Quick reference guideline for monitoring of disease modifying anti-rheumatic drug (DMARD) therapy

View the BSR and BHPR guideline: Disease-modifying anti-rheumatic drug (DMARD) therapy for further information

DRUG	TYPICAL DOSE	PRE-TREATMENT	FBC	U&E, Creat (1)	LFT	BP	URINE DipStick protein	FREQUENCY / COMMENT
Azathioprine	1mg/kg/day increase at 4-6 weekly intervals to **max** 3mg/kg/d	FBC, U&E, LFT, Creatinine, **TPMT assay (See main text)**	√	√ SIX Monthly	√	_	_	FBC and LFT **weekly for 6 weeks** and then every **2 weeks** until dose stable for **6 weeks**; then **monthly**. After dose increase - repeat FBC and LFT's after **2 weeks** and then **monthly** If dose and test results stable for **6 months** consider discussing with patient to reducing to **3 monthly**. In patients **heterozygote** for TPMT, monitoring should continue at **monthly** intervals U&E, creatinine – **6 monthly**
Ciclosporin	Start 2.5mg/kg/day in two divided doses for 6 weeks and then may be incrementally increased by 25mg at 2–4 weekly intervals until clinically effective or the maximum dose of 4mg/kg is reached	FBC, U&E, LFTCreatinine: Twice at 2 week apart – to obtain mean value Creatinine clearance or equivalent Fasting Lipids BP: ≤140/90 on 2 occasions at 2/52 apart.	√	√	√	√	_	U & E including potassium and Creatinine **every 2 wks** until dose and results stable for **3 months** and then **monthly** FBC and LFT **monthly** until dose and results stable for **3 months; thereafter 3 monthly.** Vigilance when NSAID added **particularly diclofenac**- reduce **diclofenac dose** by 50% 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 controlled, stop ciclosporin and obtain BP control before restarting ciclosporin Check fasting **lipids periodically**
I / M Gold (Myocrisin)	Test dose 10mg then 50mg weekly until a total dose 1000mg is given when efficacy should be reviewed.	FBC, U & E, LFT & Creatinine, Urinalysis	√	_	_	_	√	FBC and urinalysis at time of each injection. Provided blood results are stable, 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. Urinalysis must be done before each injection Ask each time about presence of skin rash or mouth ulcers

Drug	Typical Dose	PRE-TREATMENT	FBC	U&E, Creat (1)	LFT	BP	URINE DipStick protein	FREQUENCY / COMMENT
Hydroxychloroquine	200-400mg daily. Max 6.5mg/kg/day	FBC, U&E, LFT Ask about visual impairment not corrected by glasses. Record near visual acuity of each eye (with reading glasses if worn) using a test type or reading chart If abnormality detected refer first to an optometrist	–	–	–	–	–	Annual review either by an optometrist or enquiring about visual symptoms, rechecking visual acuity and assessing for blurred vision using the reading chart. Discuss with ophthalmologist if on treatment for >5 years **Patients should also be advised to report any visual disturbance**
Leflunomide	10mg – 20 mg daily. Maximum 20mg daily when monotherapy is used. Advised to use 10mg daily in combination with other hepatotoxic drugs such as methotrexate	FBC, U&E, LFT, Creatinine. Blood Pressure on 2 occasions 2 weeks apart. If >140/90 treat before starting Rx Body weight.	√		√	√	–	FBC, LFT **every month** for 6 months and, if stable, **2 monthly thereafter.** If co-prescribed with another immumnosuppressant or potential hepatotoxic agent then blood checks should be continued long-term, **at least once a month**. 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 specialist team. If ALT/AST >3x normal, stop drug, **recheck within 72 hours**. If still > 3x, withdraw drug and consider washout. **BP each visit**. If BP >140/90 treat in line with NICE guidance. If BP remains uncontrolled, stop leflunomide and consider washout **Weigh at each visit**. If >10% weight loss with no other cause identified, reduce dose or stop and consider washout.

Drug	Typical Dose	PRE-TREATMENT	FBC	U&E Creat (1)	LFT	BP	URINE DipStick protein	FREQUENCY/COMMENT
Methotrexate (2) Folic Acid	7.5 - 25 mg ONCE a week. Increase every 2-6 weeks to maximum dose of 25mg ONCE weekly. Rarely max 30mg/week (See main text) 5 mg ONCE weekly ≥24 hours after Methotrexate	1.FBC, U&E, LFT , CXR (within the last 6 months) & 2.Pulmonary Function Test in selected patients.	√	√	√	–	–	FBC, U&E, LFT **every 2 weeks** until dose and monitoring **stable for 6 weeks**; thereafter **monthly**, until the dose and disease is stable for a year. Thereafter based on clinical judgement and following discussion with specialist team consider reducing frequency of monitoring **to every 2 - 3 months** (see main text) Albumin – unexplained fall (in absence of active disease) – withhold and discuss New or increasing dyspnoea or dry cough – withhold and discuss urgently with the specialist team Avoid prescribing trimethoprim or cotrimoxazole to patients receiving methotrexate – greatly increases risk of marrow aplasia For discussion of use of pro-collagen III see main text
Mycophenolate Mofetil	Start 500mg daily increase **weekly** by 500mg to optimal or max. tolerated dose. Max - **3 gms /day**	FBC, U&E, LFT & CXR (within the last 6 months	√	–	–	–	–	FBC **weekly** until dose **stable for 4 weeks** then **fortnightly for 2 months.** **Monthly thereafter**, even after patient is stabilized on treatment.
D-Penicillamine	Start 125-250mg/day increase by 125 mg, 4 weekly initially to 500mg. Max dose 750mg/day **(see main text)**	FBC, U&E, Creatinine & Urinary Protein	√	–	–	–	√	FBC and urinalysis **every 2 weeks** until dose and monitoring stable for **3 months**; **monthly thereafter**. Ask about skin rash or oral ulceration at every visit
Sulfasalazine	Start at 500mg/day increasing by 500mg each weekly to maximum of 2.0–3.0 gm/day. May occasionally go above 3 gms/ day **(See main text)**	FBC, U&E, LFT, Creatinine	√	–	√	–	–	FBC, LFT **monthly for 3 months**. If dose and bloods **stable for 3 months,** then **3 monthly**. If dose increase, repeat **bloods one month after dose increase**; if stable revert to usual monitoring regime. If **after first year** dose and blood results stable, frequency of blood tests can be reduced to **every 6 months** for second year of treatment. **After 2 years** of therapy, blood monitoring can be discontinued. Ask about skin rash or oral ulceration

Please note that in addition to absolute values for haematological indices a rapid fall or rise and a consistent upward or downward trend in any value should prompt caution and extra vigilance.

(1) U/E and creatinine, CRP and ESR / PV should be checked every 6 months – this will enable monitoring of renal disease and disease activity

(2) IM/SC Methotrexate conforms to the same protocol for monitoring as oral Methotrexate.

1. General advice

- This is a summary of the most relevant monitoring requirements. Refer to full text of guideline for further information. http://www.rheumatology.org.uk/resources/guidelines
- The summary guideline does not address combination therapy – read full text of guideline for advice
- Beware drug interactions
- Review individual monitoring protocols when dose changes are implemented.
- Patients should not receive immunisation with live vaccines
- Beware infections treat vigorously - check FBC and U & E
- Beware oral ulceration/sore throats/nosebleeds/bruising/rash
- If patients come into close contact with Herpes Zoster, consider passive immunisation
- If blood pressure >140/90 manage hypertension according to NICE Hypertension Guidance

2. Consult table for test and frequency

- Any discretionary reduction in the frequency of monitoring should only be on the instruction of a Rheumatology specialist
- Enter result in patient-held record book

3. Withhold treatment & liaise with Specialist team in charge of patient's treatment if:-

- Severe rash or bruising or ulceration of mucous membranes.
- Any unexplained illness occurs including nausea or diarrhoea
- WCC falls $<3.5 \times 10^9$/l
- Neutrophils $<2.0 \times 10^9$/l
- Eosinophils $>0.5 \times 10^9$/l
- Platelet count falls below $<150 \times 10^9$/l
- MCV > 105 f/l
- Creatinine >30% of baseline
- LFTs (ALT or AST) increase > 2 fold rise above upper limit reference range (Leflunomde special rules – see above and full text)
- If urinary protein on dipstick is 2+ send a MSU for culture. If MSU confirms infection, treat appropriately. If sterile proteinuria – seek advice.