ESCA: All non-biological DMARDs (oral/subcutaneous) and agreement for transferring of DMARD Prescribing & Monitoring to GP

Dermatology/ Haematology/ Gastroenterology/ Neurology/ Ophthalmology/ Respiratory/ Rheumatology Shared Care Guideline

Approved Date: June 2017
Review Date: June 2019
NON BIOLOGICAL DMARDs

SECONDARY CARE
- Decision to initiate: by an expert in management of rheumatic diseases in conjunction with patient/carer
- Choice of DMARDS: consider comorbidities, occult infections, immunocompromised patient
- Patient information provided
- Baseline assessments
- Vaccination advice
- Specific drug advice
- Monitoring and prescribing by secondary care
- Regular patient assessments
- Communication with primary care
- Stable dose with no concerns

HANDOVER TO PRIMARY CARE
- ESCA issued
- GP informed
- Pt informed

PRIMARY CARE
- Monitoring and prescribing by primary care
- Appropriate advice:
  - Surgery
  - Infection
  - Vaccination
  - Specific drug advice
  - Complete patient recording/document if appropriate
- Consider immediate drug withdrawal
- Contact the DMARD Initiating Specialist team
- Yellow Card

Yellow Card

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ESCA: All non-biological DMARDs (oral/subcutaneous)

Dermatology/ Haematology/ Gastroenterology/ Neurology/ Ophthalmology/ Respiratory/ Rheumatology Shared Care Guideline

Agreement for transferring of DMARD Prescribing & Monitoring to GP

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose (mg) and frequency (Words and Figures please)</th>
<th>Route</th>
<th>Tick All those that apply</th>
</tr>
</thead>
<tbody>
<tr>
<td>Azathioprine</td>
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</tr>
<tr>
<td>6-Mercaptopurine</td>
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<tr>
<td>Ciclosporin</td>
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<tr>
<td>Hydroxychloroquine</td>
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<tr>
<td>Leflunomide</td>
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<tr>
<td>Mepacrine</td>
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</tr>
<tr>
<td>Methotrexate: <strong>Prescribe 2.5mg tablets only</strong></td>
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<tr>
<td>Minocycline</td>
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<tr>
<td>Mycophenolate mofetil</td>
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<tr>
<td>Sodium aurothiomalate/Myocrisin (Gold)</td>
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<tr>
<td>Sulfasalazine</td>
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<tr>
<td>Tacrolimus</td>
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</tr>
</tbody>
</table>
• I can confirm that the patient is on a stable dose of medication as detailed in the table.
• I would like to formally hand over the monitoring and prescribing of the above DMARD(s) to your care as of _ _ / _ _ / _ _ (DD/MM/YY), in line with the enclosed Effective Shared Care Agreement (ESCA).
• If there are any concerns in relation to:
  o Agreement of transfer of DMARD monitoring and prescribing.
  o Concerns in relation to the patients DMARD monitoring.

Please contact the Specialist using the contact details below:

CONTACT DETAILS:

Yours sincerely,

Specialist Name:

Specialist Designation:

Date:
ESCA: All non-biological DMARDs (oral/subcutaneous)

Dermatology/ Haematology/ Gastroenterology/ Neurology/ Ophthalmology/ Respiratory/ Rheumatology Shared Care Guideline

Introduction

This effective shared care agreement (ESCA) sets out details for the sharing of care for patients receiving non-biological DMARDs. It should be read in conjunction with the Summary of Products Characteristics (SPC; datasheet).

This ESCA has been developed following the publication of the BSR/BHPR non-biological DMARD guidelines 2016. DMARDs covered in this ESCA include:

- Azathioprine
- 6-Mercaptopurine
- Ciclosporin
- Hydroxychloroquine
- Leflunomide
- Mepacrine
- Methotrexate
- Minocycline
- Mycophenolate mofetil
- Sodium aurothiomalate/Myocrisin (Gold)
- Sulfasalazine
- Tacrolimus

The purpose of this document is to assist the provision of DMARDs. Initiation of treatment should be the responsibility of a specialist. Once the patient is stabilised on treatment, it is then appropriate for GP’s without a special interest to prescribe this drug over the longer term within the guidance of an ESCA.

This document set out the responsibilities of the Specialist and the General Practitioner in the provision of shared care. It also outlines the DMARD monitoring guidelines.
Responsibilities of the Specialist Initiating Treatment

Generic recommendations before commencing any DMARD

1. The decision to initiate DMARDs should be made in conjunction with the patient/carer and be supervised by an expert in the management of their medical condition.
2. Patients should be provided with education about their treatment to promote self-management.
3. When appropriate patients should be advised about the impact of DMARD therapy upon fertility, pregnancy and breastfeeding.
4. Baseline assessment should include height, weight, blood pressure and laboratory evaluation (FBC, calculated GFR, ALT and/or AST, albumin).
5. Patients should be assessed for comorbidities as these may influence DMARD choice, including evaluation for respiratory disease and screening for occult viral infection.
6. Vaccinations against pneumococcus and influenza are recommended. Live vaccines should be avoided, except on the advice of the initiating specialist. [For example: Zostavax (shingles live vaccine) can be offered to appropriate patients on Sulphasalazine, Prednisolone ≤ 10mg/kg/day, Methotrexate ≤ 0.4mg/kg/week and Azathioprine ≤ 3mg/kg/day, on the proviso that these drugs are not being given in combination with other immunosuppressant’s].
7. For gastroenterology patients, screen for Hepatitis B&C and Varicella Ig.

- Provide pre-treatment patient information sheets on the relevant DMARD and record baseline tests.
- Review results of safety monitoring and request additional tests as required.
- Monitor disease response to treatment and need to continue therapy.
- Continue to review the patient at agreed specified intervals, sending a written summary to the GP whenever the patient is reviewed.
- Provide any other advice or information for the GP if required.
- If the patient is tolerating their DMARD and on a stable dose then the patient may be referred for Primary Care monitoring and prescribing via this ESCA. We envisage this will be between 1-3 months of starting treatment.
Prescribing DMARDs in patients with known comorbidities

1. Pre-existing lung disease is not a specific contraindication to DMARD therapy; however caution is advised when using drugs associated with pneumonitis in patients with poor respiratory reserve.
2. In patients with deranged liver biochemistry, hepatotoxic DMARDs should be used with caution, with careful attention to trends in test results.
3. In patients with impaired liver synthetic function (e.g. cirrhosis) DMARD therapy should be used with extreme caution.
4. Patients with chronic viral hepatitis infection should be considered for anti-viral treatment prior to immunosuppressive DMARD initiation.
5. DMARDs must be used with caution in chronic kidney disease with appropriate dose reduction and increased frequency of monitoring. This can be defined in accordance with advice from the initiating specialist.
6. Cardiovascular disease and prior malignancy are not considered contraindications to DMARD therapy.

Drug specific recommendations

Methotrexate: (oral or subcutaneous):
- All patients should be co-prescribed folic acid supplementation at a minimum dose of 5mg once weekly. Folic acid should not be administered on the same day as Methotrexate and can be given 2-3 days after the day of taking Methotrexate.
- Avoid concomitant prescription of Trimethoprim or Co-trimoxazole due to risk of pancytopenia – unless specifically advised by the hospital specialist (e.g. in patients with Systemic Vasculitis receiving long-term treatment with co-trimoxazole).
- Always prescribe methotrexate in multiples of the 2.5mg tablet strength. The 10mg tablets must not be used. This is to reduce errors.
- Baseline Chest Xray should be done and consider Lung Function (including transfer factor and lung volumes) in selected patients. For example those patients with an abnormal Chest Xray.
- For Dermatology patients on Methotrexate, Procollagen type III peptide (PIIINP) should be checked at baseline and 3 monthly thereafter.
- Zlatal is the preferred formulary choice of subcutaneous methotrexate
- All cytotoxic substances should be disposed of in purple sharps bins, these are prescribable on FP10 prescription as: Sharpsafe disposal unit- purple available in a range of sizes.

Azathioprine:
- Patients should have baseline thiopurine methyltransferase (TPMT) status assessed.

Hydroxychloroquine:
- Patients should have formal ophthalmic examination with their optician annually. This should include formal visual acuity testing for distance and reading vision, fundoscopy and 10-2 central visual field testing.
• If a patient is on Hydroxychloroquine for > 5 years, the patient should be referred to ophthalmology for the above tests and in addition have an objective retinal assessment for using optical coherence tomography (OCT).

**Responsibilities of the General Practitioner/Primary Care Prescriber**

1. Prescribe the DMARD at the dose recommended by the specialist.
2. Arrange and record on-going monitoring as per the monitoring guidelines and in agreement with the specialist initiating treatment.
3. Ensure no drug interactions with other medications when prescribing new medications.
   Example: Allopurinol with Azathioprine or Trimethoprim with Methotrexate, which also should be avoided.
4. Check patient is using adequate contraception (where applicable).
5. Continued prescribing is appropriate for patients attending for regular review.
6. Check patient has had one dose of pneumococcal vaccine.
7. Vaccinations against influenza are recommended annually. Live vaccines should be avoided, except on the advice of the initiating specialist. [For example: Zostavax (shingles live vaccine) can be offered to appropriate patients on Sulphalazine, Prednisolone ≤ 10mg/kg/day, Methotrexate ≤ 0.4mg/kg/week and Azathioprine ≤ 3mg/kg/day, on the proviso that these drugs are not being given in combination with other immunosuppressant’s].
8. Passive immunisation using Varicella immunoglobulin (VZIG) should be considered in non-immune patients if exposed to chickenpox or shingles.
9. Ask about oral ulceration/sore throat, unexplained rash or unusual bruising at every consultation where clinically appropriate.
10. Report adverse events to the MHRA (via yellow card) and the specialist initiating treatment.
11. Contact the specialist team and consider interruption in treatment if any of the following develop:

<table>
<thead>
<tr>
<th>WBC &lt; 3.5x10⁹/l</th>
<th>MCV &gt;105fl/l</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neutrophils &lt;1.6x10⁹/l</td>
<td>Creatinine &gt;30% above baseline and/or calculated GFR &lt;60</td>
</tr>
<tr>
<td>Unexplained eosinophilia &gt;0.5x10⁹/l</td>
<td>ALT and/or AST &gt; 100iu/l</td>
</tr>
<tr>
<td>Platelet count &lt;140x10⁹/l</td>
<td>Unexplained fall in serum albumin</td>
</tr>
</tbody>
</table>

MTX: Dry cough or new or increasing dyspnoea, Unexplained rash/abnormal bruising

As well as responding to absolute values in laboratory tests, it is also relevant to observe trends in results (e.g. gradual decreases in WBC or albumin, or climbing liver enzymes).
For clinically urgent abnormalities, please withhold treatment AND contact the specialist teams for advice

**Drug specific recommendations**

*Methotrexate: (oral or subcutaneous):*

- All patients should be co-prescribed folic acid supplementation at a minimum dose of 5mg once weekly.
- Avoid concomitant prescription of Trimethoprim or Co-trimoxazole due to risk of pancytopenia – unless specifically advised by the hospital specialist (e.g. in patients with Systemic Vasculitis receiving long-term treatment with co-trimoxazole).
- Always prescribe methotrexate in multiples of the 2.5mg tablet strength. The 10mg tablets must not be used. This is to reduce errors as detailed in Patient Safety Alert, Reducing the harm caused by oral methotrexate, July 2004. 563; NPSA.
- For Dermatology patients on Methotrexate, Procollagen type III Peptide (PIIINP) should be checked at baseline and every 3 months thereafter. Consider onward referral to specialist for advice if abnormal.
Non-Biological DMARD Monitoring Guidelines

Recommended STANDARD DMARD blood monitoring schedule when starting or adding a new DMARD

These guidelines are for both the specialist initiating treatment and the general practitioner or primary care prescriber, who will continue monitoring and prescribing when patients is on a stable dose of their DMARD and a formal handover from the specialist (in writing) has taken place.

Check FBC, creatinine/calculated GFR, ALT and/or AST and albumin every:

- Two weeks until on stable dose for 6 weeks then
- Once on stable dose, monthly FBC, creatinine/calculated GFR, ALT and/or AST and albumin for 3 months
- Thereafter FBC, creatinine/calculated GFR, ALT, and/or AST and albumin at least every 12 weeks* we would also recommend the ESR & CRP is checked to aid in assessment of disease activity.

*More frequent monitoring is appropriate in patients at higher risk of toxicity.

Dose increases should be monitored by FBC, creatinine/calculated GFR, ALT and/or AST and albumin every 2 weeks until on stable dose for 6 weeks then revert back to above schedule.
Exceptions / additions to the monitoring schedule for specific DMARDs are included in the summary monitoring requirements table. Please see below:

Summary of monitoring requirements:

<table>
<thead>
<tr>
<th>Drug</th>
<th>Laboratory Monitoring</th>
<th>Other monitoring</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apremilast</td>
<td>No routine laboratory monitoring</td>
<td>None</td>
</tr>
<tr>
<td>Azathioprine</td>
<td>Standard monitoring schedule*</td>
<td>None</td>
</tr>
<tr>
<td>Ciclosporin A</td>
<td>Extended monthly monitoring longer-term**</td>
<td>BP and Glucose monitoring each visit</td>
</tr>
<tr>
<td>Myocrisin (Gold)</td>
<td>Standard monitoring schedule*</td>
<td>Urinalysis for blood and protein prior to each dose.</td>
</tr>
<tr>
<td>Hydroxychloroquine</td>
<td>No routine laboratory monitoring</td>
<td>Annual eye assessment (ideally including OCT) if continued for &gt;5 years</td>
</tr>
<tr>
<td>Leflunomide</td>
<td>Standard monitoring schedule*</td>
<td>BP and weight at each monitoring visit.</td>
</tr>
<tr>
<td>Mepacrine</td>
<td>No routine laboratory monitoring</td>
<td>None</td>
</tr>
<tr>
<td>Methotrexate</td>
<td>Standard monitoring schedule*</td>
<td>None</td>
</tr>
<tr>
<td>Leflunomide/Methotexate</td>
<td>Extended monthly monitoring longer-term**</td>
<td>None</td>
</tr>
<tr>
<td>Combined</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Minocycline</td>
<td>No routine laboratory monitoring</td>
<td>None</td>
</tr>
<tr>
<td>Mycophenolate Mofetil</td>
<td>Extended monthly monitoring longer-term**</td>
<td>None</td>
</tr>
<tr>
<td>Sulphasalazine</td>
<td>Standard monitoring schedule for 12 months then no routine monitoring needed.</td>
<td>None</td>
</tr>
<tr>
<td>Tacrolimus</td>
<td>Extended monthly monitoring longer-term**</td>
<td>BP and glucose at each assessment</td>
</tr>
</tbody>
</table>

*Standard monitoring as per recommended DMARD blood monitoring schedule outlined above.
Patients who have been stable for 12 months can be considered for reduced frequency monitoring on an individual patient basis. This would be under the guidance of the specialist initiating treatment.

**Perioperative DMARD management: This would be under the guidance of the specialist initiating treatment.**

1. Steroid exposure should be minimised prior to surgical procedures, and increases in steroid dose to prevent adrenal insufficiency are not routinely required.
2. DMARD therapy should not routinely be stopped in the peri-operative period, although individualised decisions should be made for high-risk procedures.

**Intercurrent infections**

1. During a serious infection Methotrexate, Leflunomide, Sulphalazine, Azathioprine, Apremilast, Mycophenolate Mofetil, Ciclosporin A, and Tacrolimus should be temporarily discontinued until the patient has recovered from the infection. For example: if the patient requires antibiotics, or has a protracted viral infection, they should withhold their DMARD treatment temporarily. The GP/primary care prescriber should seek advice from the specialist if there is any uncertainty.

**References**

2. Interface Pharmacist Network Specialist Medicines: [www.ipnsm.hscni.net](http://www.ipnsm.hscni.net)

**Contacts:**

Initiating Consultant (see details above) 01384 456111

Dudley CCG Pharmaceutical Public Health Team: 01384 321979

Medicines Information (Pharmacy, Russells Hall Hospital) 01384 244088

Dudley Group NHS Foundation Trust

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