### CICLOSPORIN for patients within adult services

<table>
<thead>
<tr>
<th>1. Background</th>
<th>Ciclosporin is a potent immunosuppressant. Indications, dose adjustments and monitoring requirements for disease modifying drugs (DMDs) (licensed and unlicensed indications) included in this Framework are in line with national guidance published by the British Society for Rheumatology 2017.</th>
</tr>
</thead>
</table>
| 2. Licensed Indications | - Rheumatoid arthritis.  
- Psoriasis in patients in whom conventional therapy is inappropriate or ineffective.  
- Atopic dermatitis when systemic therapy is required  
- Inflammatory eye disease  
**Transplant indications are not included** |
| 3. Locally agreed off-label use | - Interstitial lung disease  
- Other rheumatology indications  
- Myasthenia gravis  
- Connective tissue disease  
- Psoriatic arthritis  
- Connective tissue disease  
- Autoimmune and inflammatory kidney conditions  
- Sarcoidosis  
- Atypical neuro-inflammatory disease |
| 4. Initiation and ongoing dose regime | **Rheumatology patients managed by Wirral Trust**  
Secondary care to diagnose and provide written instructions to the GP for prescribing and escalation of treatment.  
**Other Patients**  
Transfer of monitoring and prescribing to Primary care is normally after 3 months  
**The duration of treatment will be determined by the specialist based on clinical response and tolerability**  

*Rheumatoid arthritis*  
Initiation:  
For the first 6 weeks of treatment the recommended dose is 2.5 mg/kg/day orally given in 2 divided doses. If the effect is insufficient, the daily dose may then be increased gradually as tolerability permits, but should not exceed 5 mg/kg. 

Maintenance  
The dose will be titrated individually by the specialist to the lowest effective level according to tolerability, usually 2.5 - 4mg/kg per day orally.  

*Psoriasis*  
Initiation:
The recommended initial dose is 2.5 mg/kg/day orally given in 2 divided doses. If there is no improvement after 1 month, the daily dose may be gradually increased, but should not exceed 5 mg/kg. Initial doses of 5 mg/kg/day are justified in patients whose condition requires rapid improvement.

Maintenance:
Doses have to be titrated individually to the lowest effective level, and should not exceed 5 mg/kg/day.

<table>
<thead>
<tr>
<th>Terminations of treatment will be the responsibility of the specialist.</th>
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</thead>
<tbody>
<tr>
<td><strong>Rheumatology patients managed by Wirral Trust</strong></td>
</tr>
<tr>
<td>5. Baseline investigations to be undertaken by specialist. Initial monitoring and dose titration to be undertaken by GP</td>
</tr>
<tr>
<td><strong>Other Patients</strong></td>
</tr>
<tr>
<td>5. Baseline investigations, initial monitoring and dose titration to be undertaken by specialist</td>
</tr>
<tr>
<td><strong>Baseline</strong></td>
</tr>
<tr>
<td>• Height, weight, BP, FBC, creatinine/eGFR, ALT and/or AST, albumin.</td>
</tr>
<tr>
<td>• Vaccinations against pneumococcus and influenza are recommended.</td>
</tr>
<tr>
<td>• Shingles vaccine (Zostavax) is recommended as per the JCVI for eligible patients.</td>
</tr>
<tr>
<td>• Specialist to highlight in the first clinic letter notifying the GP of the decision to initiate DMDs that the GP will need to give the shingles vaccine if the patient is older than 69 years and the pneumococcal vaccine if this has not already been given. The GP should also be advised to add the patient to the influenza vaccine list.</td>
</tr>
<tr>
<td>• Patients should be assessed for comorbidities that may influence DMD choice, including evaluation of respiratory disease and screening for occult viral infection.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Initiation</th>
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<tbody>
<tr>
<td>• FBC, creatinine/eGFR, ALT and/or AST and albumin every 2 weeks until on stable dose for 6 weeks;</td>
</tr>
<tr>
<td>• Once on stable dose, monthly FBC, creatinine/eGFR, ALT and/or AST and albumin.</td>
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</tbody>
</table>

Once patients have been stable for 12 months they can be considered for reduced frequency of monitoring, as advised by the specialist team. This monitoring consists of FBC, creatinine/eGFR, ALT and/or AST and albumin at least every 12 weeks.

BP and blood glucose should be measured at each monitoring visit.

<table>
<thead>
<tr>
<th>6. Ongoing monitoring</th>
<th>Monitoring</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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</table>
### 7. Pharmaceutical aspects

<table>
<thead>
<tr>
<th>Route of administration</th>
<th>oral</th>
</tr>
</thead>
<tbody>
<tr>
<td>Formulation</td>
<td>10mg, 25mg, 50mg, 100mg capsules, 100mg/1ml oral solution</td>
</tr>
<tr>
<td>Administration details</td>
<td>The daily doses of ciclosporin should be given in two divided doses. The solution should be diluted, preferably with orange or apple juice, however, other drinks, such as soft drinks, can be used. (Rinse with more to ensure total dose is taken). Do not mix with grapefruit juice.</td>
</tr>
<tr>
<td>Other important information</td>
<td>Concomitant intake of grapefruit juice has been reported to increase bioavailability of ciclosporin.</td>
</tr>
</tbody>
</table>

### 8. Contraindications

- Hypersensitivity to the active substance or excipients.
- Concomitant use of tacrolimus
- Abnormal renal function, uncontrolled hypertension, uncontrolled infections or any malignancy
- SPC states live vaccines should be avoided; however, JCVI and BSR recommend that oral DMD therapy at standard doses is not a contraindication in most patients, clinician discretion is advised.

### 9. Significant drug interactions

For a comprehensive list consult the BNF or Summary of Product Characteristics. [SPC]

Ciclosporin interacts with all statins and is contraindicated with rosuvastatin. [MHRA Safety alert: Statins: interactions, and updated advice for atorvastatin]

Seek advice from the initiating Specialist if there are any concerns about interactions.

### 10. Adverse Effects and managements

<table>
<thead>
<tr>
<th>Result</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abnormal bruising or severe sore throat</td>
<td>Stop drug until FBC results available, contact Specialist Nurse (SN)</td>
</tr>
<tr>
<td>Fall in WCC &lt;3.5 x 10^9/l</td>
<td>Stop drug. Contact SN for advice and management</td>
</tr>
<tr>
<td>Fall in neutrophils &lt;2.0 x 10^9/l</td>
<td></td>
</tr>
<tr>
<td>Fall in platelets &lt;140 x 10^9/l</td>
<td></td>
</tr>
<tr>
<td>Increased MCV &gt;105fl</td>
<td>Check folate, B12 &amp; TSH. Treat if abnormal, contact SN for advice if normal.</td>
</tr>
<tr>
<td>Unexplained reduction in albumin</td>
<td>Contact SN for advice and</td>
</tr>
<tr>
<td>Condition</td>
<td>Management</td>
</tr>
<tr>
<td>-----------</td>
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<tr>
<td>&lt;30g/l</td>
<td>management</td>
</tr>
<tr>
<td>Abnormal LFTs – AST or ALT &gt; 100U/l</td>
<td></td>
</tr>
<tr>
<td>'Significant' increase in fasting lipids</td>
<td></td>
</tr>
<tr>
<td>Rash:</td>
<td>Stop drug and contact SN.</td>
</tr>
<tr>
<td>Taste loss:</td>
<td>Reassure, continue drug.</td>
</tr>
<tr>
<td>Nausea, vomiting, diarrhoea</td>
<td>Discuss with SN</td>
</tr>
<tr>
<td>Increase in serum creatinine &gt;30% over period of 12 months or less OR decline in eGFR &gt; 25%</td>
<td>Contact specialist nurse if there is new or unexplained renal impairment</td>
</tr>
<tr>
<td>Hyperkalaemia:</td>
<td>Stop drug and contact SN</td>
</tr>
<tr>
<td>Hypertension:</td>
<td>Consider anti-hypertensive agent. If hypertension persists, stop drug and contact SN</td>
</tr>
<tr>
<td>Gingival hypertrophy</td>
<td>Send patient for dental advice</td>
</tr>
</tbody>
</table>

### 11. Advice to patients and carers

The specialist will counsel the patient with regard to the benefits and risks of treatment and will provide the patient with any relevant information and advice, including patient information leaflets on individual drugs.

### 12. Pregnancy and breast feeding

Ciclosporin can be used during pregnancy at the lowest effective dose after considering the potential risks and benefits. BP, renal function and drug level should be monitored.

Mothers receiving treatment with ciclosporin should not be discouraged from breastfeeding.

(“SR & BHPR guideline on prescribing in pregnancy and breastfeeding”)

### 13. Specialist contact information

See appendix 2

### 14. Additional information

Where patient care is transferred from one specialist service or GP practice to another, a new shared care agreement must be completed.

### 15. References

See appendix 2

### 16. To be read in conjunction with the following documents.

1. Policy for shared care
2. Shared care agreement form

When two or more DMDs are initiated, one shared care agreement form should be completed for all relevant drugs.
Appendix 1

Policy for Shared Care

Shared care is only appropriate if it provides an optimum solution for the patient and it meets the criteria outlined in the Shared Care section of the Pan Mersey Definitions and Criteria for Categorisation of Medicines in the Pan Mersey Formulary document.

Before prescribing responsibilities are transferred to primary care:

- Prescribing responsibility will only be transferred when the consultant and the patient’s GP agree that the patient’s condition is stable.
- All information required by the shared care framework for the individual medicine has been provided to the patient’s GP.
- Patients will only be referred to the GP once the GP has agreed to the Shared Care Agreement and returned signed copies.

**Inherent in any shared care agreement is the understanding that participation is at the discretion of the GP, subject to the availability of sufficient information to support clinical confidence.**

Specialist Responsibilities in Shared Care

- For Rheumatology patients under Wirral Trust, Specialist to ensure baseline monitoring of full blood count and biochemical profile as described by the shared care framework
- For all other patients, Specialists to initiate the medicine, prescribe, monitor for toxicity and efficacy as described by the shared care framework until the patient is stabilised.
- To ensure the patient or their carer:
  - Is counselled with regard to the risks and benefits of the medicine.
  - Provide any necessary written information to the patient with regard to the individual medicine including patient information leaflets on individual drugs.
  - Obtain and document informed consent from the patient when any medicines is prescribed for an off-label indication for any condition
- To be familiar with the shared care framework.
- To provide all information to the patient’s GP as required by the shared care framework when prescribing responsibility is initially transferred and at any subsequent times as necessary for safe and effective treatment of the patient.
• To assess the patient regularly as necessary for the duration of therapy.
• To review the patient promptly if required by the GP concerned.
• To meet any additional requirements as required by the individual medicine shared care framework.
• To communicate failure of a patient to attend a routine hospital review and advise the GP of appropriate action to be taken.

**Addition of a second DMD**: Following the addition of a new drug to an existing regime covered by a Shared Care Agreement, the Specialist must initiate, prescribe and monitor the new drug in accordance with the relevant shared care agreement including subsequent review and inform the GP of this. A new Shared Care Agreement must then be initiated for the new drug.

**Primary Care Responsibilities in Shared Care**

• To reply to a written request for Shared Care within 21 days ensuring both copies of the Shared Care Agreement are signed if appropriate.

If agreeing to shared care, the GP is asked to:

• To provide prescribe or manage and monitor the medicine as advised by the Specialist and in line with the individual Shared Care Framework.
• To review the patient as required by the Shared Care Framework
• To make appropriate and contemporaneous records of prescribing and/or monitoring and to note the existence of the Shared Care Agreement on the patient’s clinical record. A READ code of “6652 Shared Care- Specialist/GP” can be used.
• To be familiar with the individual Shared Care Framework.
• To report any adverse effects of treatment to the specialist team.
• To inform the Specialist of any relevant change in the patient’s circumstances.
• To seek Specialist advice as appropriate.
• To meet any additional requirements as required by the individual Shared Care Framework.
• To respond to Specialist communication relating to any change or addition to the patients treatment covered by the Shared Care Agreement.
Appendix 2: Shared Care Agreement

Disease modifying drugs (DMDs)
Request by Specialist Clinician for the patient’s GP to enter into a shared care agreement

Part 1
To be signed by Consultant / Prescribing member of Specialist Team

Date ____________________________
Name of patient ____________________________
Address ______________________________________
______________________________________________
Patient NHS No ____________________________
Patient hospital unit No _______________________
Diagnosed condition ____________________________

Dear Dr ____________________________

I request that you prescribe
(1) ______________________________________
(2) ______________________________________
(3) ______________________________________
(4) ______________________________________
for the above patient in accordance with the enclosed shared care framework.

Last Prescription Issued: ..... / ..... / ..... Next Supply Due: ..... / ..... / .....  
Date of last blood test: ..... / ..... / ..... Date of next blood test: ..... / ..... / .....  
Frequency of blood test: ..............................

I confirm that the patient has been stabilised and reviewed on the above regime in accordance with the Shared Care Framework and Policy.  

[ ]

I confirm that if this is a Shared Care Agreement for a drug indication which is unlicensed or off label, informed consent has been received.  

[ ]  [N/A]
Details of Specialist Clinicians

Name ___________________________ Date ________________

Consultant / Prescribing member of Specialist Team *circle or underline as appropriate

Signature ______________________________________________

In all cases, please also provide the name and contact details of the Consultant.

When the request for shared care is made by a prescriber who is not the consultant, it is the supervising consultant who takes medico-legal responsibility for the agreement.

Consultant: ____________________________________________

Contact details:

Telephone number: ___________________ Ext: ______________

Address for return of documentation

________________________________________________________________

________________________________________________________________

Part 2
To be completed by Primary Care Clinician

Patient name ____________________________

I agree to prescribe ____________________________ for the above patient in accordance with the enclosed shared care framework.

GP signature ____________________________ Date _______________

GP name ______________________________ Please print

GP: Please sign and return a copy within 21 calendar days to the address above

OR

GP- If you do not agree to prescribe, please delete the section above and provide any supporting information as appropriate below: