:

Methotrexate, Leflunomide, Sulphasalazine, Azathioprine, Apremilast, Mycophenolate, Ciclosporin, Tacrolimus

6.4 Perioperative management of DMARDS

Steroid exposure should be minimised prior to surgical procedures to reduce the risk of infection

Increases in steroid dose to prevent adrenal insufficiency are not routinely required

DMARD therapy should not routinely be stopped in the peri-operative period, although individualised decisions should be made for high-risk procedures.

6.5 Malignancy and DMARDS

Prior malignancy is not considered a contra-indication to DMARD therapy

7. References

BSR & BHPR guideline for the prescription and monitoring of non-biologic disease-modifying anti-rheumatic drugs 2017

https://www.rheumatology.org.uk/Knowledge/Excellence/Guidelines

BSR & BHPR guideline on prescribing drugs in pregnancy and breastfeeding – Part 1: standard and biological disease modifying anti-rheumatic drugs and corticosteroids

https://www.rheumatology.org.uk/Knowledge/Excellence/Guidelines

Summary of Product Characteristics http://www.medicines.org.uk/emc/

Reducing the harm caused by oral methotrexate. National Patient Safety Agency. 29 July 2004. Available via www.npsa.nhs.uk/health/alerts

Improving compliance with oral methotrexate guidelines. Patient Safety alert 13. National Patient Safety Agency. 1 June 2006. Available via www.npsa.nhs.uk/health/alerts

NPSA rapid response report on the risks of incorrect dosing of oral anti-cancer medicines (NPSA/2008/RRR001) www.npsa.nhs.uk/health/alerts

NHS England Jan 2018. Responsibility for prescribing between primary and secondary/tertiary care. https://www.england.nhs.uk/wp-content/uploads/2018/03/responsibility-prescribing-between-primary-secondary-care-v2.pdf