Appendix 3: Reference guideline for primary care monitoring of DMARD therapy

Drug	Tests required	Primary care clinician responsibility	Initiating specialist responsibility *suggested monitoring. To be amended on a patient by patient basis as required.
Azathioprine (Same monitoring regimen as **Mercaptopurine** as azathioprine is a prodrug which is converted to mercaptopurine in vivo). (Standard monitoring)	• FBC • U&E's • Creatinine • Calculated eGFR • LFT's	• Monitoring required every 3 months	• Every 2 weeks until on stable dose for 6 weeks then, monthly for 3 months • After dose increase - repeat FBC and LFTs creatinine/calculated GFR every 2 weeks until on stable dose for 6 weeks then once on stable dose, monthly for 3 months and thereafter at least every 12 weeks • More frequent monitoring is appropriate in patients at higher risk of toxicity
Ciclosporin (Extended monthly monitoring)	• FBC • U&E's • Creatinine • Calculated eGFR • LFT's • BP • Blood glucose • Fasting lipids - Periodically	• Monitoring required every 3 months • Blood pressure monitoring each attendance. BP > 140/90 on 2 consecutive readings 2/52 apart – treat hypertension before stopping ciclosporin (Note possible drug interactions). If BP cannot be controlled, stop ciclosporin and obtain BP control before restarting ciclosporin. Seek initiating specialist advice. • Vigilance when NSAID added particularly diclofenac- reduce diclofenac dose by 50% • Occasional monitoring of ciclosporin blood levels is recommended, e.g. when ciclosporin is co-administered with substances that may interfere with the pharmacokinetics or in the event of unusual clinical response (e.g. lack of efficacy or increased drug intolerance such as renal dysfunction). • Check fasting lipids periodically	• FBC and LFT creatinine/calculated GFR every 2 weeks until on stable dose for 6 weeks then, monthly • After dose increase - repeat FBC and LFTs creatinine/calculated GFR every 2 weeks until on stable dose for 6 weeks then once on stable dose, monthly • Extended monitoring required - Patients who have been stable for 12 months can be considered for reduced frequency of monitoring on an individual patient basis. • More frequent monitoring is appropriate in patients at higher risk of toxicity

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Drug	Tests required	Primary care clinician responsibility	Initiating specialist responsibility *suggested monitoring. To be amended on a patient by patient basis if required.
Hydroxychloroquine (No routine monitoring)	• No routine monitoring	• Current Kent and Medway advice is to follow the NICE guidance on hydroxychloroquine. Pathway currently under review. If a patient has ophthalmology concerns/complaints please refer urgently to ophthalmology and include all relevant PMH and DMARD prescribing. • Patients should be advised to report any visual disturbance.	• Patient should have an annual eye assessment (ideally including optical coherence tomography) if treatment continued for >5 years. (To be requested by Specialist) • Current Kent and Medway advice is to follow the NICE guidance on hydroxychloroquine. Pathway currently under review. If a patient has ophthalmology concerns/complaints please refer urgently to ophthalmology and include all relevant PMH and DMARD prescribing. • Patients should be advised to report any visual disturbance.
Leflunomide (Standard monitoring)	• FBC • U&E's • Creatinine • Calculated eGFR • LFT's • BP • Weight	• Monitoring required every 3 months • ALT/AST 2-3x upper limit normal – reduce dose to 10mg, recheck weekly. If normalised – continue 10mg; if remains elevated withdraw drug and discuss with initiating specialist. • If ALT/AST >3x normal, stop drug, recheck within 72 hours. If still > 3x, withdraw drug and consider washout. Discuss with initiating specialist. • BP each visit. If BP >140/90 treat in line with NICE guidance. If BP remains uncontrolled, stop leflunomide and consider washout. Discuss with initiating specialist. • Weigh at each monitoring visit. If >10% weight loss with no other cause identified, reduce dose or stop and consider washout. Discuss with initiating specialist.	• FBC and LFT creatinine/calculated GFR every 2 weeks until on stable dose for 6 weeks then, monthly for 3 months. • After dose increase - repeat FBC and LFTs creatinine/calculated GFR every 2 weeks until on stable dose for 6 weeks then once on stable dose, monthly for 3 months. • More frequent monitoring is appropriate in patients at higher risk of toxicity • If co-prescribed with another immunosuppressant or potential hepatotoxic agent then blood checks should be continued long-term, at least once a month.

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Methotrexate (Oral and Subcutaneous) (Standard monitoring)	• FBC • U&E's • Creatine • Calculated eGFR • LFT's	• Monitoring required every 3 months • Albumin – unexplained fall (in absence of active disease) – withhold and discuss with initiating specialist. • New or increasing dyspnoea or dry cough – withhold and discuss urgently with the specialist team. • Avoid prescribing trimethoprim or co-trimoxazole to patients receiving methotrexate – greatly increases risk of marrow aplasia.	• FBC and LFT creatinine/calculated GFR every 2 weeks until on stable dose for 6 weeks then, monthly for 3 months. • After dose increase - repeat FBC and LFTs creatinine/calculated GFR every 2 weeks until on stable dose for 6 weeks then once on stable dose, monthly for 3 months. • More frequent monitoring is appropriate in patients at higher risk of toxicity
Mycophenolate Mofetil (Standard monitoring)	• FBC • U&E's • Creatinine • Calculated eGFR • LFT's	• Monitoring required every 3 months	• FBC and LFT creatinine/calculated GFR every 2 weeks until on stable dose for 6 weeks then, monthly for 3 months. • After dose increase - repeat FBC and LFTs creatinine/calculated GFR every 2 weeks until on stable dose for 6 weeks then once on stable dose, monthly for 3 months. • More frequent monitoring is appropriate in patients at higher risk of toxicity
D-Penicillamine (Extended monthly monitoring)	• FBC • U&E's • Creatinine • Calculated eGFR • Urinalysis (Dipstick protein)	• Monitoring required every 3 months • Ask about skin rash or oral ulceration at every visit.	• FBC, LFT, Creatinine/calculated GFR and urinalysis every 2 weeks until on stable dose for 6 weeks then monthly thereafter. • Once stable for 12 months patient can be considered for reduced monitoring (every 3 months) on an individual patient basis. • More frequent monitoring is appropriate in patients at higher risk of toxicity

Sulfasalazine (Standard monitoring)	• FBC • U&E's • Creatinine • Calculated eGFR • LFT's	• Monitoring required every 3 months • Discontinue blood monitoring after 12 months. • Ask about skin rash or oral ulceration.	• FBC and LFT creatinine/calculated GFR every 2 weeks until on stable dose for 6 weeks then, monthly for 3 months. • After dose increase - repeat FBC and LFTs creatinine/calculated GFR every 2 weeks until on stable dose for 6 weeks then once on stable dose, monthly for 3 months. • More frequent monitoring is appropriate in patients at higher risk of toxicity.
Dapsone (Standard monitoring)	• FBC including reticulocyte count • LFT's • Creatinine • Calculated eGFR	• Monitoring required every 3 months • An elevated reticulocyte count of 10-15% above normal is acceptable provided that it is stable along with the haemoglobin and bilirubin levels. Contact specialist for advice and guidance. • Serum methaemoglobin levels should be measured in patients complaining of light-headedness, headache, fatigue or shortness of breath.	• FBC, Reticulocyte count, LFT and Creatinine/calculated GFR every week for 4 weeks, monthly for 3 months then 3 monthly • After dose increase - FBC, Reticulocyte count, LFT and Creatinine/calculated GFR every week for 4 weeks, monthly for 3 months then 3 monthly • Patients who have been stable for 12 months can be considered for reduced frequency of monitoring on an individual patient basis. • More frequent monitoring is appropriate in patients at higher risk of toxicity.

Tacrolimus (Extended monthly monitoring)	• FBC • LFT's • Creatinine • Calculated eGFR • BP • Blood glucose	• Monitoring required every 3 months	• FBC and LFT creatinine/calculated GFR every 2 weeks until on stable dose for 6 weeks then monthly • After dose increase - repeat FBC and LFTs creatinine/calculated GFR every 2 weeks until on stable dose for 6 weeks then once on stable dose then monthly • Extended monitoring required - Patients who have been stable for 12 months can be considered for reduced frequency of monitoring on an individual patient basis • More frequent monitoring is appropriate in patients at higher risk of toxicity.

Appendix 4 – DMARD initiation and dose increase

All DMARDs that require monitoring initiated by specialist

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Fortnightly for 6 weeks in specialist care: FBC, LFTs, Creatinine and eGFR

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Monthly for 3 months by specialist: FBC, LFTs, Creatinine and eGFR.
3 Monthly monitoring to be completed by primary care clinician

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Extended monitoring schedule

It is recognised that patients may need more frequent monitoring. If this is required, patients remain the responsibility of the initiating specialist.

⇔

Standard monitoring schedule

FBC, LFTs, Creatinine and eGFR

Quarterly (3 monthly) in primary care

For patients at low risk of toxicity e.g., normal range blood test parameters, no co-morbidities such as renal impairment/fatty liver.

As specified in specialist care treatment plan. Communicate to primary care clinician using the shared care agreement form (appendix 6)

Dose increase of DMARD

Fortnightly for 6 weeks by initiating specialist

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Resume usual patient monitoring schedule in primary care
(e.g. quarterly – 3 monthly)
FBC, LFTs, Creatinine and eGFR

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Appendix 5 – Monitoring – actions for abnormal monitoring parameters

The prescriber has responsibility for ensuring patients are adhering to monitoring guidance and respond to abnormalities of the results included in the monitoring schedule.
As well as responding to absolute values in laboratory tests, it is also relevant to observe trends in results (e.g. gradual decreases in white blood cells or albumin, or increasing liver enzymes). A rapid fall or rise and a consistent upward or downward trend in any value should prompt caution and extra vigilance.
The parameters below are suitable for the majority of patients; however Individual patient needs may vary. For some patients individual parameters may be set by the specialist and communicated to Primary Care where results outside these set limits are medically acceptable (for example a persistently raised stable MCV due to drug therapy where no alternative cause has been identified).
As a general guide action should be taken by withholding treatment and discussing with the relevant specialist department if:

Abnormality Detected	Recommended Action to include
WBC <3.5 $x10^9$/L	Withhold and discuss urgently with specialist team
Neutrophils <1.6 $x10^9$/L	Withhold and discuss urgently with specialist team
Unexplained Eosinophilia >0.5 x 10^9/L	Withhold and discuss urgently with specialist team
Platelet count <140 $x10^9$/L	Withhold and discuss urgently with specialist team
ALT and/or AST > than twice the upper limits	Withhold and discuss urgently with specialist team
Unexplained reduction in albumin <30 g/L	Withhold and discuss urgently with specialist team
Mean Cell Volume (MCV) >105 f/L	Withhold and discuss urgently with specialist team
Creatinine increase >30% over 12 months and/or calculated GFR <60 ml/min/	Withhold and discuss urgently with specialist team
Blood pressure >140/90mm Hg	Manage hypertension according to NICE hypertension guidance (If on Ciclosporin, Tacrolimus or Leflunomide – withhold and discuss with specialist team)
Unexplained new increasing dyspnoea or cough ** *(Cases of pneumonitis have been reported)*	Withhold and discuss urgently with specialist team
Dapsone	Contact specialist and consider withholding if haemoglobin decreases by 2g/dL from baseline or reticulocyte count increases >6%

*** AZATHIOPRINE, CICLOSPORIN, LEFLUNOMIDE, METHOTREXATE, MINOCYCLINE, SULPHASALAZINE, TACROLIMUS have pneumonitis listed on SPC. Cases reports of MYCOPHENOLATE pneumonitis exist.*

For up to date information on possible abnormalities and recommended actions required please click link Suggestions for drug monitoring in Adults in primary care ***Specialist pharmacy service September 2020***.

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