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1. INTRODUCTION

This document has been developed in order to standardise care of patients on disease modifying anti-rheumatic drug therapies across the primary / secondary interface.

It is a tool to be used by and assist Practice Nurses, District Nurses and General Practitioners who are undertaking the shared care of monitoring patient’s with rheumatological conditions requiring DMARD therapies.

It allows / offers access and communication at the health care interface.

It will be used in conjunction with the shared care blood monitoring booklet, which is held by the patient.

Health care professionals may use this information as a tool, to complement the management of patients monitored by them in primary care. The monitoring of trends, collating of results, patient recall etc, is to be managed by the Practice as usual.
2. AIMS OF THERAPY

- To control joint inflammation as early as possible after diagnosis
- To prevent damage/erosions leading to pain reduction
- To maintain range of joint movement
- To minimise loss of function
- To prevent deformity
- To maintain patient’s independence and mobility
- To maintain patient’s quality of life
- To ensure that the benefit of DMARD therapy outweighs the risks

The goal of treatment being:

‘to intervene in the disease before the joints are damaged’

Austen May 2000

‘to arrest the disease and to achieve remission’

ACR guidelines 1996

The American College of Rheumatology’s guidelines recommend that the commencement of DMARD therapy should not be delayed beyond three months for any patient with an established diagnosis who, in spite of adequate treatment with N.S.A.I.D. s, has ongoing joint pain, significant early morning stiffness or fatigue, active synovitis, or persistent elevation of the ESR or CRP level. (ACR 1996). This early aggressive therapeutic approach is often referred to as the ‘window of opportunity’ (ACR 2002). Oliver (2007) suggests that guidance published by the European League Against Rheumatism (Combe et al 2007) and the British Society for Rheumatology (BSR) (Luqmani et al 2006) should be used in conjunction with the ACR criteria to optimise decisions in early diagnosis and clinical management (Appendix G point 1 on page 48), and that an early referral algorithm is a practical clinical tool to aid practitioners (Emery et al 2002)(Appendix G point 2 on page49).

Monitoring should be standardised across the primary / secondary interface as variations are occurring with current practice at present. Arther et al (2001) highlights the differences in care that patient are receiving.
3. EPIDEMIOLOGY

DMARD’s play an important role in the management of inflammatory arthritis. The disease is characterised by symmetric polyarthritis that over time leads to destruction of joint cartilage and bone, and to deformities of the joint.

RA is a common condition, affecting around 1% of the population (Hochberg, Silman, Smolen, Weinblatt, Weisman 2004). Ra can present at any age, although prevalence increases with advancing years, with the peak onset falling between 35-50 years (Zvaifler 2006). Once initiated, the persistent synovitis, characteristic of RA, causes progressive joint destruction and deformity with resultant deterioration in quality of life and high cost to society. This is estimated at £1.3 billion annually in the UK (Pincus and Callahan 1993).

Most patients develop prominent impairments of joint function and recent evidence suggests RA may be associated with a shortened life span. Although the presentation and natural course of the disease may vary if left untreated, the disease has the potential to cause progressive joint destruction and reduce life expectancy. It is not a benign disease but a progressive condition with survival rates similar to those of non-Hodgkin’s lymphoma and triple heart bypass surgery of 45-50% survival over a five-year period (Pincus and Callahan 1993). Cardiovascular disease is an additional risk factor related to the inflammatory component of RA and subsequent mortality (Kumar et al 2007).

Life expectancy decreases by 3 to 7 years. Research has shown that early intervention with disease specific anti-rheumatic drugs, or disease-modifying anti rheumatic drugs is the cornerstone of treatmentand, in the early stages may be able to curb or arrest the progressive synovitis and joint destruction and thereby limit disability (Rheumatology 2008). The American College of Rheumatology (ACR) guidelines (1996), state that the timing for the initiation of DMARDs is critical. The selection of a DMARD is made on the basis of efficacy versus toxicity and latest evidence.
4. DMARDs: Monitoring
Investigations
Side Effects
Prescribing Issues
Patient Information

GENERAL INFORMATION.
DMARDs differ in their chemical make up. However they all possess common properties;

- Delayed action: a therapeutic response can be activated from six weeks but may take from three to six months. It is therefore important to encourage the patient to persevere with their therapy during this time. (ACR 1996)
- They are prescribed to patients with inflammatory arthritis; their primary function is to suppress disease activity. They are not analgesics, although they indirectly help through the control of signs and symptoms of Rheumatoid Arthritis. This includes certain blood parameters denoting inflammation, CRP, ESR, painful swollen joints and sometimes slowing down the progression of damage to the joints. (Donnelly et al 1992).
- The mechanism of most DMARD therapy is poorly understood.
- All have the potential to cause serious haematological toxicity and other adverse effects.
- Efficacy cannot be predicted for the individual patient. (ACR 1996)
  Therefore it is important that patient expectation is not falsely raised.

Monitoring of DMARDs varies across the country. The British Society for Rheumatology (BSR) has attempted to standardise practice with the publication of guidelines (Rheumatology 2008), which relate to choice of investigation, intervals at which they should be performed and relevant action to take if side effects occur. Copies of these guidelines are available from the BSR (Rheumatology 2008). For medico-legal reasons it is necessary to be familiar with the data sheet recommendations. They are the foundation of this protocol. Literature can also be obtained from pharmaceutical companies, BNF, MIMS and the Data Sheet Compendium.
**SHARED CARE ARRANGEMENTS FOR DMARDs.**

Shared Care Monitoring refers to the joint provision of care between secondary and primary care. This approach can be very convenient and beneficial to the patient. (Hill J 1998.)

Shared Care Monitoring in primary care would commence once the patient is established on the prescribed DMARD within secondary care.

Documentation for the initiation of shared care blood monitoring would include the following:

- Introductory letter to GP /Community Nurse involved in the shared care protocol
- Patient blood monitoring record booklet (updated with hospital monitoring results, including urinalysis and BP as appropriate) held by the patient
- Copy of this Shared Care Protocol (copy to be kept in GP practice, copy for Practice Nurse and District Nurse.)

All patients on DMARDs require blood results, (urinalysis and blood pressure where necessary) to be recorded in a monitoring booklet.

- This should be held by the patient and used across the primary/secondary interface.
- It will assist in shared communication across the interface.
- Serial data can be recorded allowing for easier detection of increasing/decreasing trends in blood results, hypertension, and for detection of nephrotoxicity through regular urinalysis.

**SHARED CARE MONITORING OF DMARDs**

To minimise inconvenience to patients and to utilise the particular resources of the hospital rheumatology department and of the primary health care team, a system of shared care is recommended (BSR/BHPR guidelines 2008). The following guidelines have been drawn up to standardise and formalise the current arrangement across the primary / secondary interface.
DMARD GUIDELINES

- Sulfasalazine EN (Salazopyrin EN) p.10-11
- D Penicillamine p.12-13
- Methotrexate p.14-16
- Auranofin (oral gold) p.17-18
- Ciclosporin p.19-20
- Azathioprine (Imuran) p.21-22
- Cyclophosphamide p.23-24
- Myocrisin (gold inject/sodium aurothiomalate) p.25-26
- Leflunomide p.27-30
- Mycophenolate p.31-33

The decision to start a patient on a particular DMARD should normally be taken by the Consultant. Monitoring of the early stages of treatment would usually be undertaken by the hospital team.

Once the patient is stabilised on a DMARD, the GP would normally be asked to take over the monitoring according to agreed guidelines. Routine hospital visits would continue at six monthly intervals usually for overall review of patient assessment and management policy.

The hospital team would be readily available for advice to the primary care team / patient for any problems / concerns that arise at any time with regard to DMARD therapy or any aspect of patient care or treatment. See telephone contact numbers in section 8.

The hospital team must be informed without delay of any side effects, which have led to withdrawal of the DMARD, and the patient would normally be reviewed at the next hospital appointment. It is essential that clinicians remember to report (yellow card system) any serious adverse events (SAE) related to the use of DMARDs.

The decision to stop DMARDs because of lack of efficacy / response should be taken by the Consultant.

Some DMARDs can be taken concomitantly as prescribed by the Consultant. Monitoring is performed as per guidelines for each drug.

See Appendix section for management of drug reactions and side effects.

Patients should continue to take prescribed non-steroidal anti-inflammatory drugs and analgesics when taking DMARD therapy. Caution should be taken where Methotrexate is prescribed - refer to prescribing literature. However, if required the dose / frequency may be reduced at the time when symptoms reduce / subside, following shared care guidelines.
This protocol includes the most common adverse reactions to second line drugs and their monitoring requirements. However it is not exhaustive and all adverse reactions should be documented and most require some form of action. It is strongly recommended that the reader refers to national guidelines and other pharmacology texts for further reading, eg. data sheets.

On commencement of DMARD therapy the patient will given information and counselling as appropriate, the main contents of which can be found at the end of each DMARD section and ARC leaflets supplied to the patient are available from www.arc.org.uk.

See section 8 for rheumatology department contact telephone numbers.
SULFASALAZINE EN (SALAZOPYRIN EN enteric coated)

A typical dose regimen may be:- 500mg/day increasing by 500mg weekly to 2.0-3.0g/day.

Pretreatment Assessment:- FBC, LFT's, U&E'S. Check Varicella antibody status

Monitoring:-
Stabilising in secondary care FBC and LFT's fortnightly for the first 12 weeks, then initiate shared care once stable.
Primary care FBC and LFT's 12 weekly. If during the first year of treatment blood results have been stable 6 monthly tests will suffice for the second year. Thereafter, monitoring of blood for toxicity may be discarded. Patient should be asked about the presence of rash or oral ulceration at each visit.
Following dose changes Repeat FBC, LFT one month after dose increases.

Action to be taken:-

<table>
<thead>
<tr>
<th>Condition</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>WB&lt;3.5x10^9 /l</td>
<td>withhold until discussed with rheumatologist</td>
</tr>
<tr>
<td>Neutrophil &lt;2.0x10^9 /l</td>
<td>withhold until discussed with rheumatologist</td>
</tr>
<tr>
<td>platelets &lt; 150x10^9/l</td>
<td>withhold until discussed with rheumatologist</td>
</tr>
<tr>
<td>&gt;2-fold rise in AST, ALT or Alk. Phos (from upper limit of reference range)</td>
<td>withhold until discussed with rheumatologist</td>
</tr>
<tr>
<td>rash or oral ulceration normal</td>
<td>withhold until discussed with rheumatologist</td>
</tr>
<tr>
<td>MCV&gt;105fl</td>
<td>investigate and if B12 or folate and TSH. If abnormal, treat any underlying abnormality. If normal, discuss with rheumatologist.</td>
</tr>
<tr>
<td>nausea/dizziness/ headache</td>
<td>if possible continue, may have to reduce dose or stop if symptoms severe.</td>
</tr>
<tr>
<td>Abnormal bruising or sore throat</td>
<td>withhold until FBC result available</td>
</tr>
<tr>
<td>Unexplained acute widespread rash</td>
<td>Withhold, seek specialist advice</td>
</tr>
<tr>
<td>Oral ulceration</td>
<td>withhold until discussed with rheumatologist</td>
</tr>
</tbody>
</table>

If in doubt use the contact telephone number. A rapid fall or a consistent downward trend in any value should prompt caution and extra vigilance.
**SIDE EFFECTS**

These are commonest in the first 3 months of treatment and may be transient.
- Nausea, vomiting, anorexia, indigestion, abdominal pain and diarrhoea
- Malaise
- Sore mouth and mouth ulcers
- Headache ‘muzzy head’
- Can stain contact lenses yellow
- Can stain urine orange – not an indication of abnormality
- Oligospermia - reversible on discontinuation of drug
- Rash, pruritis, photosensitivity, exfoliate dermatitis
- Vertigo, tinnitus, insomnia, depression
- Sore throat / fever – query this and check for a reduction in the WBC count
- Leucopenia
- Rarely Steven-Johnson syndrome or exfoliative dermatitis
- Thrombocytopenia
- Agranulocytosis

**PRESCRIBING ISSUES**

Check results prior to the issuing of further prescriptions
- A total daily dose of 2g (or more) can be prescribed
- This drug should not be given to patients with allergies / sensitivity to salicylates or sulphonamides
- Can reduce the uptake of digoxin and folate

**PATIENT INFORMATION**

- It is not a pain killer.
- Take with food to reduce stomach upset.
- Can take alcohol in moderation.
- Even though tablets are large, swallow whole not broken crushed or chewed.
- It is slow acting therefore can take up to 3 months before improvement is felt.
- Don’t be discouraged and try to persevere, particularly if suffering from transient side effects.
- Check with chemist when buying over the counter medicines, or newly prescribed medicines.
- Indigestion remedies should not be taken at the same time. 2 hours before or after. This is because you will not absorb your medicine properly.
- Report unexplained bleeding, bruising, sore throat, fever or malaise.
- If side effects persist consult your Nurse / Dr.
- Importance of blood monitoring and responsibility for use of shared care blood monitoring booklet.
PENICILLAMINE (Distamine, Pendramine)

A typical dose regimen may be:- 125mg/day increasing by 125mg every 4 weeks to 500mg/day. If no response after a further 3 months increase by 125mg every 4 weeks to 750mg/day. If no response after a further 3 months a further increase by 125mg every 4 weeks to 1g/day may be considered. If no response after 3 months on the maximum dose stop treatment.

Pretreatment assessment:- FBC, urinalysis, U&E's. Check Varicella antibody status

Monitoring:-
Stabilising in secondary care Fortnightly urinalysis and FBC until on a stable dose
Primary care FBC and urinalysis monthly. Patient should be asked about the presence of rash or oral ulceration at each visit.

Action to be taken:-
WBC<3.5.0x10^9/l withhold until discussed with rheumatologist
Neutrophils<2.0x10^9/l withhold until discussed with rheumatologist
Platelets<150x10^9/l withhold until discussed with rheumatologist
2+ proteinuria on >1 occasion check MSU: If evidence of infection treat appropriately. If sterile and 2+proteinuria persists, withhold until discussed with rheumatologist
Rash or oral ulceration withhold until discussed with rheumatologist
Late rashes are more serious than early ones
Alteration of taste continue treatment (usually settles spontaneously)

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. If in doubt use the telephone contact number.
SIDE EFFECTS

Unexplained bruising / bleeding
Aplastic anaemia
Fever, infections, fatigue, muscle weakness.
Proteinuria is frequent, may progress to nephrotic syndrome
Anorexia, nausea, vomiting, oral ulceration, taste impairment
Pruritis, urticaria, rash
Thrombocytopenia, Leucopenia, Agranulocytosis
Rarely –
Haematuria (withdraw immediately)
Myasthenia gravis, Goodpastures syndrome
Polymyositis, Pancreatitis, Haemolytic anaemia

PRESCRIBING ISSUES

Check results prior to the issuing of further prescriptions
Start dose 125mg nocte. Increase by 125mg nocte every 4 weeks until response, this is undertaken within the secondary setting.
Must be taken on an empty stomach. Best at night time with water
Patients are not to take oral iron within 2 hours of taking drug. Penicillamine is a metal chelator and mops up essential metals, including oral iron.
Patients are not to take antacids within 2 hours of taking the drug as they hinder the absorption of the drug
No live vaccines to be given whilst on this medication
You can take alcohol in moderation.
Avoid pregnancy, and for 3 months after stopping the drug. Use a reliable contraceptive.

PATIENT INFORMATION

It is not a pain killer.
Take at night on an empty stomach with water. The drug can bind to food / liquids if they contain milk and so will not work because it will not be absorbed.
Swallow whole, do not crush or chew.
The full dose can be taken at once.
You can take alcohol in moderation.
Tablets come in 2 strengths therefore check dose and number of tablets taken. 125mg, 250mg.
It is slow acting and can take up to 3 months before improvement is felt and continues to work for 6 months. Don’t be discouraged and try to persevere, particularly if suffering from transient side effects such as nausea, metallic taste.
Check with chemist when buying over the counter medicines.
Use a reliable contraceptive. Avoid pregnancy whilst on the drug and for 3 months after.
Report unexplained bleeding, bruising, sore throat, fever or malaise.
If side effects persist consult your Nurse / Dr.
Importance of blood monitoring and responsibility for use of shared care blood monitoring booklet.
METHOTREXATE

A typical dose regimen may be: - 7.5mg weekly increasing by 2.5mg every 6 weeks to a maximum of 25mg. Lower doses should be used in the frail elderly or if there is significant renal impairment. Regular folic acid supplements are thought to reduce toxicity. Cotrimoxazole or trimethoprim must be avoided in patients taking methotrexate. Excess alcohol should be avoided. Live vaccines should be avoided in patients taking methotrexate. NSAIDs in addition to the above doses of methotrexate are not contraindicated. Annual flu vaccine should be given.

Pretreatment assessment: - FBC, U&E's, LFT's, Chest Xray (unless CXR done within the last 6 months), PFT should be considered in selected patients. Check Varicella antibody status

Monitoring: -
Stabilising in secondary care FBC U&E's and LFT's fortnightly until 6 weeks after last dose increase and provided it is stable monthly thereafter. Once stable initiate shared care.
Primary care Monthly FBC, LFT's and U&E's 6-12 monthly (more frequently if there is any reason to suspect deteriorating renal function).

Action to be taken: -
WBC <3.5.0x10^9/l withhold until discussed with rheumatologist
Neutrophils <2.0x10^9 withhold until discussed with rheumatologist
Platelets<150x10^9 /l withhold until discussed with rheumatologist
>2-fold rise in AST, ALT withhold until discussed with rheumatologist

(from upper limit of reference range)

Unexplained fall in albumin withhold until discussed with rheumatologist
In absence of active disease
Rash or oral ulceration, withhold until discussed with rheumatologist
diarrhoea, nausea and vomiting
New or increasing dyspnoea or cough withhold until discussed urgently with rheumatologist

MCV>105fl investigate and if B12 or folate low start
start appropriate supplementation, check TFT
Mild to moderate renal impairment withhold until discussed with rheumatologist

Abnormal bruising or sore throat withhold until immediate 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. If in doubt use rheumatology contact number
**Side effects**

Non productive cough, dyspnoea  
Anorexia, nausea, vomiting, diarrhoea, weight loss, stomatitis, mouth ulcers  
Rash, alopecia, urticaria  
Leucopenia, thrombocytopenia, megaloblastic anaemia, pancytopenia  
cutaneous vasculitis, transient oligospermia, teratogenic effects, liver toxicity, bone marrow suppression.  
Pulmonary fibrosis.

**Prescribing issues**

Check results prior to the issuing of further prescriptions  
Start dose 5-10mg weekly orally. Increased if no response within the first 3 months. This is done in the secondary setting.  
Caution this drug is to be taken on a weekly basis only  
This drug is co prescribed with folic acid 5 mg, taken 3 days post methotrexate or more often depending on the consultant prescribing.  
This helps to reduce minor side effects.  
This medication is manufactured in two strengths. 10mg and 2.5 mg. Both are of similar size, colour and are scored. Ensure patient is aware of this in order to prevent drug over dosage.  
If the patient is not sure or cannot remember taking the dose it must not be taken again  
Alcohol should be avoided (special occasions only)  
No live vaccines to be given whilst on this medication  
Consider varicella-zoster immunoglobulin after exposure to chickenpox or herpes-zoster  
Care with co prescribing. Check BNF (septrin, trimethoprim, phenytoin have antifolate action.)  
Avoid in patients (both men and women) of child bearing age. Must use contraception and for to 6 months after stopping the drug

**Patient information**

It is not a pain killer  
Take with or after food. Swallow whole and do not crush or chew the tablet(s)  
Tablet strengths are similar and colour and size is similar take care when taking mixed strengths. Hospital pharmacy dispenses 2.5mg strength tablets only.  
Take dose same day each week and take folic acid 3 days after or as prescribed by the Consultant. This helps to reduce side effects  
Only take weekly (even if package states daily.)  
Take your tablet from the bottle, and then put the bottle back where you keep it so you don’t become confused or uncertain and take too many.  
If you are uncertain of having taken your medicine, do not take it until it is next due.  
Alcohol should not be taken (special occasions only) due to effects on the liver.  
It is slow acting and can take up to 3 months before improvement is felt. Don’t be discouraged and try to persevere, particularly if suffering from transient side effects.  
Check with chemist when buying over the counter medicines.
For both men and women, fertility is affected and contraception must be used if you are of child bearing age and for 6 months after stopping this medicine. You need to stop the drug prior to conception so it is important that you speak to your Dr / Nurse first. You cannot breast feed if the drug is restarted after the baby is born. This drug should not be used as a contraceptive. Do not take indigestion remedies within 6 hours of taking the drug. Avoid septrin (cotrimoxazole) and trimethoprim. Live vaccines should not be administered – check if going abroad. Avoid aspirin based medicines or other anti-inflammatory's unless prescribed by your clinician. Avoid Alka Selzer and especially obtaining over the counter. Avoid close contact with patients recently vaccinated with live polio vaccine because of the risk of infection from faecal excretion / babies nappies. Report unexplained bleeding, bruising, sore throat, fever or malaise. If side effects persist consult your Nurse / Dr Importance of blood monitoring and responsibility for use of shared care blood monitoring booklet.
AURANOFIN (ORAL GOLD) RIDAURA

A typical dose regimen may be:- 3mg b.d. increasing to 3mg t.i.d. after 4-6 months if necessary.

Pretreatment assessment:- FBC, urinalysis, U&E's, LFT's. Check Varicella antibody status

Monitoring:-
Stabilising in secondary care Monthly FBC and urinalysis, and once stable initiate shared care
Primary care Monthly FBC and urinalysis. Patient should be asked about the presence of rash or oral ulceration at each visit.

Action to be taken:-

WBC<3.5x10^9 /l withhold until discussed with rheumatologist
Neutrophils<2.0x10^9 /l withhold until discussed with rheumatologist
Eosinophilia >0.5x10^9/l Caution with increased vigilance required
Platelets<150x10^9 /l withhold until discussed with rheumatologist
2+ proteinuria or more check MSU: If evidence of infection treat appropriately. If sterile and 2+proteinuria persists withhold until discussed with rheumatologist
Rash or oral ulceration withhold until discussed with rheumatologist
Abnormal bruising or sore throat withhold until immediate 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. If in doubt use the rheumatology contact number.
**Side effects**

Profuse diarrhoea, nausea, vomiting, mouth ulcers, stomatitis  
Cramps, headache, rash, altered taste  
Rash, dermatitis, irreversible skin pigmentation in sun exposed skin  
Proteinuria, haematuria  
Eosinophilia, leucopenia, agranulocytosis, thrombocytopenia, anaemia, pancytopenia, neutropenia, bruising, bleeding  
Rarely –  
Alopecia, colitis, peripheral neuritis, pulmonary fibrosis, nephrotic syndrome

**Prescribing issues**

Check results prior to the issuing of further prescriptions  
Start dose is 3mg (one tablet) daily for four weeks. This can be increased.  
This is done within the secondary setting  
Preferable to avoid live vaccines  
Alcohol in moderation  
Contraception should be used in patients of child bearing age.  
Pregnancy should be avoided whilst on this drug and for 3 months after stopping the drug

**Patient information**

It is not a painkiller  
Take with water after meals at the same time each day. This will help to reduce stomach upsets. Swallow whole and do not crush or chew.  
Alcohol can be taken in moderation  
It is slow acting and can take up to 3 months before improvement is felt Don’t be discouraged and try to persevere particularly if you are suffering from transient side effects  
Check with the chemist when buying over the counter medicines  
Avoid pregnancy and for 3 months after stopping the drug. If you are planning a family speak to your Nurse / Dr  
If side effects persist consult your Nurse / Dr. Report any fever, infection, bleeding, bruising, metallic taste, rashes, mouth ulcers, breathlessness, cough  
Importance of blood monitoring and responsibility for use of shared care blood monitoring booklet
CICLOSPORIN

A typical dose regimen may be:- 2.5mg/kg/day in 2 divided doses increasing after 4 weeks by 25mg increments to a maximum of 4mg/kg/day. Ciclosporin is contraindicated in patients with abnormal renal function or uncontrolled hypertension. There are numerous drug interactions involving ciclosporin and it is recommended that the data sheet is consulted at the time of first prescription and if any other drugs are introduced. In particular, the dose of diclofenac should be halved if ciclosporin is co-prescribed. Colchicine and nifedipine should be avoided. Potassium sparing diuretics should be used with caution. Grapefruit juice should be avoided. Live vaccines should be avoided in patients taking ciclosporin. Experience with ciclosporin in rheumatoid arthritis is relatively short. 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 data sheet.

Pretreatment assessment:- FBC, U&E's (x2), creatinine (x2, 2 weeks apart to obtain a mean value), creatinine clearance, LFT’s, fasting lipids. Blood pressure: should be ≤ 140/90 on 2 separate occasions (2 weeks apart) prior to treatment. If greater than this treat hypertension before starting ciclosporin. Check Varicella antibody status.

Monitoring:-
Stabilising in secondary care HIGHLIGHT TARGET DOSE FOR MONITORING NURSES IN NOTES AND GP LETTER. Watch when NSAID added, particularly diclofenac
FBC, LFTs, U&E’s and BP fortnightly until the dose has been stable for 3 months and thereafter monthly. Monthly until dose stable for 3 months and then 3 monthly and at this point initiate shared care
Primary care BP (maintain ≤ 140/90), U&E’s, LFT’s and FBC, 3 monthly and serum lipids 6 monthly. Annual flu vaccine should be given.

Action to be taken:-
Creatinine rises by 30% of baseline Repeat in one week and if still >30% above baseline withhold until discussed with rheumatologist
Abnormal bruising withhold until discussed with rheumatologist
Potassium rises to above normal range withhold until discussed with rheumatologist
BP rise to abnormal range ≥140/90 two consecutive readings 2 weeks apart Treat BP before stopping ciclosporin (note interactions with several anti-hypertensives). If BP cannot be controlled, stop ciclosporin and obtain BP control before restarting. Discuss with rheumatologist
Significant rise in lipids withhold until discussed with rheumatologist
Platelets<150x10^9 /l withhold until discussed with rheumatologist
>2-fold rise in AST, ALT or Alk. Phos (from upper limit of reference range) withhold LFT result available

Use contact telephone number if in doubt
Side effects
Nausea, vomiting, abdominal discomfort, dose dependent rise in serum creatinine and urea
Less common-
Tinnitus, tremor, paraesthesia, muscle weakness, fatigue, cramps, headaches,
Gum hyperplasia, sore throats, weight gain, skin rashes, increased body hair
Hypertension
Haematuria, proteinuria,
Hyperkalaemia, hyperuricaemia, hepatotoxicity
Rise in lipids

PRESCRIBING ISSUES
Check results prior to the issuing of further prescriptions
Several important drug interactions include, erythromycin, ketoconazole, calcium channel blockers (except nifedipine), aminoglycosides, amphotericin b, ciprofloxacin, trimethoprim, can affect certain oral contraceptives. Check BNF before co prescribing
Teratogenic effects
Patient to avoid grapefruit juice and grapefruit
The drug is available in capsules or solution. The taste of the liquid can be improved by dilution with orange juice, squash or apple juice
The drug can affect the clearance of steroids and non-steroidal anti-inflammatory drugs so great care should be taken monitoring the renal function
No live vaccines should be given whilst on this therapy and other vaccinations may be less effective, but flu vaccine should be given

Patient information
It is not a pain killer
Take drug with a glass of water after a meal. Avoid grape fruit juice whilst on this drug as it can increase the risk of side effects, cause a build up of the drug in your system and interfere with the drug uptake in your system
You can take alcohol in moderation
Daily treatment is 150mg to 175mg and varies depending on your weight
It is slow acting therefore can take up to 3 months before improvement is felt. Don’t be discouraged and try to persevere particularly if suffering from transient side effects
Check with chemist when buying over the counter medicines. Avoid over the counter non-steroidal anti-inflammatory and aspirin based medicines eg Anadin, AlkaSeltzer. Also indigestion remedies or medication for blood pressure or heart disease. You must check with your Dr first, especially if you are taking treatment for gout.
Women of child bearing age must use a reliable method of contraception and for 3 months after stopping the drug
If side effects persist consult your Dr / Nurse
Importance of blood monitoring and responsibility for use of shared care monitoring booklet
AZATHIOPRINE (IMURAN)

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. If allopurinol is co-prescribed the dose of azathioprine must be cut to 25% of the original dose. Live vaccines should be avoided in patients taking azathioprine.

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&E’s, creatinine, LFT’s. Check TMPT status

Monitoring:
Stabilising in secondary care FBC and LFT’S weekly for 6 weeks and continue every 2 weeks until stable for 6 weeks; then monthly, 2 and 4 weeks after each dose increase and thereafter monthly.
Primary care Monthly FBC and LFT’s and if remains stable consider discussing with the patient to reduce monitoring to 3 monthly. U&E’s should be repeated 6 monthly. In people heterozygote for TPMT, monitoring should continue at monthly intervals at minimum. Pneumovax and annual ‘flu vaccine should be given.
Following dose change repeat FBC and LFT’s after dose change then monthly.

Action to be taken:-
WBC <3.5.0x10^9/l withhold until discussed with rheumatologist
Neutrophils<2.0x10^9 /l withhold until discussed with rheumatologist
Platelets<150x10^9 /l withhold until discussed with rheumatologist
>2-fold rise in AST, ALT or Alk. Phos (from upper limit of reference range) withhold until discussed with rheumatologist
Rash or oral ulceration withhold until discussed with rheumatologist
MCV>105fl investigate and if B12 or folate low start appropriate supplementationcheck TSH.

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. If in doubt use the contact number.
**Side effects**
Malaise, dizziness, skin rashes, sore throat, fever
Vomiting, nausea, diarrhoea, rarely pancreatitis
Bone marrow suppression, pancytopenia, neutropenia, bruising, bleeding
Fever, rigours, susceptibility to infections, jaundice, hypertension
Rarely- alopecia, pancreatitis and pneumonitis

**Prescribing issues**
Check results prior to the issuing of further prescriptions
Start dose is 25-50 mg daily orally. Patients are stabilised within the secondary setting.
Tablets are in 25mg, 50mg strengths and are similar
Several important drug interactions including allopurinol (reduce dose with concomitant allopurinol). Check BNF before co prescribing
No live vaccines to be given whilst on this medication
Consider patient for varicella-zoster vaccine after exposure to chickenpox or herpes-zoster
Teratogenic effects

**PATIENT INFORMATION**
It is not a pain killer
Tablet strengths look similar. Take care when taking mixed strengths
Take with a glass of water after a meal
Alcohol can be taken in moderation
It is slow acting therefore can take up to 3 months before improvement is felt. Don’t be discouraged and try to persevere, particularly if you are suffering from transient side effects
Check with the chemist when buying over the counter medicines
No live vaccines whilst on this medication
Avoid pregnancy and for 3 months after stopping the drug. Use reliable contraceptives. No breast feeding
Avoid close contact with patients recently vaccinated with live polio vaccine because of the risk of infection from faecal excretion/babies nappies
If side effects persist consult your Dr / Nurse
Importance of blood monitoring and responsibility for use of shared care monitoring booklet
If you notice a continuing sore throat, or you feel as if you are suffering from a heavy cold you should contact your DR immediately. You may need to have a blood sample taken and adjustment of your Azathioprine dose.
**CYCLOPHOSPHAMIDE**

IT IS RARE TO HAVE SHARED CARE MONITORING OF PATIENTS ON THIS DRUG. For completeness, monitoring information has been included in this protocol. IF IN ANY DOUBT, CONTACT CONSULTANT.

Prior to treatment in the secondary setting: FBC, U&E’s, Creatinine, Urinalysis, Check Varicella antibody status

**Investigations**
- FBC
- Urinalysis
- LFT’s
- U&E’s

**Monitoring**
At commencement of therapy: every week for three months whilst the patient is stabilised in the secondary setting then monthly as shared care is initiated with the GP, PrN, DN. Abnormal results can be discussed with the rheumatology team.

**FBC**
Stop if
- WBC < 3.5 x10^9/L
- Neutrophils < 2.0 x10^9/L
- Platelets < 150 x 10^9/L
Or if sequential fall of >10% in three counts

**Macrocytosis**
Check B12 and folate levels

**LFT’s**
Stop if transaminase twice normal

**U+E’s**
Stop and seek advice

**Renal Impairment**
Stop if
- Proteinuria + +
- Haematuria + +
Unless MSU shows infection

**Urinalysis**
Stop if

**Rash, Mouth ulcers**
Stop

**Unexplained fever/flu like illness**
Stop
Side effects
Bone marrow suppression, leucopenia, thrombocytopenia, anaemia
Nausea and vomiting, mouth ulcers
Irregular menstrual periods
Alopecia, hyper-pigmentation of the skin
Teratogenic effects
Gastric toxicity
Rare but very serious - Haemorrhagic cystitis
If in doubt use tel contact no. A rapid fall or a consistent downward trend in any value should prompt caution and extra vigilance.

Prescribing issues
Check results prior to the issuing of further prescriptions. Prescribed by experienced practitioners only.
Start dose 50-100mg per day. It depends on body weight. Low doses of tablets can be taken once per day. High doses can be taken less often.
Patients are stabilised within the secondary setting
Due to gastric toxicity patients are maintained on Ranitidine 150mg throughout treatment. In addition adjustment to the dose is vital if there is significant renal impairment.
Mesna can be prescribed to help prevent symptoms of cystitis.
ANY SUGGESTION OF CYSTITIS STOP AND DO NOT RESTART
No live vaccines to be given whilst on this medication
Consider patient for varicella-zoster immunoglobulin after exposure to chickenpox or herpes-zoster
Check BNF when co-prescribing. Drug interactions include Allopurinol, Sulphonylureas

Patient information
It is not a pain killer
Take with or after food and plenty of water. Swallow whole and do not crush or chew.
Alcohol in moderation
It is slow acting therefore can take up to 3 months before improvement is felt. Don’t be discouraged and try to persevere, particularly if suffering from transient side effects
Check with the chemist when buying over the counter medicines
Avoid close contact with patients recently vaccinated with live polio vaccine because of the risk of infection from faecal infection
Reliable contraception is required (for both men and women) and pregnancy should be avoided. Consult your Nurse / Dr if you wish to become pregnant prior to stopping the drug. No breast feeding.
Report any blood in your urine to the Dr / Nurse immediately. You should increase the number of non-alcoholic drinks each day to the equivalent of 8-10 glasses of water.
The Dr may prescribe a drug to reduce the risk of cystitis
You can be more likely to develop infections. If you do contact your Dr
If you have any side effects consult your Dr or Nurse immediately
Importance of blood monitoring and responsibility for use of sharedcare blood monitoring booklet
MYOCRISIN (GOLD INJECTION) SODIUM AUROTHIOMALATE

A typical dose regimen may be: 10mg test dose (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 1g has been administered no response has occurred treatment should be stopped.

Pretreatment assessment: FBC, urinalysis, U&E's, serum creatinine, LFTs. Check Varicella antibody status

Monitoring: Stabilising in secondary care FBC and urinalysis at the time of each injection. (This is usually weekly for 3/12) 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.

Primary care Monthly FBC and urinalysis

Action to be taken:

- WBC<4.0x10^9/l withhold until discussed with rheumatologist
- Neutrophils<2.0x10^9/l withhold until discussed with rheumatologist
- Platelets<150x10^9/l withhold until discussed with rheumatologist
- >1+ proteinuria on >1 occasion withhold until discussed with rheumatologist
- Rash or oral ulceration withhold until discussed 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. If in doubt use the contact number.
**Side effects**

Mouth ulcers, stomatitis, altered taste  
Skin rash, pruritus  
Bruising, bleeding, epistaxis  
Diarrhoea (persistent), nausea, vomiting  
Leucopenia, eosinophilia, agranulocytosis, thrombocytopenia, anaemia, pancytopenia  
Proteinuria, haematuria  
Skin pigmentation  
Rarely - pulmonary fibrosis, colitis, nephrotic syndrome, alopecia peripheral neuropathy

**PRESCRIBING ISSUES**

Check results prior to giving injection and issuing of further prescriptions  
Test dose is 10 mg. 20-50mg weekly for 3 months or until there is a response.  
The patient is stabilised within the secondary setting. 50mg monthly thereafter  
Test dose to check for reaction  
Wait 30 mins post injection  
Teratogenic effects

**Patient information**

Not a pain killer  
Test dose given initially  
Injection in muscle on a weekly basis then less often once stabilised  
Injection site rotated  
May increase joint pain and stiffness a few hours after the injection  
Re schedule injections for holidays  
You can take alcohol in moderation  
It is slow acting therefore can take up to 3 months before improvement is felt.  
Don’t be discouraged, particularly if suffering from transient side effects  
Check with chemist when buying over the counter medicines  
Avoid pregnancy and for 3 months after stopping the drug. Use a reliable form of contraception. No breast feeding  
If side effects persist consult your Dr / Nurse  
Importance of blood monitoring and responsibility for use of shared care monitoring booklet
LEFLUNOMIDE (Arava)

A typical dose regimen may be: - 100mg daily for three days followed by 20mg daily. This can be reduced to 10mg daily if poorly tolerated. Loading dose 100mg per day for three days (regime may vary depending on consultant). Maintenance dose 10 – 20mg per day.

Pretreatment assessment: - FBC, LFTs, U&Es and Blood pressure. Blood pressure: should be ≤ 140/90 on 2 separate occasions (2 weeks apart) prior to treatment. If greater than this treat hypertension before starting. (Exclude pregnancy). Weight: to allow assessment of weight loss: this may be attributable to leflunomide. Check Varicella antibody status

Monitoring:
Stabilising in secondary care Weight, FBC, LFT’s and blood pressure four weeks for the first six months and then if stable eight weekly. Once stable initiate shared care. If co-prescribed with another immunosuppressant or potentially hepatotoxic agent monthly monitoring should be undertaken.
Primary care FBC, LFT’s and BP and weight every 8 weeks. If co-prescribed with another immunosuppressant or potentially hepatotoxic agent monthly monitoring should be undertaken.

Action to be taken: -

WBC < 3.5x10^9/l 
withhold until discussed with rheumatologist

Neutrophils < 2x10^9/l 
withhold until discussed with rheumatologist

Platelets < 150x10^9/l 
withhold until discussed with rheumatologist

>2-fold rise in ALT or AST 
(withdraw until discussed with rheumatologist)
(from upper limit of reference range)

If the current dose is more than 10mg daily reduce the dose to 10mg daily and recheck weekly until normalized. If the AST & ALT is returning to normal, leave on 10mg daily. If LFT’s remain elevated withdraw the drug and discuss with the rheumatologist.

Rash, itch or mouth ulcers 
withhold until discussed with rheumatologist

Consider dosage reduction with or without antihistamines: if severe stop and consider washout procedure. See Appendix D.

Hair loss 
Consider dosage reduction: if severe stop and consider washout procedure. See Appendix D.
Abnormal bruising or sore throat  withhold until immediate FBC result
Available

Hypertension  
If BP >140/90 treat in line with NICE Guidance. If remains uncontrolled, stop Leflunomide and consider washout (Appendix D)

Headache  
if severe consider dosage reduction
If persist consider washout (Appendix D)

GI upset (nausea, diarrhoea)  
if loading dose has been used, give symptomatic treatment. If steady state has been reached, give symptomatic treatment and consider dosage reduction. If symptoms are severe or persistent, stop and consider washout (Appendix D)

Weight loss  
monitor carefully. If >10% weight loss with no cause identified, reduce dosage and stop. Consider washout (Appendix D)

Breathlessness  
if increasing shortness of breath occurs, Stop and consider washout (Appendix D)

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. If in doubt ring the contact telephone number.
Side effects

Leflunomide may cause blood dyscrasias, hepatotoxicity, mouth ulcers, skin rash (including Stevens–Johnson syndrome and toxic epidermal necrolysis), mild increase in blood pressure, GI upset, weight loss, 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 8G tid or activated charcoal 50G qid, each for 11 days is available. Leflunomide increases susceptibility to infections which should be treated promptly.

Live vaccines are contraindicated.
Diarrhoea, nausea, vomiting, anorexia, oral mucosal disorders, abdominal pain, weight loss, alopecia, eczema, rash, pruritis, leucopenia

Hypertension, headache, dizziness, asthenia, paraesthesia, tenosynovitis,

Rarely –

Epidermal necrolysis
Hypophosphataemia, anaemia, hypokalaemia, eosinophilia,
thrombocytopenia, pancytopenia

Liver dysfunction
Taste disturbance
Anxiety
Tendon rupture
Stevens Johnson syndrome

Drug eliminating wash out procedure available. See appendix C
If in doubt use contact telephone number

Prescribing issues
Usually used in those who have failed other DMARDs
Check results prior to issuing a new prescription
Loading dose 100mg per day for three days (regime may vary depending on consultant). Maintenance dose 10 – 20mg per day. Patient is stabilised within the secondary setting
Nb several important drug interactions (including warfarin, phenytoin, tolbutamide, cholestyramine and rifampicin). Check BNF before co prescribing

Care prior to treatment if on other DMARDs. Can lead to increased side effects, such as hepatoxicity, haematoxicity
Long half life
Avoid hepatic impairment, pregnancy.
Essential contraception and for 2 years after stopping the drug in women.
Male and female patients should not procreate within 2 years of discontinuing leflunomide.

Men wishing to father a child should be referred back to the Consultant, and must use adequate contraception in the interim.
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. Blood concentrations of its active metabolite should be measured 2 years after discontinuation before pregnancy occurs

Patient information
It is not a pain killer
Tablet(s) should be swallowed whole, not crushed or chewed. Take with liquids and can be taken with or without food. It is slow acting therefore can take up to 3 months before improvement is felt. Don’t be discouraged and try to persevere, particularly if suffering from transient side effects. Check with the chemist before buying over the counter medicines. Reliable contraceptives must be used as pregnancy must be avoided whilst on this medicine and for two years after stopping treatment for women. You must contact your Dr / nurse immediately if you suspect you are pregnant or if you wish to plan for a family. No breast feeding. Both male and females should use contraception for 6 months after stopping treatment. Alcohol should be avoided. If side effects persist consult your Dr / Nurse. Importance of blood monitoring and responsibility for use of shared care monitoring booklet.
MYCOPHENOLATE (MOFETIL, CELLCEPT)

A typical dose regimen may be:- 500mg daily for the 1st week, 500mg and increase it gradually by 500mg twice daily for the 2nd week and increase it gradually by 500mg each week until the optimal or maximum tolerated dose is achieved. Typical dose is 1-2g/day, maximum dose is up to 3g/day. (250mg capsules). Excess alcohol should be avoided. Live vaccines should be avoided. Annual flu vaccine should be given.

Pretreatment assessment:- FBC, U&E's, LFT's, Chest X-ray. Exclude pregnancy

Monitoring:-
Stabilising in secondary care FBC weekly for 4 weeks, fortnightly for 8 weeks and when stable monthly thereafter. Once stable initiate shared care.
Primary care Monthly FBC

Action to be taken:-
WBC <3.5x10^9/l withhold until discussed with rheumatologist
Neutrophils<2.0x10^9 withhold until discussed with rheumatologist
Platelets<150x10^9 /l withhold until discussed with rheumatologist
Abnormal bruising or sore throat withhold until immediate 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. If in doubt use rheumatology contact number.
**Side effects**

GI disturbance including nausea, vomiting, diarrhoea, weight loss, intestinal ulceration
Hepatitis, jaundice, pancreatitis
Oedema, tachycardia, hypertension, hypotension
Vasodilatation, cough, dyspnoea
Tremor, dizziness, headache
Influenza-like syndrome
Infections; viral, bacterial and fungal – CAUTION vigilance required
Rash, alopecia, acne
arthralgia
Leucopenia, thrombocytopenia, pancytopenia, anaemia
Increased susceptibility to skin cancer
Disturbances of electrolytes and blood lipids
Malignancies – increased incidence of non-Hodgkin’s lymphoma

**Prescribing issues**

Check results prior to the issuing of further prescriptions
Start dose 500mg once daily with option of increasing to twice daily depending on disease control and consultant. This is done in the secondary setting.
Alcohol on special occasions only
No live vaccines to be given whilst on this medication particularly yellow fever
Consider varicella-zoster immunoglobulin after exposure to chickenpox or herpes-zoster
Care with co prescribing – check BNF
Mycophenolate can reduce the absorption of Digoxin
Absorption of Mycophenolate reduced by antacids, Phenytoin, Iron,
Colestyramine and plasma concentrations reduced by Sevelamer
Avoid concomitant use Clozapine due to increase risk of agranulocytosis
Mycophenolate increases plasma concentrations of some antivirals – check BNF
Avoid in patients (both men and women) of child bearing age. Must use contraception and for to 6 weeks after stopping the drug

**Patient information**

It is not a pain killer
Take with or after food. Swallow whole and do not crush or chew the capsule(s)
Tablet strength 500mg.
Alcohol should not be taken in small amounts (special occasions only) due to effects on the liver.
It is slow acting and can take up to 3 months before improvement is felt. Don’t be discouraged and try to persevere, particularly if suffering from transient side effects.
Let your health care professional know if you have infection or flu like symptoms
Check with chemist when buying over the counter medicines.
Avoid exposure to strong sunlight
For both men and women, fertility is affected and contraception must be used if you are of child bearing age and for 6 months after stopping this medicine. You need to stop the drug prior to conception so it is important that you speak to your Dr / Nurse first. You cannot breast feed if the drug is restarted after the baby is born. This drug should not be used as a contraceptive. Live vaccines should not be administered – check if going abroad. Avoid close contact with patients recently vaccinated with live polio vaccine because of the risk of infection from faecal excretion / babies nappies. Report unexplained bleeding, bruising, sore throat, fever or malaise. If side effects persist consult your Nurse / Dr. Importance of blood monitoring and responsibility for use of shared care blood monitoring booklet.
5. CLINICAL RESPONSIBILITY

Nurses should be familiar with:

The NMC’s Code of Professional Conduct 2000

The NMC’s ‘Guidelines for the Administration of Medicines’ Oct 2000 which is currently under review.

The NMC’s ‘Guidelines for Records and Record Keeping’ (1993).

The NMC’s ‘Scope for Professional Practice’ (1992)

The patient on DMARD therapy must be seen by a qualified health care professional in order to be assessed for side effects and to undertake any action necessary according to this protocol.
6. PATIENT EDUCATION AND TEACHING

Patient information highlighted in this document is that which is given to patient in the secondary setting, as they are stabilised on their treatment. It is intended to raise health care professionals’ awareness of the information, which has been given to the patient. It can therefore also be used to reinforce the same information to the patient when seen in the primary health care setting. This patient information must be given alongside the manufacturer’s patient information leaflet.

Patients have a legal, ethical and moral right to information about their medication. Information given should reflect standards, protocols and guidelines used in the delivery of care.

Patients being treated with DMARD therapy should have a clear understanding of their medication including dosage, route, mode of action, side effects and goals of therapy.

The importance of attending appointments for blood monitoring must also be reinforced, alongside patient responsibility and ownership of their treatment and care.

Patients must be made aware of the importance of seeking help should side effects cause concern and have the contact telephone numbers for ease of access to the appropriate health care professionals.

0191 3332333 is the contact no for UHND and ask to be put through to the rheumatology department. Also see list of contacts in section 8. It is important that the patient is kept fully informed of their treatment regimen and reasons for adjustments in dosages.

Patients should be instructed about the appropriate way to take their medication and the consequences of non-compliance.

Patient ownership / sharing responsibility of DMARD therapy may be reinforced by all health care professionals across the interface. The patient must be encouraged to be an active participant in care.

To assist with this process there are a number of resources available:

- Clinical Nurse Specialist in Rheumatology
- Blood Monitoring Nurses
- Patients own Consultant / GP
- Pharmacist
- Patients shared care information booklet
- Patients information leaflets
- ARC information leaflets
- Shared care blood monitoring protocol
- Pharmaceutical literature as discussed
7. SUMMARY
of the shared care protocol
and what to do in the PHCT GP surgery

1. Establish which DMARD(s)

2. Determine which investigations to be undertaken:
   blood
   urinalysis
   blood pressure

3. Check previous results and development of any side effects.

4. Repeat prescriptions should only be prescribed if monitoring results are within normal limits.

5. Monitoring results which are not within normal limits should be discussed with the GP / Dr prior to refilling of prescription.

6. Contact numbers are available should further discussion or information be required with Consultant or Specialist Nurse.

7. Check shared care monitoring book for changes in dosage prescribed, and any previous blood monitoring results.


9. Assess patients understanding and compliance of prescribed drug, particularly if recently increased and where differing strengths of the same DMARD are required to make up the dose.

10. Arrange next appointment for monitoring.

11. If in doubt at any stage, seek advice.
8. CONTACTS

DEPARTMENT OF RHEUMATOLOGY
UNIVERSITY HOSPITAL OF NORTH DURHAM
NORTH ROAD
DURHAM
DH1 5TW
TEL: 0191 3332333
FAX: 0191 3332581

CLINICAL NURSE SPECIALIST’s in RHEUMATOLOGY

LYNDA GETTINGS (Lead) (Not Monday)
0191 – 3332333
BLEEP 2581

BELINDA ROBINSON (Biologics) (Wednesday and Friday only)
0191 – 3332333
PAGER 07699621034

CONSULTANT RHEUMATOLOGISTS
0191 – 3332333
DR A CHUCK (Not Monday)
EX 2584 / 2588

DR P MANGION (Locum)
EX 2580 / 2581

DR S HAILWOOD
EX 2582 / 2583 (Not Thursday)

Dr N KUMAR
EX 2507 / 2583 (Not Friday)

SPECIALIST REGISTRAR
BLEEP 2091

BLOOD MONITORING NURSES:
S/N JOANNE GARDNER (UNIVERSITY HOSPITAL OF NORTH DURHAM)
EX.2380 (OUT PATIENTS DEPT.)

S/N KAREN KENNEDY (SHOTLEY BRIDGE GENERAL HOSPITAL)
TEL. 01207 214503 (OUT PATIENTS DEPT)

S/N BELINDA ROBINSON (CHESTER-LE-STREET) (Monday, Tuesday and Thursday)
EX. 3632/ 3631 (OUT PATIENTS DEPT.)

PHARMACY DEPT. UHND
EX. 2458
9. GLOSSARY OF TERMS

**ACR**  American College of Rheumatology

**Agranulocytosis**  severe acute deficiency of neutrophils as a result of toxic drugs. It is characterised by fever, with ulceration of the mouth and throat. May lead to rapid prostration and death.

**BSR**  British Society for Rheumatology

**CRP**  c-reactive protein

**DMARD**  disease modifying anti-rheumatic drug

**ESR**  erythrocyte sedimentation rate

**FBC**  full blood count

**Haemolytic anaemia**  anaemia due to the destruction of red blood cells

**Hb**  haemoglobin

**Leucopenia**  a reduction of the no. of leucocytes in the blood

**LFT’s**  liver function tests

**Neutropenia**  a decrease of the no. of neutrophils in the blood. Occurs in aplastic anaemias, agranulocytosis and acute leukaemias. It results in an increased susceptibility to infections.

**NSAID**  non steroidal anti-inflammatory drug

**Megaloblastic anaemia**  a megaloblast is an abnormal form of erythroblast. Megaloblast are usually large and their nuclei fail to mature in the normal way; they are seen in the bone marrow in certain anaemias due to deficiency of vitamin b12 or folic acid.

**RA**  rheumatoid arthritis

**Teratogenesis**  the process leading to developmental abnormalities in the fetus

**Thrombocytopenia**  a reduction of the no. of platelets in the blood. Results in purpura, spontaneous bruising and prolonged bleeding after injury.

**Transaminase**  enzyme involved in the transamination process involved in the metabolism of amino acids. Lfts.

**Pancytopenia**  a simultaneous decrease in the number of red cells, white cells and platelets in the blood.
10. APPENDIX

APPENDIX A: INVESTIGATIONS

NORMAL LABORATORY VALUES ARE INDICATED ON RESULT FORMS. Abnormal values are highlighted in bold print and marked with a star **BUT BE AWARE OF WBC and NEUTROPHIL VALUES** as these will not be highlighted. Guidance values differ to values to be monitored and these are not highlighted with stars when out side of the range being monitored.

HAEMATOLOGICAL

Haemoglobin (Hb) The typical anaemia of RA is normochromic normocytic anaemia and probably results from an suppressing bone marrow activity by active inflammation. A microcytic (low mean corpuscular volume MCV) is mainly due to iron deficiency and may indicate gastointestinal blood loss often attributed to the use of non-steroidal anti-inflammatory drugs. The use of sulfasalazine EN (salazopyrin EN)and methotrexate can cause a folate deficiency anaemia (macrocytic anaemia.)

White blood cell count (WBC) This should be reviewed with the differential WBC showing the proportion of neutrophils and lymphocytes that make up the total number of circulating WBC’s. Leucocytopenia, neutropenia and thrombocytopenia can occur in a patient with RA due to marrow suppression from DMARD.

Platelet count. A reduction can be due to a bone marrow suppressing DMARD, or occasionally as a feature of active disease.

Erythrocyte sedimentation rate (ESR) If inflammation is present in the body the ESR rises. This is partly due to the changes in the red blood cells and also due to inflammatory proteins that are present in the patients blood. It is a standard test in rheumatology units to measure and evaluate disease activity, although some areas may use plasma viscosity (PV).

BIOCHEMICAL

Renal function. Urea and electrolytes together with creatinine are usually measured. A raised creatinine level indicates renal impairment. The renal toxicity caused by DMARDs is most likely to be seen on dipstick testing first.

Acute phase reactant (CRP) This is an inflammatory marker and is raised in an acute phase of RA. It can be used to monitor disease activity and treatment effectiveness.

Liver function tests (LFT’s) These tests reflect hepatic function and they can also indicate active. Gamma glutamyl transpeptidase (GGT) is a more specific test of hepatic damage or alcohol abuse. Alkaline phosphotase (ALP, Alk Phos) is often raised in active RA. Alanine aminotransferase (ALT) and aspartate aminotransferase (AST) are usually normal, however when dmards can cause hepato-toxicity, (abnormal LFT’s where the ALT and AST rise – transient rises of up to twice the upper limits of normal are tolerated)
APPENDIX B: VACCINATIONS

IF IN ANY DOUBT CONTACT HOSPITAL PHARMACY DEPARTMENT AND REFER TO BNF

Live vaccines should be avoided in patients taking methotrexate, cyclophosphamide, azathioprine, ciclosporin or high doses of steroids.

LIVE VACCINES:  MEASLES
RUBELLA
BCG
MUMPS
POLIOMYELITIS (OPV)
YELLOW FEVER
TYPHOID (ORAL)

INACTIVATED VACCINES:
INFLUENZA
TYPHOID (INJECTED)
POLIOMYELITIS (IPV INJECTED named patients only)
CHOLERA
DIPHTHERIA
HAEMOPHILIS INFLUENZA type B (Hib)
HEPATITIS A
HEPATITIS B
MENINGOCOCCAL A and C Conjugate
PNEUMOCOCCUS
TETANUS

(RYAN.S.1999)
APPENDIX C
VARICELLA EXPOSURE MANAGEMENT

- Varicella status should be checked at baseline prior to commencement of DMARD
- If patient unsure of status and has been exposed:
  - Window of opportunity to treat is 7 days from exposure
  - Check bloods for varicella status and IgG
  - Treat
  - Contact rheumatology department
APPENDIX D

LEFLUNOMIDE WASHOUT PROCEDURE

Wash out procedure undertaken by Consultants

Leflunomide has a long half life

To aid drug elimination in case of serious adverse events

Before starting another DMARD

Prior to conception – consult literature

1. Stop treatment
2. Give either a. Cholestyramine 8 g 3 times daily for 11 days
   b. Activated charcoal 50g 4 times daily for 11 days

The concentration of the active metabolite after washout should be less than 20 micrograms/litre measured on 2 occasions at 14 days apart.

1 day washout gets rid of \( \frac{1}{2} \)

2 day washout gets rid of \( \frac{2}{3} \)

3 day washout gets rid of \( \frac{3}{4} \)

4 day washout gets rid of \( \frac{4}{5} \) and so on
APPENDIX E:
MANAGEMENT OF SIDE EFFECTS

THE NURSE SHOULD STOP THE MEDICATION IF SIDE EFFECTS ARE SEVERE AND THERE IS NO IMMEDIATE ACCESS TO A DOCTOR. THE DOCTOR / CONSULTANT SHOULD BE INFORMED / CONTACTED AS SOON AS POSSIBLE.

IF IN DOUBT SEEK HELP AND USE THE CONTACT TELEPHONE NUMBERS

If a patient presents with:

1. A rash
   - Ask if they have recently changed their detergent, or other chemical contact. Consider sunburn, insect bites, soap, moisturisers etc
   - If isolated to an odd patch advise E45 cream
   - If unsure or severe seek help

2. Itching:
   - Ask if they have recently changed detergent, soap, moisturiser, perfume
   - Advise E45 cream if mild
   - Unbearable itching (affecting sleep) seek advice

3. With proteinuria
   - A trace or one + in isolation ignore
   - ++ on repeat testing send msu. If infection present contact patient, GP or Consultant
   - If symptomatic send msu
   - If msu reveals no infection but ++ persists contact Consultant

4. With haematuria
   - Confirm the patient is not menstruating
   - A trace or one + in isolation ignore
   - If ++ send msu and continue treatment
   - If patient has observed blood loss inform Dr
   - Contact Consultant if persistent and no infection

5. A sore mouth
   - Check dentures if worn are fitted correctly
   - For minor ulcers (ie 1 or 2 in isolation continue treatment and suggest Bonjela, Bioral gel, mouth rinse.
   - Advise to avoid hot / spicy liquids / food
   - If severe contact GP, Consultant

If the patient presents with G.I. tract side effects
- Anorexia, nausea, dyspepsia can occur with any drug
- Remember G.I. intolerance can occur with non-steroidal anti-inflammatory drugs
- DMARD dosage may be split, reduced or taken at night, depending on which DMARD it is. Seek advice from GP / Consultant

It is essential that clinicians remember to report (yellow card system) any serious adverse events (SAE) related to the use of DMARDs.
# APPENDIX F

## BLOOD COLLECTION INFORMATION

<table>
<thead>
<tr>
<th>TEST</th>
<th>TUBE</th>
<th>INSTRUCTIONS</th>
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<tbody>
<tr>
<td>Autoantibodies</td>
<td>White with yellow ring</td>
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</tr>
<tr>
<td>B12 and Folate</td>
<td>Ochre / Lavender</td>
<td></td>
</tr>
<tr>
<td>Biochemistry</td>
<td>Ochre</td>
<td></td>
</tr>
<tr>
<td>Calcium</td>
<td>Ochre</td>
<td></td>
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<td>Complements</td>
<td>Ochre</td>
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<tr>
<td>Circulating Immune Complex</td>
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<tr>
<td>CRP</td>
<td>Ochre</td>
<td></td>
</tr>
<tr>
<td>ESR</td>
<td>Black top glass tube</td>
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<tr>
<td>FBC</td>
<td>Lavender</td>
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<td>Ferritin</td>
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<td>FSH</td>
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<td>Protein and Electrophoresis</td>
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<td>Reticulocyte Count</td>
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<td>Thyroid</td>
<td>Ochre</td>
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<td>U &amp; E</td>
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<td>H Pylori</td>
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<td>Microbiology</td>
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For a comprehensive list, ring lab at UHND.
APPENDIX G

EARLY DIAGNOSIS AND REFERRAL:

1. DIAGNOSTIC CRITERIA FOR RHEUMATOID ARTHRITIS

American Rheumatism Association (ACR) 1987 revised criteria for the classification of rheumatoid arthritis (RA)

- Morning stiffness – in and around the joint areas; soft tissue swelling or fluid (not bony overgrowth alone) in at least 3 joints simultaneously; possible joint areas; proximal interphalangeal; metacarpophalangeal; wrist; elbows; knee; ankle; or metatarsophalangeal.

- Arthritis of hand joints – at least one joint area swollen in wrist, proximal interphalangeal or metacarpophalangeal joints.

- Symmetrical arthritis – simultaneous involvement of the joint areas as above on both sides of the body (bilateral involvement of proximal interphalangeal, metacarpophalangeal or metatarsophalangeal joints is acceptable without symmetry).

- Rheumatoid nodules – subcutaneous nodules over bony prominences or extensor surfaces or in juxta-articular regions.

- Serum rheumatoid factor – demonstration of abnormal amounts of serum rheumatoid factor by any method that has been positive in less than 5% of normal control subjects.

- Radiographic changes – radiographic changes typical of RA on posterior/anterior hand and wrist radiographs, which must include erosions or unequivocal bony decalcification localised in, or most marked adjacent to, the involved joints (osteoarthritis changes alone do not qualify).

Note: For classification purposes a patient has RA if at least 4 of these criteria are satisfied (criteria 1 to 4 must have been present for at least six weeks).

European League Against rheumatism (EULAR) recommendations for the management of early arthritis:

- Arthritis of one joint with swelling, pain and stiffness should be seen by a rheumatologist ideally within 6 weeks after the onset of symptoms.

- Clinical examination is the method of choice in detecting synovitis. Doppler ultrasound and magnetic resonance imaging might also be helpful in detecting synovitis.

- In patients presenting with early arthritis to the rheumatologist, the following factors predict persistent and erosive disease and should be measured. These include number of tender and swollen joints, erythrocyte sedimentation rate (ESR) or C-reactive protein (CRP), levels of rheumatoid factor and anti-cyclic citrullinated peptide antibodies and radiographic erosions.

- Exclusion of disease other than RA requires careful history taking and clinical examination and ought to include at least the following laboratory tests; complete blood cell count, urinalysis; transaminases and anti-nuclear antibody.
• Patients at risk of developing persistent and/or erosive disease should be started with disease-modifying anti-rheumatic drugs (DMARDs) as early as possible even if they do not yet fulfill established classification criteria for inflammatory rheumatological diseases.

• Patient information concerning the disease and its treatment and outcomes is important. Education programmes aiming at coping with pain, disability and maintenance of work ability may be employed as adjunct interventions.

• Non-steroidal anti-inflammatory drugs have to considered in symptomatic patients after evaluation of gastrointestinal, renal and cardiovascular status.

• Systemic glucocorticosteroids reduce pain and swelling and should be considered as an (mainly tempory) adjunct therapy as part of the DMARD strategy. Intra-articular glucocorticosteroid injections should be considered for the relief of local symptoms of inflammation.

• Among DMARDs, methotrexate is considered the anchor drug, and should be used first in patients at risk of developing persistent disease.

• The main goal of DMARD therapy is to achieve remission. Regular monitoring of disease activity and adverse event should guide decisions on choice and changes in treatment strategies (DMARDs including biologicals).

• Non-pharmacological interventions such as dynamic exercises, occupational therapy and hydrotherapy can be applied as treatment adjuncts to pharmacological interventions in patients with early arthritis.

• Monitoring of disease activity should include tender and swollen joint count, patient's and physician's global assessments, ESR and CRP. Arthritis activity should be assessed at 1 and 3 month intervals as long as remission is not achieved. Structural damage should be assessed by radiographs of hands and feet every 6 to 12 months during the first few years of treatment. Functional assessment, for example health assessment questionnaires, can be used to complement the disease activity and structural damage monitoring.

2. CLINICAL GUIDANCE IN EARLY DIAGNOSIS OF RA

Clinical suspicion of rheumatoid arthritis may be supported by the presence of any of the following:

• Three swollen joints

• Morning stiffness that lasts more than 30 minutes

• Rheumatoid factor (positive), raised acute phase reactants, and erosions on X-ray are associated with poor outcome. The absence at presentation should not preclude diagnosis or referral.

• Non-steroidal anti-inflammatory drugs may mask signs and symptoms at presentation.

• Corticosteroids should not be prescribed without accurate diagnosis
### 11. REFERENCES

<table>
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