Tameside and Glossop Acute Services NHS
NHS Trust

AZATHIOPRINE

Typical dose: 1 mg/kg/day—increasing after 4–6 weeks to 2–3 mg/kg/day.

If allopurinol is co-prescribed, the does of azathioprine must be cut to 25% of the original dose. Azathioprine inhibits anticoagulant effect of warfarin so higher doses of warfarin may be required. Co-prescription of azathioprine with Angiotensin-converting enzyme (ACE) inhibitors may cause anaemia (if significant, consider alternative to ACE inhibitor or different DMARD). Cotrimoxazole or trimethoprim must be avoided in patients taking azathioprine.

Live vaccines are contraindicated. However, annual flu vaccine is recommended.

Pre-treatment assessment: FBC, U&E, LFTs and TPMT assay

Monitoring: FBC and LFT's weekly for 6 weeks and continue every 2 weeks until dose stable for 6 weeks; then monthly. If maintenance dose is achieved and stable for 6 months consider discussing with patient to reduce monitoring to 3 monthly.
In people heterozygote for TPMT, monitoring should continue at monthly intervals at minimum. U&E should be repeated 6-monthly

Following changes in dose: Repeat FBC and LFT's 2 weeks after dose change and then monthly.

Actions:

WBC<3.5 x 10^9/l	*Withhold until discussed with specialist team.*
Neutrophils<2.0 x 10^9/l	*Withhold until discussed with specialist team.*
Platelets<150 x 10^9/l	*Withhold until discussed with specialist team.*
AST, ALT >2-fold rise (upper limit of reference range)	*Withhold until discussed with specialist team.*
Albumin-unexplained fall (in absence of active disease)	*Withhold until discussed with specialist team.*
Rash or oral ulceration	*Withhold until discussed with specialist team*
MCV>105 fl	*Withhold and check serum B12, Folate and TFT and discuss with specialist team if necessary*

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

Tameside and Glossop Acute Services NHS
NHS Trust

CICLOSPORIN

Typical RA starting dose: 2.5 mg/kg/day in two divided doses for 6 weeks and then may be increased at 2–4 weeks intervals by 25mg until clinically effective or the maximum dose of 4 mg/kg/day is reached. Maintenance dose: often effective between 2.5–3.2 mg/kg/day.

Live vaccines are contraindicated. However, annual flu vaccine is recommended.

Grapefruit including grapefruit juice must be avoided for 1 hr before or after taking ciclosporin tablets as bioavailability is increased. Dose of diclofenac should be reduced if co-prescribed with ciclosporin. The maximum dose of simvastain should be 10mg/day. Digoxin levels may be increased if by ciclosporin. Use nifedipine with caution. St John's Wort reduces ciclosporin activity. Ciclosporin interacts with many drugs. Please refer to BNF for further advicee.

Pre-treatment assessment: FBC including differential white cell count, U&E, creatinine: (check twice, 2 weeks apart, to obtain a mean value for creatinine), LFT, fasting lipids, creatinine clearance prior to starting the drug.
Blood pressure to be < 140/90 before treatment on two measurements 2 weeks apart. If greater than this, treat hypertension before starting ciclosporin.

Monitoring: FBC & LFT: once a month until dose and trend stable for 3 months and then 3 monthly. Serum electrolytes including potassium and creatinine every 2 weeks until dose and trend stable for 3 months and then monthly. Watch when NSAID is added, particularly diclofenac. Check fasting lipids periodically.
Check blood pressure each time patient attends monitoring clinic and maintain < 140/90.

Actions:

Creatinine rises >30% from baseline	*Repeat in 1 week and if still >30% above baseline withhold until discussed with the specialist team.*
Potassium rises to > reference range	*Withhold until discussed with the specialist team.*
Platelets<150 x 10^9/l	*Withhold until discussed with the specialist team.*
'Significant' rise in fasting lipids	*Withhold until discussed with the specialist team.*
High BP: >140/90 on two consecutive readings 2 weeks apart	*Treat blood pressure before stopping the ciclosporin (note interactions with several anti-hypertensives). If BP cannot be controlled, stop ciclosporin and obtain BP control before restarting ciclosporin. Discuss with the specialist team.*
AST, ALT or alkaline phosphatase more than 2 x upper limit of reference range	*Withhold until discussed with the specialist team. Check any other reason such as alcohol, drug interaction including over the counter medication.*
Abnormal bruising	*Check FBC immediately and withhold until discussed with the specialist team.*

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

Tameside and Glossop Acute Services NHS
NHS Trust

INTRA-MUSCULAR GOLD (MYOCRISIN)

Typical dose: 10mg test dose (which should be given in the clinic followed by 30 min observation to look for signs of allergic reaction) followed by 50 mg weekly until there is a significant response or a total dose of 1000 mg has been given. In patients who respond, the interval between doses may be increased by stages from 50 mg per week to 50 mg every 4 weeks.

Live vaccines are contraindicated.

Pre-treatment assessment: FBC, urinary dipstick for protein, U&E, LFTs.

Monitoring: FBC and urinalysis at the 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 should be carried out just before each injection. The patient should be asked about presence of rash or mouth ulcers before each injection.

Actions:

WBC<3.5 x 10^9/l	Withhold until discussed with specialist team.
Neutropaenia<2.0 x 10^9/l	Withhold until discussed with specialist team.
Eosinophilia>0.5 x 10^9/l	Caution and increase vigilance required.
Platelets<150_109/l	Withhold until discussed with specialist team.
2+ proteinuria or more	Check MSSU: If infection present treat appropriately. If sterile and 2+ proteinuria or more persists, withhold until discussed with specialist team.
Rash (usually itchy) or oral ulceration	Withhold until discussed with specialist team.
Abnormal bruising or severe sore throat	Check FBC immediately and withhold until results are available.

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

Tameside and Glossop Acute Services NHS
NHS Trust

LEFLUNOMIDE

Typical dose: 10–20 mg once a day. Leflunomide may inhibit the metabolism of warfarin, phenytoin and tolbutamide. It has an extremely long elimination half life and interactions with these drugs and with other DMARDS may occur even after leflunomide has been discontinued. Patient should be asked to limit alcohol intake well within national limits 4–8 units a week.

Leflunomide is teratogenic and so women of childbearing potential should use effective contraception during treatment and up to 2-years after treatment discontinuation. If a woman wishes to become pregnant and this waiting time is considered impractical, *contact specialist team as washout procedure would need to be initiated**. Blood concentrations should be checked prior to planned pregnancy especially if within 2 years of stopping leflunomide or following wash out. For men wishing to father a child, the same washout procedure as recommended for women with subsequent measurement of blood concentrations should be considered. Men should use effective contraception for 3 months after stopping leflunomide. Notify pharmaceutical company in the event of pregnancy while on leflunomide.

Live vaccines are contraindicated. However, annual flu vaccine is recommended.

Pre-treatment assessment: FBC, U&E's and LFTs. Blood pressure: If>140/90 on two consecutive readings 2 weeks apart treat hypertension before starting drug. Weight (see below)

Monitoring: FBC and LFT every 2 weeks for 6 months, then 8-weekly. Blood pressure and weight should be checked at each monitoring visit.

Actions:

WBC<3.5 x 10^9/l	*Withhold until discussed with specialist team.*
Neutrophils<2.0 x 10^9/l	*Withhold until discussed with specialist team.*
Platelets<150 x 10^9/l	*Withhold until discussed with specialist team.*
AST, ALT between two and three times the upper limit of reference range	*If the current dose is more than 10mg daily reduce the dose to 10mg daily and recheck weekly until normalized. If the AST & ALT is returning to normal, leave on 10mg a day. If LFTs remain elevated withdraw drug and discuss with the specialist team.*
AST, ALT more than three times the upper limit of reference range	*stop drug and consider washout*.*
Rash or itch	*Consider dosage reduction with or without antihistamines; if severe, stop and consider washout*
Hair loss	*Consider dosage reduction; if severe, stop and consider washout*.*
Abnormal bruising or severe sore throat	*Check FBC immediately and withhold until results are available.*
Hypertension	*If BP>140/90 treat in line with NICE guidance. If BP remains uncontrolled, stop leflunomide and consider washout*.*
Headache	*If severe, consider dosage reduction. If headaches persist, stop and consider washout**
GI upset (nausea,diarrhoea)	*Give symptomatic treatment and consider dosage reduction. If symptoms are severe or persistent, stop and consider washout**
Weight loss	*If >10% weight loss with no other cause identified, reduce dosage or stop and consider washout**
Breathlessness	*If increasing shortness of breath occurs, stop leflunomide and consider washout**

****if washout considered, contact specialist team*.**

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

Tameside and Glossop Acute Services NHS
NHS Trust

METHOTREXATE

Typical dose: 7.5–25mg ONCE weekly; starting dose may vary depending on the severity of the condition and patient characteristics such as age, renal function and other co-morbid conditions. The initial dose may be 5–10 mg once weekly, increasing by 2.5–5mg every 2–6 weeks until disease stabilized. The maximum licensed dose in RA is 25 mg/week. Rarely, the maximum dose can be 30 mg/week Lower doses should be considered for frail elderly patients who often have poor renal function. If maximum oral dose is not effective or causes intolerance, consider i.m. or subcutaneous route of administration before discontinuation of the drug.

Regular folic acid supplements are recommended with a typical dose 5mg once weekly, preferably the day after the methotrexate. Folic acid can be given any day as long as it is not on the same day as methotrexate. Folic acid reduces toxic effects and improves continuation of therapy and compliance.

Cotrimoxazole or trimethoprim must be avoided in patients taking methotrexate. Patients should be advised to limit their alcohol intake well within national recommendations. NSAIDs in addition to the above doses of methotrexate are not contraindicated.

Live vaccines are contraindicated. However, annual flu vaccine is recommended.

Pre-treatment assessment: FBC, U&E, LFTs and chest x-ray (in the previous 6 months)

Monitoring: FBC, U&E, LFT every 2 weeks until dose of methotrexate and monitoring stable for 6 weeks; thereafter monthly

Actions:

WBC<3.5 x 10^9/l	*Withhold until discussed with specialist team.*
Neutrophils<2.0 x 10^9/l	*Withhold until discussed with specialist team.*
Platelets<150 x 10^9/l	*Withhold until discussed with specialist team.*
AST, ALT >2-fold rise (upper limit of reference range)	*Withhold until discussed with specialist team.*
Albumin-unexplained fall (in absence of active disease)	*Withhold until discussed with specialist team.*
Rash or oral ulceration, nausea, vomiting, diarrhoea.	*Withhold until discussed with specialist team*
New or increasing dyspnoea or dry cough	*Withhold and discuss urgently with specialist team.*
MCV>105 fl	*Withhold and check serum B12, Folate and TFT and discuss with specialist team if necessary.*
Mild to moderate renal impairment (refer BNF).	*Withhold until discussed with specialist team*
Severe sore throat. abnormal bruising	*Immediate FBC and withhold until the result of FBC is available.*

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

Tameside and Glossop Acute Services NHS
NHS Trust

SULFASALAZINE

Typical dose: 500 mg/day increasing by 500mg weekly to 2.0–3.0 g/day.
Occasionally doses above 3.0 g/day are prescribed. Sulfasalazine can be prescribed to men of childbearing potential although there may be transient reversible oligospermia

Pre-treatment assessment: FBC, U&E's, LFTs.

Monitoring: FBC and LFTs (including AST/ALT) fortnightly for 3 months, monthly for the next 3 months and then 3 monthly thereafter. If, following the first year, dose and blood results have been stable, frequency of blood tests can be reduced to every 6 months for the second year of treatment.
Patient should be asked about the presence of rash or oral ulceration at each visit.

Following dose changes: Repeat FBC, LFT one month after dose increases.

Actions:

WBC<3.5 x 10^9/l	*Withhold until discussed with specialist team.*
Neutrophils<2.0 x 10^9/l	*Withhold until discussed with specialist team.*
Platelets<150 x 10^9/l	*Withhold until discussed with specialist team.*
AST, ALT>twice upper limit of reference range	*Withhold until discussed with specialist team.*
MCV>105 fl	*Check B12, folate and TSH. If abnormal, treat any underlying abnormality. If normal, discuss with the specialist team.*
Nausea/dizziness/headache	*If possible continue, may have to reduce dose or stop if symptoms severe. Discuss with specialist team.*
Abnormal bruising or severe sore throat	*Check FBC immediately and withhold until results available. Discuss with the specialist team, if necessary.*
Unexplained acute widespread rash	*Withhold seek urgent specialist (preferably dermatological) advice.*
Oral ulceration	*Withhold until discussed with specialist team.*

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