

Rheumatology Shared Care Guidelines

1. Introduction

Rheumatoid Arthritis (RA) is a chronic, progressive inflammatory disease of the synovial lining of peripheral joints. The goals of management of RA are to relieve pain and inflammation, to prevent joint destruction and to preserve or improve a patient's function. Rheumatoid arthritis is the commonest type of inflammatory arthritis but similar drug treatments are used in other forms such as psoriatic arthritis.

Early introduction of disease-modifying anti-rheumatic drugs (DMARDs) is now recognised as being vital in order to minimise the risk of irreversible joint damage. General practitioners are becoming more involved in active management of the condition with the recognition that patients should be referred early for specialist advice and the initiation of disease modifying drugs.

It is clearly inappropriate for patients on drugs which still require further specialist experience in use to be monitored in primary care, but there is a place for the monitoring of patients on *widely used and accepted drugs* within a general practice setting. Patients on these drugs need regular but infrequent consultant follow up but frequent monitoring of side effects, which may be more appropriately carried out in primary care.

These guidelines look at the shared care management of patients treated with disease-modifying anti-rheumatic drugs.

2. Patient selection

Shared care may be appropriate in the following situation:

- Patients with rheumatological conditions who have been referred to secondary care for assessment and recommendation of a treatment regimen.
- Patients receiving *conventional* disease modifying therapy, as in the attached information sheets.
- DMARDs recommended by the secondary care clinician and a treatment outline defined for that particular patient, communicated to the GP and kept under regular review.

N.B. Where "consultant" is referred to throughout this document, a designated deputy may undertake the role depending on the systems in place.

3. Drug treatment, indications and management plan

See the attached information sheets for each drug.

4. Procedure for initiating shared care arrangements

The NHS Management Executive issued guidance in 1991 (*Responsibility for prescribing between hospitals and GPs* EL(91)127) and 1994 (*Purchasing and prescribing* EL(94)72) which reinforced the basic premise that:

- The doctor who has clinical responsibility for a patient should undertake prescribing
- If care is to be shared there should be proper hand-over procedures from hospital specialists to GPs.

Aligning clinical and prescribing responsibility enhances patient safety because the individual signing prescriptions will also be responsible for ensuring that any necessary monitoring has been undertaken and will have access to the results of this.

In the case of rheumatology, when an agreement to manage a patient under a shared care guideline is in place, the general practitioner will be responsible for ensuring the continued monitoring of the patients with rheumatological conditions is undertaken and the prescribing of recommended drugs. The rheumatology department will provide all patients with a shared care booklet to record their blood results in. This will allow both consultant and GP to have access to blood results.

Shared care must be agreed before the patient is directed to primary care. Patients must not be put in a position where they are unsure where to obtain supplies of their medication

5. Regimen management

a) Aspects of care for which the consultant is responsible

- The consultant will confirm the patient's diagnosis and carry out any baseline tests necessary.
- The consultant will ensure that the patient is educated and provided with written information about their treatment and the importance of attending monitoring appointments.

The consultant will initiate the DMARD and continue to prescribe until the patient's drug dose and monitoring interval are stable. Dose changes in previously stable patients should be initiated in secondary care but prescribing and monitoring can continue in primary care with any changes in dosage and monitoring clearly communicated to the GP and patient in writing.

- Transfer of prescription and monitoring to primary care would normally take place at 3 months after the patient has been on a stable dose of the DMARD. Exceptions to this are for Hydroxychloroquine (transfer after 3 months) and Leflunomide (transfer after 6 months). Please note that mycophenolate mofetil is not licensed for treatment of RA and all monitoring will be done in secondary care.
- The consultant will then determine whether shared care is appropriate for the patient's condition and will contact the GP via letter (see Appendix 1)
- The consultant will issue the patient with a patient-held shared care booklet and a letter informing them of the shared care process (Appendix 2). Mechanisms must be in place to ensure that the shared care booklet is updated.
- The consultant will provide the patient's general practitioner with the following information:
 - Diagnosis of the patient's condition with the relevant clinical details.
 - Details of any treatment to date and treatments to be provided by the GP.
 - A copy of the Rheumatology Shared Care Guidelines.

GP information sheet for the relevant drugs detailing monitoring arrangements (Appendix 3).

- Whenever the consultant sees the patient, he/she will send a written summary within 14 days to the patient's GP. Urgent information, e.g. dose changes, will be given to the patient to take to the practice.

- The consultant or his representative will be available for information or advice to the GP.
- The consultant will ensure that the patient is given the appropriate appointments for secondary care follow up and that defaulters from follow up are contacted to arrange alternative appointments.

b) Aspects of care for which the GP is responsible

- Ensuring that he/she has sufficient information and knowledge to understand the therapeutic issues relating to the patients clinical condition.
- Agreeing to the principles & responsibilities of this shared care agreement. Agreeing that in his/her opinion a particular patient should receive shared care for the diagnosed condition unless good reasons exist for the management to remain within secondary care.
- Producing all prescriptions in an accurate, legible form according to the guidance in the current BNF. It is important to stress that the individual signing a prescription carries the legal liability for the consequences of prescribing the drug.
- Following initiation and stabilisation of DMARD treatment by the consultant, prescribing treatment on the recommendation of the consultant and continuing therapy in accordance with advice from the supervising consultant.
- The GP will ensure that the patient is monitored according to the British Society of Rheumatology guidelines and will take the advice of the supervising consultant if there are any amendments to the suggested monitoring schedule.
- Keeping the patient held shared care booklet up to date with the results of investigations, changes in dose and alterations in management.
- Reporting any adverse effects in the treatment of the patient to the consultant.
- It is the GP's responsibility, after discussion with the consultant, to decide whether to continue treatment in a patient who does not attend appointments required for follow up and monitoring, but in general, the prescription should not be issued if blood monitoring is not being done. A system should be in place to ensure detection of non-attenders.

c) Aspects of care for which the patient or carer is responsible

- Taking medicines as prescribed or informing doctors if they have not been taken.
- Making appointments for monitoring at the advised intervals.
- Attending for monitoring and follow up as required and rearranging appointments if unable to attend for whatever reason.
- Making their shared-care booklet available to be updated.
- Reporting of any side effects to their GP
- Informing their GP and consultant of any other medication they may be taking including products purchased "over the counter" and herbal medicines.
- Ensuring they have a clear understanding of their treatment.

Support, education and information

Advice should be available from the hospital trust, both from the consultant and more junior medical staff and from nurse practitioners where appropriate. The hospital trust will lead or participate in educational sessions for GPs and practice nurses where appropriate.

Queries regarding specific drugs may be directed where appropriate to the hospital trust's Medicines Information Department.

Advice and education will also be available from the DMARD monitoring service.

Contact details

Consultant rheumatologists

Dr Neil Snowden	0161 720 2602
Dr Beverley Harrison	0161 720 2598
Dr Sophia Naz	0161 720 2598
Dr Martin Pattrick	0161 720 2622

Nurse practitioners

Margaret Miller	0161 720 4752
Karen Williams	0161 720 4752

Rheumatology helpline (ansaphone – calls normally answered within 24 hours) 720 2380

Medicines Information Department 0161 720 2152

Other useful contacts:

Arthritis Care	www.arthritiscare.org.uk
Arthritis Research Campaign	www.arc.org.uk
British Rheumatology Society	www.rheumatology.org.uk

References

BSR guidelines for DMARD therapy (Rheumatology 2008; 47: 924-5) - also available on the BSR website (www.rheumatology.org.uk - under Guidelines)

British National Formulary No. 57 March 2009

NHS Management Executive, *Responsibility for prescribing between hospitals and GPs* (EL(91) 127)

NHS Executive, *Purchasing and prescribing* (EL(94)72)

These guidelines are based on those from South Manchester, Central Manchester, Trafford and East Cheshire PCTs, South Manchester University Hospitals NHS Trust, East Cheshire NHS Trust and Trafford Healthcare NHS Trust (adapted from guidelines produced by North Nottinghamshire Prescribing Strategy Group). They have been approved by the Manchester PCT Prescribing Subgroup (North) and the Pennine Acute Hospitals NHS Trust Drug & Therapeutics Committee.

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Auranofin (Ridaura)

A typical dose regimen may be:- 3mg twice a day increasing to 3mg three times a day after 4-6 months if necessary.

Pretreatment assessment:- FBC, urinalysis, U&Es, LFTs.

Monitoring:- Monthly FBC and urinalysis. Patient should be asked about the presence of rash or oral ulceration at each visit.

Action to be taken:-

WBC < $3.5 \times 10^9 / l$	withhold <u>until discussed</u> with rheumatologist
Neutrophils < $2.0 \times 10^9 / l$	withhold <u>until discussed</u> with rheumatologist
Eosinophils > $0.5 \times 10^9 / l$	caution required
Platelets < $150 \times 10^9 / l$	withhold <u>until discussed</u> with rheumatologist
>1+ proteinuria on >1 occasion	check MSU. If no infection, withhold <u>until discussed</u> with rheumatologist
Rash or oral ulceration	withhold <u>until discussed</u> with rheumatologist
Diarrhoea	increase fibre content of diet or add fibre supplements. May need to reduce dose or if severe stop treatment
Abnormal bruising or sore throat	withhold until FBC result available

Please note that in addition to absolute values for haematological indices a rapid fall or a consistent downward trend in any value should prompt caution and extra vigilance.

Pregnancy and breastfeeding:-

The manufacturer advises of teratogenicity in animal studies. Effective contraception should be used during and for at least six months after treatment. Avoid in breastfeeding. Discuss management with rheumatologist.

See BSR guidelines for DMARD therapy (Rheumatology 2008; 47: 924-5) and manufacturer's summary of product characteristics for further information.

Azathioprine

A typical dose regimen may be:- 1mg/kg/day increasing after 4 to 6 weeks to 2-3mg/kg/day. Lower doses if there is significant renal or hepatic impairment

Pneumovax and annual 'flu vaccine should be given. Passive immunisation should be carried out using Varicella zoster immunoglobulin (VZIG) in non-immune patients if exposed to chickenpox or shingles.

Pretreatment assessment:- FBC, U&Es, creatinine, LFTs, TPMT assay

TPMT deficiency: Patients who are homozygous should not be given Azathioprine. Heterozygotes should be given a lower dose and co-prescription of aminosallylates is contra-indicated.

Monitoring:- FBC & LFTs weekly for 6 weeks, then every 2 weeks until dose stable for 6 weeks and thereafter monthly. If monitoring stable for 6 months, can reduce to 3 monthly. However, if heterozygous for TPMT deficiency, patients should be monitored at least monthly. **U+E, creat every 6 months.**

Action to be taken:-

WBC $<3.5 \times 10^9/l$	withhold <i>until discussed</i> with rheumatologist
Neutrophils $<2.0 \times 10^9/l$	withhold <i>until discussed</i> with rheumatologist
Platelets $<150 \times 10^9/l$	withhold <i>until discussed</i> with rheumatologist
>2 -fold rise in AST or ALT (from upper limit of reference range)	withhold <i>until discussed</i> with rheumatologist
Rash or oral ulceration	withhold <i>until discussed</i> with rheumatologist
MCV $>105fl$	investigate and if B12 or folate low start appropriate supplementation. Check TFT.
Abnormal bruising or sore throat	withhold until FBC result available

Please note that in addition to absolute values for haematological indices a rapid fall or a consistent downward trend in any value should prompt caution and extra vigilance.

Notable interactions:- (refer to BNF)

Allopurinol - If allopurinol is co-prescribed the dose of azathioprine must be cut to 25% of the original dose.

Co-trimoxazole & trimethoprim can cause life threatening haematotoxicity

Aminosallylates (sufasalazine, mesalazine, olsalazine, balsalazide) can cause bone marrow toxicity

Live vaccines (e.g. oral polio, oral typhoid, MMR, BCG, yellow fever, varicella zoster) should be avoided in patients taking azathioprine.

Sunscreens should be encouraged to reduce sunlight exposure

Pregnancy and breastfeeding:-

Discuss with rheumatologist.

See BSR guidelines for DMARD therapy (Rheumatology 2008; 47: 924-5) and manufacturer's summary of product characteristics for further information.

Ciclosporin (Neoral)

A typical dose regimen may be:- 2.5mg/kg/day in 2 divided doses increasing after 6 weeks by 25mg increments every 2-4 weeks to a maximum of 4mg/kg/day. Ciclosporin is contraindicated in patients with abnormal renal function or uncontrolled hypertension. Experience with ciclosporin in rheumatoid arthritis is relatively short.

Pneumovax and annual 'flu vaccine should be given. Passive immunisation should be carried out using Varicella zoster immunoglobulin (VZIG) in non-immune patients if exposed to chickenpox or shingles.

Pretreatment assessment:- FBC, U&Es (x 2), creatinine (x 2), LFTs, lipids. Blood pressure should be normal on two separate occasions prior to treatment.

Monitoring:- U+E, creatinine and BP fortnightly until the dose has been stable for three months and thereafter monthly. FBC, LFTs monthly until dose stable for three months and then every three months, serum lipids every six months.

Action to be taken:-

Creatinine rises by 30% of baseline	withhold <u>until discussed</u> with rheumatologist
Abnormal bruising rheumatologist	check FBC & withhold <u>until discussed</u> with
Potassium above normal range	withhold <u>until discussed</u> with rheumatologist
BP rise to abnormal range	discuss with rheumatologist
Significant rise in lipids	withhold <u>until discussed</u> with rheumatologist
Platelets < 150 x 10 ⁹ /l	withhold <u>until discussed</u> with rheumatologist
>2-fold rise in AST, ALT or Alk. Phos (from upper limit of reference range)	withhold <u>until discussed</u> with rheumatologist

Please note that in addition to absolute values for haematological indices a rapid fall or a consistent downward trend in any value should prompt caution and extra vigilance.

Other side-effects:-

In addition to potentially serious toxicity there appears to be a large number of troublesome non-serious side-effects too numerous to mention. If in doubt please consult the summary of product characteristics or discuss with a rheumatologist. Examples include:

Gastrointestinal disturbance (abdominal pain, anorexia, nausea, vomiting, diarrhoea) – continue if possible. If troublesome, discuss with rheumatologist.

Burning sensation of hands or feet – may occur during the first week of treatment but should subside.

Interactions:-

There are numerous drug interactions involving ciclosporin and it is recommended that the manufacturer's summary of product characteristics is consulted at the time of first prescription and if any other drugs are introduced. In particular, note the following:

- Diclofenac – the dose of diclofenac should be halved if ciclosporin is co-prescribed.
- Colchicine and nifedipine should be avoided.
- Maximum dose of simvastatin is 10mg
- Potassium sparing diuretics & other drugs that can cause hyperkalaemia (e.g. ACE inhibitors & angiotensin II antagonists should be used with caution).
- Grapefruit juice should be avoided for 1 hour before & after taking ciclosporin
- Live vaccines (oral polio, oral typhoid, MMR, BCG, yellow fever, varicella zoster) should be avoided in patients taking ciclosporin.

Pregnancy and breastfeeding:- Discuss with rheumatologist.

See BSR guidelines for DMARD therapy (Rheumatology 2008; 47: 924-5) and manufacturer's summary of product characteristics for further information.

Leflunomide (Arava®)

A typical dose regimen may be:- 10-20mg daily

Pneumovax and annual 'flu vaccine should be given. Passive immunisation should be carried out using Varicella zoster immunoglobulin (VZIG) in non-immune patients if exposed to chickenpox or shingles.

Pretreatment assessment:- FBC, LFTs, U&Es, creatinine, blood pressure and weight

Monitoring:- FBC, LFTs, BP & weight every month for the first six months and then every 2 months.. (or every month if on another hepatotoxic or immunosuppressive drug)

Action to be taken:-

WBC < $3.5 \times 10^9/l$	withhold <u>until discussed</u> with rheumatologist
Neutrophils < $2 \times 10^9/l$	withhold <u>until discussed</u> with rheumatologist
Platelets < $150 \times 10^9/l$	withhold <u>until discussed</u> with rheumatologist
>2-fold rise in ALT or AST (from upper limit of reference range)	withhold <u>until discussed</u> with rheumatologist
Rash or itch	consider dosage reduction and/or antihistamines or withhold <u>until discussed</u> with rheumatologist
Severe sore throat or abnormal bruising	check FBC & withhold until results available
BP > 140/90	Treat hypertension
> 10% weight loss	reduce dosage or stop
Breathlessness	withhold <u>until discussed</u> with rheumatologist

Please note that in addition to absolute values for haematological indices a rapid fall or a consistent downward trend in any value should prompt caution and extra vigilance.

Other side effects:-

Leflunomide may also cause mouth ulcers, skin rash (including Stevens–Johnson syndrome and toxic epidermal necrolysis), gastrointestinal upset, headaches, dizziness, tenosynovitis and hair loss. If a severe undesirable side effect of leflunomide occurs or for any other reason rapid removal of its active metabolite is required a washout procedure with cholestyramine 8 grams three times a day or activated charcoal 50 grams four times a day, each for 11 days is available. Leflunomide increases susceptibility to infections which should be treated promptly.

Interactions:-

- Leflunomide may inhibit the metabolism of warfarin, phenytoin and tolbutamide. It has an extremely long elimination half life and interactions with these drugs and with other DMARDs may occur even after leflunomide has been discontinued.
- Live vaccines (e.g. oral polio, oral typhoid, MMR, BCG, yellow fever, varicella zoster) are contraindicated.
- Alcohol should be avoided (or limited to max. 8 units weekly) due to an increased risk of hepatotoxicity.

Pregnancy and breastfeeding:-

It is important that women of childbearing potential do not start leflunomide until pregnancy has been excluded and both men and women must use reliable contraception. If, during treatment, there is a delay in onset of menstruation or other reason to suspect pregnancy then the patient must notify their GP and consultant as soon as possible. It is possible that rapidly lowering the blood level of the active metabolite through the drug washout procedure the risk to the foetus may be reduced. Male and female patients should not plan a pregnancy

within two years of discontinuing leflunomide. Blood concentrations of its active metabolite should be measured two years after discontinuation (should be < 20µg/L on two occasions, 14 days apart) before pregnancy occurs (this waiting time may be reduced by using the drug washout procedure).

Women must not breastfeed while they are taking leflunomide.

See BSR guidelines for DMARD therapy (Rheumatology 2008; 47: 924-5) and manufacturer's summary of product characteristics for further information.

Methotrexate

A typical dose regimen may be:- 7.5mg **once weekly** increasing by 2.5 - 5mg every 2- 6 weeks to a usual maximum of 25mg (higher doses are sometimes used). Lower doses should be used in the frail elderly or if there is significant renal impairment. Methotrexate is available in 2.5mg and 10mg tablets – to minimise the chance of drug overdose occurring if the two strengths are confused it is recommended that **only 2.5mg tablets are used and this should be specified on the prescription**. Regular folic acid supplements are thought to reduce toxicity and a dose of 5mg once a week should be prescribed (taken at any time except on day of MTX).

PLEASE NOTE THAT THIS GUIDANCE IS FOR ORAL METHOTREXATE ONLY AND THAT PARENTERAL (IM OR SC) METHOTREXATE IS PRESCRIBED AND MONITORED ENTIRELY IN SECONDARY CARE

Pneumovax and annual 'flu vaccine should be given. Passive immunisation should be carried out using Varicella zoster immunoglobulin (VZIG) in non-immune patients if exposed to chickenpox or shingles.

Pretreatment assessment:- FBC, U&Es, creatinine, LFTs, Chest Xray. If CXR abnormal, need HRCT & KCO.

Monitoring:- FBC, U+E, LFTs fortnightly until 6 weeks after last dose increase and provided it is stable monthly thereafter. If stable for 1 year, the frequency of monitoring can be reduced after d/w rheumatologist.

Action to be taken:-

WBC <3.5 x10 ⁹ /l	withhold <i>until discussed</i> with rheumatologist
Neutrophils <2.0x10 ⁹	withhold <i>until discussed</i> with rheumatologist
Platelets <150x10 ⁹ /l	withhold <i>until discussed</i> with rheumatologist
>2-fold rise in AST, ALT (from upper limit of reference range)	withhold <i>until discussed</i> with rheumatologist
Unexplained fall in albumin	withhold <i>until discussed</i> with rheumatologist
Rash or oral ulceration	withhold <i>until discussed</i> with rheumatologist
New or increasing dyspnoea or cough	withhold <i>until discussed</i> urgently with rheumatologist
MCV >105fl	investigate and if B12 or folate low start appropriate supplementation. Check TFT.
Significant deterioration in renal function	withhold <i>until discussed</i> with rheumatologist
Abnormal bruising or sore throat	withhold until FBC result available
Folinic acid rescue (20mg IV then 15mg orally qds for 2 days) can be used for severe haematological toxicity, renal failure or MTX overdose.	

Please note that in addition to absolute values for haematological indices a rapid fall or a consistent downward trend in any value should prompt caution and extra vigilance.

Other side-effects:-

Nausea – should subside. If troublesome, consider an anti-emetic.
Hair loss – usually mild, rarely significant.

Interactions:-

- Co-trimoxazole or trimethoprim must be avoided in patients taking methotrexate (increased antifolate effect).
- Phenytoin: antifolate effect is increased

- NSAIDs reduce tubular excretion of methotrexate and thereby enhance toxicity but clinically significant interaction is rare.
- Live vaccines (e.g. oral polio, oral typhoid, MMR, BCG, yellow fever, varicella zoster) should be avoided in patients taking methotrexate.
- Excess alcohol should be avoided (or limit to max. 6 units per week)

Pregnancy and breastfeeding:-

Methotrexate is teratogenic and is contraindicated in pregnancy and breastfeeding. Both men and women receiving methotrexate should use contraception throughout the treatment period and for at least three months after stopping.

See BSR guidelines for DMARD therapy (Rheumatology 2008; 47: 924-5) and manufacturer's summary of product characteristics for further information.

Penicillamine

A typical dose regimen may be:- 125mg/day increasing by 125mg every four weeks to 500mg/day. If no response after a further three months increase by 125mg every four weeks to 750mg/day. If no response after a further three months a further increase by 125mg every four weeks to 1g/day may be considered. If no response after three months on the maximum dose, stop treatment.

Pretreatment assessment:- FBC, urinalysis, U&Es and creatinine.

Monitoring:- Urinalysis and FBC every two weeks until on a stable dose and thereafter monthly. Patient should be asked about the presence of rash or oral ulceration at each visit.

Action to be taken:-

WBC<3.5 x10 ⁹ /l	withhold <u>until discussed</u> with rheumatologist
Neutrophils<2.0x10 ⁹ /l	withhold <u>until discussed</u> with rheumatologist
Platelets<150x10 ⁹ /l	withhold <u>until discussed</u> with rheumatologist
>1+ proteinuria on >1 occasion	check MSU. If sterile, withhold <u>until discussed</u> with rheumatologist
Rash or oral ulceration	withhold <u>until discussed</u> with rheumatologist
Alteration of taste	continue treatment (usually settles spontaneously)
Dyspepsia	most likely secondary to NSAID but reduce dose if severe
Abnormal bruising or sore throat	withhold until FBC result available

Please note that in addition to absolute values for haematological indices a rapid fall or a consistent downward trend in any value should prompt caution and extra vigilance.

Interactions

Should not be taken within 2 hours of indigestion remedies or medicines containing zinc or iron due to reduced absorption of penicillamine.

Pregnancy and breastfeeding

Avoid in pregnancy or breastfeeding – discuss with rheumatologist.

See BSR guidelines for DMARD therapy (Rheumatology 2008; 47: 924-5) and manufacturer's summary of product characteristics for further information.

Sodium aurothiomalate (Myocrisin®)

A typical dose regimen may be:- 10mg test dose by deep intramuscular injection (which should be given in the *clinic* followed by 30 minutes observation) followed by weekly injections of 50mg until significant response. Thereafter, either 50mg monthly **or** 50mg fortnightly for three months, 50mg three weekly for three months, and then 50mg monthly. If after a total dose of 1gram has been administered no response has occurred treatment should be stopped.

Pretreatment assessment:- FBC, urinalysis, U&Es, serum creatinine, LFTs.

Monitoring:- FBC and urinalysis at the time of each injection. The results of the FBC need not be available before the injection is given but must be available before the next injection i.e. it is permissible to work one FBC in arrears. Patient should be asked about the presence of rash or oral ulceration before each injection.

Action to be taken:-

WBC < $3.5 \times 10^9/l$	withhold <u>until discussed</u> with rheumatologist
Eosinophils > 0.5	withhold <u>until discussed</u> with rheumatologist
Neutrophils < $2.0 \times 10^9/l$	withhold <u>until discussed</u> with rheumatologist
Platelets < $150 \times 10^9/l$	withhold <u>until discussed</u> with rheumatologist
>1+ proteinuria on >1 occasion	check MSU. If sterile, withhold <u>until discussed</u> with rheumatologist
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Rash or oral ulceration	withhold <u>until discussed</u> with rheumatologist
Abnormal bruising or sore throat	withhold until FBC result available

Please note that in addition to absolute values for haematological indices a rapid fall or a consistent downward trend in any value should prompt caution and extra vigilance.

Live vaccines (e.g. oral polio, oral typhoid, MMR, BCG, yellow fever, varicella zoster) should be avoided in patients taking Myocrisin.

Pregnancy and breastfeeding:-

Avoid in pregnancy and breastfeeding – discuss with rheumatologist.

See BSR guidelines for DMARD therapy (Rheumatology 2008; 47: 924-5) and manufacturer's summary of product characteristics for further information.

Sulfasalazine (enteric coated tablets / Salazopyrin EN-Tabs®)

A typical dose regimen may be:- 500mg/day increasing by 500mg weekly to 2 – 3 grams/day. Only the enteric coated preparation is licensed for treating inflammatory arthritis).

Pretreatment Assessment:- FBC, U+ E, creat & LFTs.

Monitoring:- FBC and LFTs (including AST or ALT) every month for the first 3 months and every 3 months thereafter. If during the first year of treatment blood results have been stable, six monthly tests will suffice for the second year and, thereafter, monitoring of blood for toxicity could be discarded. Patient should be asked about the presence of rash or oral ulceration at each visit.

Action to be taken:-

WB $<3.5 \times 10^9$ /l	withhold <i>until discussed</i> with rheumatologist
Neutrophil $<2.0 \times 10^9$ /l	withhold <i>until discussed</i> with rheumatologist
platelets $< 150 \times 10^9$ /l	withhold <i>until discussed</i> with rheumatologist
>2 -fold rise in AST, ALT (from upper limit of reference range)	withhold <i>until discussed</i> with rheumatologist
rash or oral ulceration	withhold <i>until discussed</i> with rheumatologist
MCV >105 fl	investigate and if B12 or folate low start appropriate supplementation. Check TFT.
nausea/dizziness/ headache	if possible continue, may have to reduce dose or stop if symptoms severe.
Abnormal bruising or sore throat	withhold until FBC result available

Please note that in addition to absolute values for haematological indices a rapid fall or a consistent downward trend in any value should prompt caution and extra vigilance.

Other side effects:-

Orange tears and urine – sulfasalazine is excreted in secretions and can stain some contact lenses.

Reversible reduction in sperm count – usually returns to former level 60 days after stopping the drug.

Pregnancy and breastfeeding

Sulfasalazine should be used with caution in pregnancy and not in doses > 2 g/day. Folic acid supplements should be given before conception & during pregnancy. Small amounts of the drug may be excreted in breast milk, although these are not thought to be a risk to a healthy infant. Need to discuss with rheumatologist.

See BSR guidelines for DMARD therapy (Rheumatology 2008; 47: 924-5) and manufacturer's summary of product characteristics for further information.

Hydroxychloroquine (Plaquenil®)

A typical dose regimen may be:- 400mg daily initially, in divided doses. This may be reduced to 200mg daily after 3 months if patient weighs less than 60kg.

Pretreatment assessment:-

- FBC, U&E, LFTs
- Visual screening – ask about visual impairment (which is not corrected by glasses). Record near visual acuity of each eye (with glasses where appropriate) using test type or reading document as recommended by the Royal College of Ophthalmologists (see BNF). Refer to an optician if abnormal.

Monitoring:-

- Patients should be monitored yearly, enquiring about visual symptomatology, rechecking acuity and assessing for blurred vision using a reading chart. This assessment may be done by an optician, with referral to an ophthalmologist if necessary.

Relative contraindications

- Psoriasis.
- Pre-existing maculopathy of the eye.
- Epilepsy

Interactions

Refer to BNF & SPC

Pregnancy and breastfeeding

Hydroxychloroquine has been used relatively safely in pregnancy but need to d/w rheumatologist. Women should not breastfeed whilst on hydroxychloroquine.

See BSR guidelines for DMARD therapy (Rheumatology 2008; 47: 924-5) and manufacturer's summary of product characteristics for further information.

Mycophenolate mofetil (CellCept®)

A typical dose regimen may be:- 500mg/d for 1 week then increase by 500mg per week until optimal dose reached (usually 1-2g/d) up to a maximum of 3g/day.

Pneumovax and annual 'flu vaccine should be given. Passive immunisation should be carried out using Varicella zoster immunoglobulin (VZIG) in non-immune patients if exposed to chickenpox or shingles.

Pretreatment assessment:- FBC, U&Es, LFTs and CXR.

Monitoring:- FBC weekly until dose stable for 4 weeks, then every 2 weeks for 2 months & thereafter, monthly

Action to be taken:-

WBC $<3.5 \times 10^9/l$	withhold <i>until discussed</i> with rheumatologist
Neutrophils $<2.0 \times 10^9/l$	withhold <i>until discussed</i> with rheumatologist
Platelets $<150 \times 10^9/l$	withhold <i>until discussed</i> with rheumatologist
Abnormal bruising or sore throat	withhold until FBC result available

Please note that in addition to absolute values for haematological indices a rapid fall or a consistent downward trend in any value should prompt caution and extra vigilance.

Notable interactions:- (refer to BNF)

Live vaccines (e.g. oral polio, oral typhoid, MMR, BCG, yellow fever, varicella zoster) should be avoided in patients taking mycophenolate

Pregnancy and breastfeeding:-

Mycophenolate is contra-indicated during pregnancy & breastfeeding. Contraception should be used for 6 weeks after stopping the drug.

See BSR guidelines for DMARD therapy (Rheumatology 2008; 47: 924-5) and manufacturer's summary of product characteristics for further information.

Appendix 1

Draft letter for GPs re Shared Care process

The Pennine Acute Hospitals

NHS Trust

Consultant:	Secretary:	Direct No:
Dr B J Harrison Dr S M Naz <i><u>Dr M G Patrick</u></i>	Amanda Parry Jeanette McDonagh	720 2598 720 2622
Dr H N Snowden	Jane Cohen Janet Froggatt Eileen Taylor	720 2602 720 2146 922 3537
Nurse Practitioners: Margaret Miller Karen Williams	Anne Byrne	720 4752

Department of Rheumatology

**North Manchester General Hospital
Delaunays Road
Crumpsall
Manchester M8 5RB
Tel: 0161 720 2598
Fax: 0161 720 2626**

Re: Shared Care Process for patients on DMARDs

Dear

Your patient was started on(drug) on(month/year) by Dr(consultant). He/she is now on a stable dose of(dose) and blood monitoring has been satisfactory. As such, he/she is now suitable for transfer to the Shared Care process in which prescribing and monitoring can be undertaken in primary care

As part of the process, the GP is responsible for prescribing and monitoring the drug after initial stabilisation in secondary care. Your patient has been issued with a shared care booklet in which you can record the blood test results. The patient is responsible for ensuring that the results are kept up-to-date and for presenting the booklet at all hospital and GP visits.

If you have any questions about the Shared Care process or about DMARD monitoring / toxicity, please contact any of the consultant rheumatologists or specialist nurses.

Kind Regards

Dr Neil Snowden, Dr Beverley Harrison, Dr Sophia Naz
Consultant Rheumatologists

Appendix 2

Draft letter to patients about to transfer to shared care monitoring of DMARDs

The Pennine Acute Hospitals

NHS Trust

Consultant:	Secretary:	Direct No:
Dr B J Harrison	Amanda Parry	720 2598
Dr S M Naz <i><u>Dr M G Patrick</u></i>	Jeanette McDonagh	720 2622
Dr H N Snowden	Jane Cohen	720 2602
	Janet Froggatt	720 2146
	Eileen Taylor	922 3537
Nurse Practitioners:		
Margaret Miller	Anne Byrne	720 4752
Karen Williams		

Department of Rheumatology

North Manchester General Hospital
Delaunays Road
Crumpsall
Manchester M8 5RB
Tel: 0161 720 2598
Fax: 0161 720 2626

Re: Shared Care process for patients on DMARDs

Dear

You have recently been started on treatment withwhich is a disease-modifying anti-rheumatic drug (DMARD). Your rheumatologist has now accepted that you are on a stable dose and that your blood monitoring has been satisfactory. As such you can be transferred to the Shared Care process for DMARD monitoring. This means that your GP will now be responsible for prescribing and monitoring the drug.

You should now make arrangements with your GP practice to have regular blood tests (according to a defined protocol). You should have been issued with a shared care booklet (from the hospital Rheumatology department) in which these results will be recorded. Please ensure that you attend for the blood tests as requested. If you are unable to attend any appointments, or if you stop your medication, then please advise your GP accordingly. You will also need to make sure that the results are kept up to date in your booklet and that you bring the booklet to all your appointments with your rheumatologist or GP.

You should already have received education and an information sheet about your medication from the Rheumatology department at the hospital. If you have any concerns about the monitoring process or possible side effects of the drug, you can either discuss that with your GP or contact the Rheumatology Helpline (ansaphone – most calls returned within 24 hrs) on 0161 720 2380. Alternatively, please contact one of the Rheumatology team on the telephone numbers listed above.

Yours sincerely

Dr Neil Snowden, Dr Beverley Harrison, Dr Sophia Naz
Consultant Rheumatologists