Paediatric Rheumatology Drug Monitoring Guidelines

Based on: Shared Care Agreement (2007) for Oxford and Heatherwood & Wexham Park; NHS-Prodigy Guidelines; British Society for Paediatric and Adolescent Guidelines

This Shared Care protocol provides a monitoring schedule for routine disease modifying anti-rheumatic drugs (DMARDs), which may be used individually or in combination.

‘Shared care’ is here defined as ‘The joint participation of general practitioners and hospital consultants in the planned delivery of care for patients with chronic inflammatory musculoskeletal disorders, informed by an enhanced information exchange over and above the routine clinic, discharge and referral letters.’ (Hickman et al 1994)

This Protocol covers:

<table>
<thead>
<tr>
<th>DMARD</th>
<th>History, examination</th>
<th>Laboratory tests</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adalimumab</td>
<td>Mouth ulcers, Fever, chills, Bruising, pallor, Signs of other autoimmunity</td>
<td>FBC, LFTs, U&amp;Es, Monthly for 3 months; then 3 monthly dsDNA yearly</td>
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<tr>
<td>Anakinra</td>
<td>Respiratory signs and symptoms</td>
<td>FBC, Monthly for 3 months; then 3-monthly</td>
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<tr>
<td>Azathioprine</td>
<td>Fever, bruising, pallor</td>
<td>FBC, LFTs, Every 2 weeks for 6 weeks; then every 1–3 months</td>
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<tr>
<td>Ciclosporin</td>
<td>Peripheral oedema, Mouth ulcer, rash, Blood pressure</td>
<td>FBC, U&amp;Es, creatinine, Fortnightly for 6 weeks; then 1-2 monthly LFTs monthly especially if concomitant NSAIDs. Lipids every 6 months.</td>
</tr>
<tr>
<td>Cyclophosphamide (IV)</td>
<td>Fever, bruising, pallor</td>
<td>FBC, U&amp;Es, LFTs, urine dipstick, 10 days after last dose and 2 days before next</td>
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<tr>
<td>Etanercept</td>
<td>Mouth ulcers, Fever, chills, Bruising, pallor, Signs of other autoimmunity</td>
<td>FBC, LFTs, U&amp;Es, 1-3 Monthly dsDNA yearly</td>
</tr>
<tr>
<td>Hydroxychloroquine</td>
<td>Annual Visual acuity</td>
<td>—</td>
</tr>
<tr>
<td>Leflunomide</td>
<td>Mouth ulcer, rash, Blood pressure, Weight loss</td>
<td>FBC, LFTs, 2weekly for 1 month; Monthly for 12 months; then every 8 weeks</td>
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<tr>
<td>Infliximab</td>
<td>Mouth ulcers, Fever, chills, Bruising, pallor, Signs of other autoimmunity</td>
<td>FBC, LFTs, U&amp;Es, Before each infusion dsDNA yearly</td>
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<tr>
<td>Methotrexate</td>
<td>Fever, bruising, pallor, Mouth ulcer, Respiratory signs and symptoms</td>
<td>FBC, U&amp;Es, LFTs, urine dipstick, 2 weekly for 1 month; then every 1–3 months</td>
</tr>
<tr>
<td>Mycophenolate</td>
<td>Fever, bruising, pallor, Mouth ulcer</td>
<td>FBC weekly for 4 weeks; then monthly LFTs U&amp;Es ESR and CRP monthly.</td>
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<tr>
<td>Sulfasalazine</td>
<td>Mouth ulcers, Fever, chills, Bruising, pallor</td>
<td>FBC, LFTs, Fortnightly for 2 months; then 3 monthly</td>
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</tbody>
</table>

Slight variations in monitoring requirements may occur and this should be read in conjunction with:
1. The medication specific information provided by the rheumatology unit
2. manufacturers data sheet

N Wilkinson (Nov 07); based on Rheumatology Monitoring Information for GPs v4/ September 2007 / M Cox / N Kennedy / Dr Paul Bowness / Nuffield Orthopaedic Centre
Drug monitoring actions to be taken:

General guidelines:
These guidelines apply to DMARD therapy including azathioprine, methotrexate, sulphasalazine, mycophenalate, cyclosporin, and biologic treatment (anti-TNF and anakinra).

Please contact us as described below or if you have any other concerns beyond that described here.

We advise withholding medication and contacting one of the OxPARC medical team if there is:

- A rapid fall or a consistent downward trend in any value and prompt extra vigilance.
- Abnormal bruising or sore throat – withhold until FBC result available
- Unusual rash or oral ulceration that may be attributed to medication
- Unexpected fall in albumin
- New or increasing dyspnoea or cough in absence of asthma or respiratory infection

<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
<th>Action</th>
<th>Contact us:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neutrophil count</td>
<td>&lt; 1.5</td>
<td>Withhold for 2 weeks (doses) and recheck 3-4 days before 3rd dose. If returns to normal restart at usual dose</td>
<td></td>
</tr>
<tr>
<td>Platelet count</td>
<td>&lt; 140</td>
<td></td>
<td></td>
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<tr>
<td>WCC</td>
<td>&lt; 2.5</td>
<td></td>
<td></td>
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<tr>
<td>AST or ALT</td>
<td>&gt; 120</td>
<td></td>
<td></td>
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<tr>
<td>Creatinine</td>
<td>50% above normal</td>
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Drug specific guidelines:

Cyclosporin Withhold if
- Potassium rises to above 6.5
- BP rises to systolic BP > 95% for age/height

Anti-TNF therapy Withhold if
- Major surgery
- Infection requiring hospitalisation or if unusual
- Referral for medical assessment of abnormal symptom
- Presence of a positive dsDNA titre

If medication is withheld please contact us
Shared care principles and responsibilities

Background for use of DMARDs
The ultimate goals in managing rheumatological inflammatory diseases are to prevent or control joint or organ damage, prevent loss of function (physical and organ specific), and decrease pain. There is clear evidence from placebo controlled trials that DMARDs reduce symptoms, improve global well being, function, long term outcome and survival (references).

DMARDs are no different to other long term medications and present some risk to the patient of adverse events. Regular monitoring of blood tests is required to detect any side effects early, monitor disease activity and general health. The incidence of side effects is significantly reduced if monitoring is carried out in a well-organised way close to the patient’s home. It is emphasised to all patients that unless regular monitoring of blood tests is undertaken they will be unable to continue taking the medication.

The hospital will issue the patient with a yellow “shared care” booklet for recording blood results. The patient will bring this booklet to their primary care and hospital consultations.

The Rheumatology Consultant will be responsible for provision of:
• Pre treatment assessment and recommendation of the appropriate DMARD and dose.
• Pre treatment counselling to include rationale for treatment, benefits, potential side effects, precautions and monitoring requirements.
• Issue of written patient drug information, shared care monitoring booklet and contact telephone number.
• Regular review in the out-patient clinic to assess disease activity and recommend any adjustments to treatment.
• Telephone support in the event of any serious adverse reactions by a member of the medical team.
• Additional support for patients, via the rheumatology telephone help-line.
• Provision of formal or informal training as necessary to ensure that clinical staff within the primary care team have the necessary skills to ensure safe practice.

The General Practitioner will be responsible for:
• Provision of services related to the shared care agreement as listed in the GMS contract, in respect of near patient testing
• Prescribing the DMARD as per recommendation of consultant
• Ensuring blood tests are taken in accordance with the rheumatology unit information sheets and National Guidelines for the monitoring of Second Line drugs (BSR 2007)
• Checking and recording of blood test results.
• Notification to the consultant rheumatologist of any changes in the patient’s condition, any adverse drug reactions, or if the patient fails to attend for blood monitoring.
• Ensuring that all clinical staff involved in the provision of this service have the relevant knowledge and skills.

The patient will be responsible for:
• Attending for blood monitoring
• Ensuring shared care card is kept up to date
• Reporting any adverse side effects to medication to the GP or a member of the hospital rheumatology team.
• Ensuring that they bring the shared care card and a list of all medications to the surgery and out patient consultations.
Common problems and concerns

- **Side effects and drug interactions.** See individual drug monitoring sheets.
- **Patients not attending for routine blood tests.** Should your patient fail to attend for routine blood testing on more than one occasion the patient should be contacted to ascertain the reason for non attendance. It should be stressed that non attendance for blood testing may lead to withdrawal of the medication. Further help and advice can be sought from the clinical nurse specialist in paediatric rheumatology.

Instructions for referring back to the consultant team

- **Intolerance to side effects of DMARDs.** If the patient has been established on DMARD therapy, withdrawal of treatment may result in a relapse of symptoms. Therefore it is important to consider alternative therapy in the event of side effects.
- **Severe side effects/ Potential overdose.** Urgent referral to rheumatology unit or A&E.
- **Non compliance with medication or monitoring.** Refer to CNS for help and advice

Contact Numbers

<table>
<thead>
<tr>
<th>E Mail enquiries</th>
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<tbody>
<tr>
<td>Rheumatology Advice line (Answer phone)</td>
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<tr>
<td>Clinical Nurse Specialist in rheumatology</td>
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<tr>
<td>Nuffield Orthopaedic Centre. Rheumatology Registrar on call</td>
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<td></td>
</tr>
</tbody>
</table>

References / Further Information.
2. Shared Care Agreement 2007 for Rheumatology Departments in Oxford and Heatherwood & Wexham Park
3. NHS-prodigy guidelines -
   http://www.prodigy.nhs.uk/monitoring_people_on_dmards/view_whole_guidance
4. British Society for paediatric and Adolescent Guidelines -