SCHEDULE 2 – THE SERVICES

A. Service Specifications

Service Specification No.	
Service	Monitoring of High Risk Drugs and those with Essential Shared Care Agreements
Commissioner Lead	NHS Shropshire CCG
Provider Lead	GP Practice
Period	1st April 2019 to 31st March 2020
Date of Review	October 2019

1. Population Needs

1.1 National Context and Evidence Base

All practices are expected to provide essential services and those additional services, which they are contracted to provide, to all their patients. This enhanced service specification is designed to cover enhanced aspects of clinical care of the patient, which are beyond the scope of essential services. No part of the specification by commission, omission or implication defines or redefines essential or additional services.

The treatment of several diseases within the field of medicine, particularly in rheumatology, is increasingly reliant on drugs which, while clinically effective, require regular monitoring. This is due to the potentially serious side-effects, which these drugs can occasionally cause. It has been shown that the incidence of side-effects can be reduced significantly if this monitoring is carried out in a structured manner.

Any GP, who prescribes medication, legally assumes responsibility for the drug and the consequences of its use. Prescribers therefore have a duty to keep themselves informed about the medicines they prescribe, including their appropriateness and effectiveness. They should also keep up to date with the relevant guidance on the use of medicines and on the management of the patient's condition.

1.2 Local Context

Shropshire Clinical Commissioning Group has a population of approximately 312,000. It consists of 41 GP member practices, which are working together to ensure that the local population is provided with sustainable, high quality, healthcare services.

The drug list included within this specification has been updated to reflect current prescribing for the relevant disease areas and the latest monitoring guidelines published by the British Society of Rheumatologists. It is recognized that prescribing patterns and requirements for monitoring evolve therefore these specifications shall be reviewed on an annual basis. As this is a local enhanced service, practitioners have the option of opting out; practices, however, are encouraged to participate in this enhanced service.

Aligning clinical and prescribing responsibility enhances patient safety because the individual signing the prescription, shall also be responsible for ensuring that any necessary monitoring has been undertaken and should have access to the results of this.

2. Outcomes

2.1 NHS Outcomes Framework Domains and Indicators

Domain 1	Preventing people from dying prematurely	✓
Domain 2	Enhancing quality of life for people with long term conditions	✓
Domain 3	Helping people to recover from episodes of ill-health or following injury	✓
Domain 4	Ensuring people have a positive experience of care.	✓
Domain 5	Treating and caring for people in a safe environment and protecting them from avoidable harm	✓

2.2 Local Defined Outcomes

To provide equitable patient access to high risk drug monitoring testing services within the local community.

3. Scope

3.1 Aim and Objectives of Service

The aim of this monitoring service is to ensure that patients are prescribed high risk drugs safely and it is supported by the following objectives:

(i) Medication should only be started for appropriate indications and time periods
(ii) Patient's medication doses should follow a dosing schedule recommended by secondary care clinicians and should be adequately monitored (and managed) in primary care
(iii) The service is convenient to the patient
(iv) The need for the continuation of therapy is reviewed regularly
(v) The therapy is discontinued when appropriate
(vi) The use of resources by the National Health Service is efficient
(vii) The agreed monitoring protocols should be followed by both primary and secondary care.

3.2 Service Description/Care Pathway

This service shall fund the monitoring of the following drugs:

Drugs Requiring Monitoring
5-Aminosalicylates - Balsalazide, Mesalazine, Olsalazine (for first 12 months only)
Amiodarone
Azathioprine
Ciclosporin
Denosumab
Dronedarone
Eplenerone
Leflunamide
Methotrexate (oral and parenteral)
Sodium aurothiomalate (Gold, Myocrisin)
Sulfasalazine (for first 12 months only)

Essential shared care agreements (ESCAs) are documents, which provide clear guidance to General Practitioners (GPs) and hospital prescribers on the procedures to be adopted when the responsibility for prescribing a patient's treatment is transferred from secondary to primary care.

Drugs included within this service specification are those which, a GP can prescribe but would not normally prescribe without assessment and recommendation from a specialist in secondary care and which require blood monitoring more frequently than once a year.

In order to qualify for payment for this Monitoring Service, the Provider shall have to fulfil the following criteria as a minimum requirement:-

(i) *A register* To produce and maintain an up-to-date register of all shared care drug monitoring service patients which includes: patient name; date of birth; the indication and intended duration of treatment; date of last hospital appointment and a schedule of monitoring results.

(ii) *Call and recall system* To ensure that systematic call and recall of patients on this register is taking place either in a hospital or general practice setting.

(iii) *Education of newly diagnosed patients* To ensure that all newly diagnosed / treated patients (and/or their carers when appropriate) have received appropriate education and advice on management and prevention of secondary complications of their condition and the drugs prescribed to manage it. This should include written information where appropriate.

(iv) *Continuing information for patients*. To ensure that all patients (and/or their carers and support staff when appropriate) are informed of how to access appropriate and relevant information

(v) *Individual management plan*. To ensure that the patient has been given a copy of an individual management plan which gives: the reason for treatment; the planned duration; the monitoring timetable and if appropriate, the therapeutic range to be obtained.

(vi) *Professional links*. To work together with other professionals when appropriate. Any health professionals involved in the care of patients should be appropriately trained.

Significant elements of (iii) to (vi) may be undertaken by rheumatology specialist nurses in secondary care.

(vii) *Referral policies.* Where appropriate to refer patients promptly to other necessary services and to the relevant support agencies using locally agreed guidelines where these exist.

(viii) *Record keeping*. To maintain adequate records of the service provided, incorporating all known information relating to any significant events e.g. hospital admissions or deaths, of which the practice has been notified.

(ix) *Training.* Each practice shall ensure that all members of staff involved in providing any aspect of care under this scheme have the necessary training and skills to do so.

(x) *Annual review*. All Providers shall perform an annual review, which should include:

a) Brief details as to the arrangements for each of the requirements in (i) to (viii)
b) Details of any computer-assisted decision-making equipment used and arrangements for internal and external quality control.
c) Details of any testing equipment used and arrangements for internal and external quality assurance
d) Details of the training and education relevant to this monitoring service), which has been undertaken by staff
e) Details of the standards used for the control of the relevant condition of the patient
f) Assurance that any staff member responsible for prescribing shall have the necessary skills to prescribe safely

Accreditation

Doctors who have previously provided services similar to the proposed enhanced service and who satisfy at appraisal and revalidation that they have such continuing medical experience, training and competence as is necessary to enable them to contract for the enhanced service, shall be deemed professionally qualified to do so.

3.3 Population Covered

The registered populations of all patients within the 41 GP Practices, which comprise Shropshire CCG.

3.4 Acceptance and Exclusion Criteria and Thresholds

This service does not apply to the Shropshire Walk in Centre as this has alternative commissioning arrangements.

Patient transport arrangements do not form part of this service specification. Patients shall be expected to make their own transport arrangements. Those patients who are entitled to assistance with transport under existing NHS arrangements should be able to access this service through their GP Practice as per local arrangements.

3.5 Interdependence with other Services/Providers

This service should be delivered as part of a seamless service for patients. This service should be delivered in collaboration with other Providers and within the arrangements of the relevant Essential Shared Care Agreements.

4. Applicable Service Standards

The service shall comply with the following guidance and policies where applicable.

4.1 National Standards e.g. NICE

NICE Guidance and recommended pathways http://guidance.nice.org.uk/

4.2 Standards set out in Guidance and/or Issued by a Competent Body e.g. Royal Colleges

BSR and BHPR guideline for the prescription and monitoring of non-biologic disease-modifying anti-rheumatic drugs https://doi.org/10.1093/rheumatology/kew479

4.3 Local Standards

Incidents Requiring Reporting

It is a condition of participation in this service that, practitioners should give notification to the Head of Medicines Management at Shropshire CCG, of all **emergency admissions or deaths** of any patient covered under this service, where such admission or death **is or may be due to usage of the drug(s)** in question or attributable to the relevant underlying medical condition, which is being treated and monitored under this specification. Notification shall take place within 72 hours of the information becoming known to the practitioner and should be reported via DATIX. This is in addition to their statutory obligations.

5. Applicable Quality Requirements and CQUIN Goals

Applicable Quality Requirements (See Schedule 4 parts [A-D]

Applicable CQUIN Goals (See Schedule 4 part [E]

6. Location of Provider Premises

The provider shall deliver this service from the GP Practice

Appendix 1 Shared Care Guidelines – Monitoring Protocols

Introduction

These guidelines look at the shared care management of patients treated with a range of disease modifying anti-rheumatic drugs (DMARDs) and drugs for other conditions which require specific monitoring. They are intended to guide prescribers in the safe prescribing of and monitoring requirements for these drugs

Drug treatment, indications and management plan

See the attached protocols for each drug.

Procedure for initiating shared care arrangements

The NHS Management Executive issued guidance in 1991 (Responsibility for prescribing between hospitals and GPs EL (91)127) and 1994 (Purchasing and prescribing EL (94)72) which reinforced the basic premise that:

- The doctor who has clinical responsibility for a patient should undertake prescribing.
- If care is to be shared there should be proper hand-over procedures from hospital specialists to GPs.

Aligning clinical and prescribing responsibility enhances patient safety because the individual signing prescriptions shall also be responsible for ensuring that any necessary monitoring has been undertaken and should have access to the results of this.
Shared care shall be agreed before the patient is directed to primary care. Patients shall not be put in a position where they are unsure where to obtain supplies of their medication. In the event that a GP declines to take on shared care of a patient, the matter should be referred to the Head of Medicines Management at Shropshire CCG for resolution.

The British Society for Rheumatology makes the following recommendations:

Generic Recommendations before Commencing any DMARD

(i) The decision to initiate DMARDs should be made in conjunction with the patient/carer and be supervised by an expert in the management of rheumatic diseases.
(ii) Patients should be provided with education about their treatment to promote self-management.
(iii) When appropriate, patients should be advised about the impact of DMARD therapy upon fertility, pregnancy and breastfeeding.
(iv) Baseline assessment should include height, weight, blood pressure and laboratory evaluation [full blood count (FBC), calculated glomerular filtration rate (GFR), alanine aminotransferase (ALT) and/or aspartate aminotransferase (AST) and albumin].
(v) Patients should be assessed for co-morbidities because these may influence DMARD choice, including evaluation for respiratory disease and screening for occult viral infection.
(vi) Vaccinations against pneumococcus and influenza are recommended.

Prescribing DMARDs in Patients with known Co-morbidities

(i) 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.
(ii) In patients with deranged liver biochemistry, hepatotoxic DMARDs should be used with caution, with careful attention to trends in test results.
(iii) In patients with impaired liver synthetic function (e.g. cirrhosis), DMARD therapy should be used with extreme caution.
(iv) Patients with chronic viral hepatitis infection should be considered for anti-viral treatment prior to immunosuppressive DMARD initiation.
(v) DMARDs should be used with caution in chronic kidney disease, with appropriate dose reduction and increased frequency of monitoring.
(vi) Cardiovascular disease and prior malignancy are not considered contraindications to DMARD therapy.

The following information should be read in conjunction with the Summary of Product Characteristics for each drug, available from www.medicines.org.uk

and the full Shared Care Agreement for each drug, available from www.shropshireccg.nhs.uk

Please note that there is inherently greater risk in having these drugs on 'repeats'.

Protocol number: 1

5-Aminosalicylates – Balsalazide, Mesalazine and Olsalazine

1. General guidance

This protocol outlines the shared care arrangements for patients taking 5 - Aminosalicylates.

2. Background

5-ASA drugs are widely use for the treatment of inflammatory bowel disease, as well as for rheumatological conditions. They should be used with caution in patients with renal impairment and avoided in patients with severe renal impairment or hypersensitivities to salicylates, sulphonamides or co-trimoxazole.

3. Pre-treatment assessment

FBC, LFTs, U&Es and creatinine.

4. Dosing

Dose and up titration shall be at the recommendation of the hospital consultant and should be recorded at the practice.

5. Monitoring

Ensure results from tests performed within relevant time period are available at time of signing prescription.
Repeat FBC, LFTs, U&Es and creatinine every 3 months for the first year.
Thereafter if results are stable repeat FBC and LFTs and U&Es every six months or annually based on patient's risk factors and monitor renal function annually or more frequently in renal failure.
Consider repeating bloods 1 month after any dose increases.
Ask about skin rash or oral ulceration at each visit.

Consider monitoring more frequently if also taking azathioprine or 6-mercaptopurine due to increased risk of haematological toxicity.

	Urgent Action to be Taken
• WBC <4.0 x 10^9/l	monitor carefully - if continues to fall, withhold until discussed with patient's consultant
• Neutrophils <2.0 x 10^9/l	monitor carefully - if continues to fall, withhold until discussed with patient's consultant
• Platelets <150 x 10^9/l	monitor carefully - if continues to fall, withhold until discussed with patient's consultant
• > 2 fold rise above upper limit of normal reference range for ALT/AST	withhold until discussed with patient's consultant team; ultrasound liver
• Rise of creatinine level above normal range (or rise of >20% above baseline)	withhold until discussed with patient's consultant team; urinalysis for proteinuria; renal ultrasound
• Severe abdominal pain	check amylase level; consider ultrasound or CT scanning
• Unexplained acute widespread rash	withhold and seek urgent specialist (preferably dermatological) advice
• Abnormal bruising, oral ulceration or Sore throat	check FBC and withhold until discussed with patient's consultant team
• Nausea, dizziness, headaches or worsening diarrhoea	If troublesome reduce dose or stop treatment and consider alternative

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

Protocol number: 2

Anti-arrhythmic drugs – Amiodarone and Dronedarone

1. General guidance

This protocol outlines the shared care arrangements for patients taking AMIODARONE and DRONEDARONE. The full Shared Care Agreements are available from **www.shropshireccg.nhs.uk**

AMIODARONE

2. Background

Amiodarone's license, its Summary of Product Characteristics and the British National Formulary state that it should be used for severe cardiac rhythm disorders when other treatment is ineffective or contra-indicated
It is the responsibility of the initiating specialist to ensure that a clear care plan, including indication, dose and duration of amiodarone therapy and hospital follow up, is sent to the patient's GP before expecting the GP to assume ongoing prescribing responsibility. If the initiating specialist is not a cardiologist, and there is not an end date for prescribing amiodarone then the patient should be referred to a cardiologist for a long term care plan.
General Practitioners should never initiate amiodarone therapy

3. Pre-treatment assessment - see also table below

Baseline investigations by the specialist: thyroid and liver function tests; serum U&E's; chest X-ray (if no recent investigation undertaken); echocardiogram; pulmonary/respiratory function tests (including DLCO) if underlying lung disease or abnormal chest X-ray and baseline slit-lamp examination, if visual impairment or symptoms,

4. Dosing

Amiodarone should only be initiated by specialists and the entirety of the loading dose should be under specialist supervision. Care should be taken to ensure that only the ongoing dose is used for prescribing by any other doctor.

After the initial period the dosage should be reduced to 200mg daily or less if appropriate. Rarely the patient may require a higher maintenance dose. The scored 100mg tablet should be used to titrate the minimum dosage required to maintain control of the arrhythmia. The maintenance dose should be regularly reviewed, especially where this exceeds 200mg daily.

5. Monitoring

Monitoring requirements for Amiodarone are summarised in the table below

Monitoring	TFTs	U&Es	Ophthalmologic Examination	ECG	LFTs	Chest X-ray	Lung Function Test	GP or Consultant
Baseline	✓	✓		✓	✓	✓	✓	Consultant
Week 1				✓				Consultant
Month 6	✓	✓		✓	✓			GP
Month 12	✓	✓	✓	✓	✓			GP
Thereafter	6 Monthly	6 Monthly	Annually (optometrist)	Annually	6 Monthly		Annually	GP

DRONEDARONE

6. Background

Dronedarone is indicated for the maintenance of sinus rhythm after successful cardioversion in adult clinically stable patients with paroxysmal or persistent atrial fibrillation (AF). Due to its safety profile, dronedarone should only be prescribed after alternative treatment options have been considered.

Dronedarone (Multaq®) should not be given to patients with left ventricular systolic dysfunction or to patients with current or previous episodes of heart failure.

7. Pre-treatment assessment

Baseline tests: LFTs, U&Es, ECG, Pulmonary Function Tests (PFTs)

On-going specialist responsibilities:

- 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.
- ECG every 6 months
- PFTs annually
- Provide any other advice or information for the GP including dose adjustments.

8. Dosing

The recommended dose is 400 mg twice daily with food (available as 400mg tablets). Prescribe dronedarone according to dose advised by specialist.

9. Monitoring

Arrange and record ongoing monitoring as agreed with specialist:

- **LFT:** 1 week after initiation of treatment; 1 month after initiation of treatment, then monthly for 6 months then at month 9 and 12 and periodically thereafter. If ALT levels are > 3 x upper limit of normal (ULN), treatment should be stopped and contact the specialist who reviews the patient in secondary care.
- **U&E:** plasma creatinine: 1 week after initiation, if an increase is seen, serum creatinine should be re-measured after a further 7 days. If no further increase is seen, this value should be used as the new reference baseline. If serum creatinine continues to rise, contact the specialist who reviews the patient in secondary care for advice.
- **Onset of dyspnoea or non-productive cough** may be related to pulmonary toxicity, contact the specialist who reviews the patient in secondary care for advice.
- Report adverse drug reactions to specialist and usual bodies (e.g. MHRA).
- Ensure no drug interactions with other medicines.

Protocol number: 3

Azathioprine

1. General guidance

This protocol outlines the shared care arrangements for patients taking AZATHIOPRINE. The full Shared Care Agreement is available from **www.shropshireccg.nhs.uk**

2. Background

Azathioprine is an immunosuppressant and a disease modifying anti-rheumatic drug. It requires blood monitoring because of the incidence of side effects such as neutropenia and thrombocytopenia. It is used in gastrointestinal disease and dermatology as well as rheumatoid disease.
Avoid live vaccine in patients taking azathioprine. Allopurinol and ACEIs increase blood levels of azathioprine and should not be started without discussing with patient's consultant.
An increased number of skin tumours have occurred in patients during treatment with azathioprine. They have been observed mainly on areas of skin exposed to the sun. Patients should be advised to use sun protection.
During a serious infection, azathioprine should be temporarily discontinued until the patient has recovered from the infection.

3. Pre-treatment assessment

Height, weight, blood pressure, FBC, creatinine/calculated GFR, ALT and/or AST and albumin. Patients should have baseline thiopurine methyltransferase (TPMT) status assessed. Avoid in TPMT deficiency or reduce dose if low levels.

4. Dosing

Dose and up titration shall be at the recommendation of the specialist and should be recorded within the practice.

5. Monitoring

Ensure results from tests performed within relevant time period are available at time of signing prescription.
FBC creatinine/calculated GFR, ALT and/or AST and albumin every 2 weeks until dose stable for 6 weeks; then 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. More frequent monitoring is appropriate in patients at higher risk of toxicity.
After dose increases repeat FBC, creatinine/calculated GFR, ALT and/or AST and albumin every 2 weeks until on stable dose for 6 weeks then revert to previous schedule.

Urgent Action to be Taken

Contact rheumatology team urgently and consider interruption in treatment if any of the following develop:

• White cell count	$<3.5 \times 10^9$/l
• Mean cell volume	>105 fl
• Neutrophils	$<1.6 \times 10^9$/l
• Creatinine increase	>30% over 12 months and/or calculated GFR <60ml/min
• Unexplained eosinophilia	$>0.5 \times 10^9$/l
• ALT and/or AST	>100 U/l
• Platelet count	$<140 \times 10^9$/l
• Unexplained reduction in albumin	<30g/l
• If Alk Phos or γ GT abnormal at baseline, then if either become	withhold until discussed with patient's consultant team $\geq$2 x upper level of normal
• Rash or oral ulceration	withhold until discussed with patient's consultant team
• Abnormal bruising or sore throat	withhold until discussed with patient's consultant team
• Diarrhoea	increase fibre content of diet or add fibre supplements. May need to reduce dose or if severe stop treatment

Prescribing of **trimethoprim or co-trimoxazole** increases the risk of haematological abnormalities

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

Protocol number: 4

Ciclosporin

1. General guidance

This protocol outlines the shared care arrangements for patients taking CICLOSPORIN. The full Shared Care Agreement is available from **www.shropshireccg.nhs.uk**

2. Background

Ciclosporin is widely use for the treatment of severe rheumatoid arthritis, short-term treatment of severe atopic dermatitis, severe psoriasis and (unlicensed) severe ulcerative colitis and a number of other conditions

3. Pre-treatment assessment

FBC, creatinine/calculated GFR, ALT and/or AST and albumin, height, weight, blood pressure and blood glucose.
On-going specialist responsibilities:

- Review results of safety monitoring and request additional tests as required.
- Perform trough drug levels and adjust dose if 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 including dose adjustments.

4. Dosing

Dose and up titration shall be at the recommendation of the hospital consultant and should be recorded at the practice.

5. Monitoring

Always prescribe Ciclosporin by brand (as initiated by specialist)

Arrange and record on-going monitoring as agreed with specialist

- Creatinine/ calculated GFR, blood glucose and blood pressure: every 2 weeks until dose stable for 6 weeks then monthly thereafter (if diastolic BP> 95mm Hg on 2 consecutive occasions, consider treating hypertension before stopping ciclosporin, also discuss with the initiating specialist team)
- FBC, ALT and/or AST and albumin every 2 weeks until dose stable for 6 weeks; then monthly.
- Fasting Lipids: six monthly
- ESR & CRP (Rheumatology only) may be required 3 monthly

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

If ciclosporin dose is adjusted monitor FBC, creatinine/calculated GFR, blood pressure, blood glucose, ALT and/or AST and albumin every 2 weeks until on stable dose for 6 weeks then revert to previous schedule.

Patients who have been stable for 12 months can be considered for reduced frequency monitoring on an individual patient basis.

Identify and report adverse drug reactions to initiating specialist and usual bodies (e.g. MHRA)

Ensure no drug interactions with other medicines

Administer influenza vaccine annually unless otherwise advised by the initiating specialist

Check patient has had ONE DOSE of pneumococcal vaccine (revaccination is not recommended except every five years in patients whose antibody levels are likely to have declined more rapidly e.g. asplenia.) - see BNF or Green Book

Passive immunisation using Varicella immunoglobulin (VZIG) should be considered in nonimmune patients exposed to chickenpox or shingles

Ask about oral ulceration/sore throat; unexplained rash or unusual bruising at every consultation

Urgent Action to be Taken

Contact rheumatology team urgently and consider interruption in treatment if any of the following develop:

- White cell count <3.5 x 10^9/l
- Mean cell volume >105 fl
- Neutrophils <1.6 x 10^9/l
- Creatinine increase >30% over 12 months and/or calculated GFR <60ml/min
- Unexplained eosinophilia >0.5 x 10^9/l
- ALT and/or AST >100 U/l
- Platelet count <140 x 10^9/l
- Unexplained reduction in albumin <30g/l
- Potassium > 5.5mmol/L
- Blood Pressure > 160/95 (or > 50% of baseline) despite addition of standard antihypertensive therapy
- Lipids Significant rise in lipids
- Oral Ulceration / sore throat
- Unexplained rash / abnormal bruising

Please note: A rapidly increasing or decreasing trend in any values should prompt caution and extra vigilance. Some patients may have abnormal baseline values, specialist should advise

Protocol number: 5

Denosumab

1. General guidance

This protocol outlines the shared care arrangements for patients taking DENOSUMAB. The full Shared Care Agreement is available from **www.shropshireccg.nhs.uk**

2. Background

Denosumab is a monoclonal antibody, which is licensed for the treatment of osteoporosis in postmenopausal women who are at increased risk of fractures. Patients should also meet the criteria in NICE TA204.

3. Pre-treatment assessment

None by practice. Specialist is responsible for checking calcium levels before each of first two doses and within two weeks of initial dose, in patients at a high risk of hypocalcaemia e.g. patients with an eGFR<30ml/min.

4. Dosing

The recommended dose of denosumab is 60mg, administered as a single subcutaneous injection once every six months in the thigh, abdomen or back of the arm. This can be administered by the practice or the patient can be taught to self-administer. The first two doses should be administered within secondary care.

5. Monitoring

Calcium levels should be checked every six months, at least two weeks before each dose and if suspected symptoms of hypocalcaemia occur.
Ensure results from tests performed within relevant time period are available at time of signing prescription.

Urgent Action to be Taken

• Skin infections (e.g. cellulitis)	Patient should seek prompt medical attention
• Symptoms of hypocalcaemia e.g. muscle spasms, twitches, cramps, numbness or tingling in fingers, toes or around the mouth	Should be reported to GP. Calcium levels to be checked and advice sought from specialist if necessary.
• Symptoms of osteonecrosis of the jaw e.g. pain, swelling, dental mobility, non-healing oral sores or discharge	Should be reported to GP and dental surgeon
• If an atypical femoral fracture is suspected	Patient should be referred to specialist for evaluation and discontinuation of treatment should be considered until patient has been evaluated

The GP is also responsible for:

- Ensuring patient maintains an adequate intake of calcium and vitamin D
- Checking for any possible drug interactions with current and any newly prescribed concurrent treatment
- Reporting any adverse events to the MHRA

Protocol number: 6

Eplerenone for heart failure

1. General guidance

This protocol sets out details for the monitoring of patients prescribed EPLERENONE for heart failure.

2. Background

Eplerenone is an effective drug for patients with Chronic Heart Failure who remain symptomatic despite optimal doses of ACE inhibitors (or Angiotensin II receptor blockers) and β -blockers or where spironolactone is not tolerated e.g. gynaecomastia; eplerenone is then substituted. Spironolactone is the drug of first-choice in this drug group for chronic heart failure.

Eplerenone should only be commenced on the recommendation of a specialist.

Eplerenone may be considered for patients who develop symptomatic heart failure in the immediate post MI period and remain symptomatic at 3-14 days. It should only be commenced by a hospital consultant, in these circumstances.

3. Pre-treatment assessment

None by practice

4. Dosing

Dose and up-titration shall be at the recommendation of the hospital consultant and should be recorded within the practice.

5. Monitoring

Ensure results from tests performed within relevant time period are available at time of signing prescription.

Measure U&Es at 2 weeks post initiation, 3 monthly thereafter for 1 year and then 6 monthly

Urgent Action to be Taken

Stop eplerenone immediately and seek advice from the hospital if:

- **creatinine** (on routine monitoring – see above) increases to 250 µmol/L or by ≥ 25% from baseline (e.g. from 80 to 100 µmol/L
- **urea** (on routine monitoring – see above) with previous reading <12, increases to ≥ 18 mmol/L; or if previous reading ≥12, increases by ≥ 50% e.g. 12 to 18
- **potassium** increases (on routine monitoring – see above) to ≥ 5.5mmol/L
- **sodium and water depletion occurs e.g.**
    - patient develops inter-current illness causing sodium and water depletion e.g. diarrhoea and vomiting
    - patient is not drinking fluids
    - patient has been in a hot climate, perspiring excessively.
    - any other cause of sodium and water loss

Symptoms/signs of sodium and water depletion are

- postural dizziness / light-headedness
- excessive and sustained fall in blood pressure
- significant and sustained weight loss (e.g. > 1 Kg, sustained over >1 week)

If patient has any such symptoms, measure U&Es immediately and seek advice from the hospital.

Ensure patient has written information about reporting symptoms and issues around sodium and water depletion.

Protocol number: 7

Leflunomide

1. General guidance

This protocol outlines the shared care arrangements for patients taking LEFLUNOMIDE. The full Shared Care Agreement is available from **www.shropshireccg.nhs.uk**

2. Background

Leflunomide is an immunosuppressant similar in efficacy to sulfasalazine and methotrexate. Its effect starts after 4-6 weeks and improvement can continue for 4-6 months.

3. Pre-treatment assessment

FBC, creatinine/calculated GFR, ALT and/or AST and albumin, height, weight and blood pressure.

4. Dosing

Dose and up titration shall be at the recommendation of the hospital consultant and should be recorded within the practice.

5. Monitoring

Ensure results from tests performed within relevant time period are available at time of signing prescription.
FBC, creatinine/calculated GFR, ALT and/or AST and albumin, every 2 weeks until on stable dose for 6 weeks
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.

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

Blood pressure and weight should be checked at each visit. If >10% weight loss with no other cause identified, reduce dose or stop and consider washout (contact consultant team if washout is thought necessary). If co-prescribed with another immunosuppressant or potential hepatotoxic agent then blood checks should be continued long term, at least monthly.

If ALT/AST is 2-3 times the upper limit of normal – reduce dose to 10mg and re-check weekly. If normalised – continue with10mg dose. If level remains elevated withdraw drug and discuss with specialist team.

If ALT/AST is >3 times normal, stop drug and re-check within 72 hours. If level remains > 3 times normal, withdraw drug and consider washout (contact consultant team if washout is thought necessary).

If given in conjunction with methotrexate - extend monthly monitoring longer term (patients who have been stable for 12 months can be considered for reduced frequency monitoring on an individual patient basis).

Increases in dose should lead to a repeat of FBC, creatinine/calculated GFR, ALT and/or AST and albumin every 2 weeks until on stable dose for 6 weeks then revert to previous schedule.

Urgent Action to be Taken

Contact rheumatology team urgently and consider interruption in treatment if any of the following develop:

• White cell count	<3.5 x 10^9/l
• Mean cell volume	>105 fl
• Neutrophils	<1.6 x 10^9/l
• Creatinine increase	>30% over 12 months and/or calculated GFR <60ml/min
• Unexplained eosinophilia	>0.5 x 10^9/l
• ALT and/or AST	>100 U/l
• Platelet count	<140 x 10^9/l
• Unexplained reduction in albumin	<30g/l
• Rash, itch or oral ulceration	withhold until discussed with consultant team
• Abnormal bruising or sore throat	withhold until discussed with consultant team
• Blood pressure >140 syst or >90 diast	continue treatment for 3 months. Re-measure blood pressure. If still elevated, discuss with consultant team

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

Do not use live vaccines in patients taking leflunomide.

Advise no procreation while patient is taking leflunomide nor within 2 years of stopping it (women) and 3 months (men)

Patients should be advised not to drink alcohol while taking leflunomide.

During a serious infection, lefunomide should be temporarily discontinued until the patient has recovered from the infection.

Protocol number: 8

Methotrexate (Oral and Parenteral)

1. General guidance

This protocol outlines the shared care arrangements for patients taking ORAL or PARENTERAL METHOTREXATE. The full Shared Care Agreement is available from **www.shropshireccg.nhs.uk**

2. Background

Methotrexate is an effective second-line drug used in the treatment of rheumatoid arthritis, psoriasis, some cancers and occasionally other autoimmune disorders. It has both immunosuppressant and anti-inflammatory effects.

3. Pre-treatment assessment

Check height, weight, blood pressure, FBC, creatinine/calculated GFR, ALT and/or AST and albumin. If drug is recommended in a patient with abnormal LFTs at pre-treatment assessment, then guidance should be given about how to deal with further deterioration in liver function. The specialist initiating treatment should ensure that the patient gets a chest x ray if they have not had one within the preceding 6 months. (Pulmonary function tests may be requested in patients with underlying respiratory disease at baseline).

4. Dosing

Dose and up titration shall be at the recommendation of the hospital consultant and should be recorded within the practice. All patients should be co-prescribed folic acid supplementation at a minimal dose of 5mg once weekly.

Methotrexate should be withheld during the treatment of acute infections. **Trimethoprim and co-trimoxazole** should be avoided as they greatly increase the risk of marrow aplasia.

5. Monitoring

Ensure results from tests performed within relevant time period are available at time of signing prescription.
Check FBC, creatinine/calculated GFR, ALT and/or AST and albumin every 2 weeks until dose and monitoring stable for 6 weeks, then monthly for 3 months. Thereafter reduce to at least every 12 weeks. More frequent monitoring is appropriate in patients at higher risk of toxicity.

If given in conjunction with leflunomide - extend monthly monitoring longer term (patients who have been stable for 12 months can be considered for reduced frequency monitoring on an individual patient basis).

Increases in dose should lead to a repeat of FBC, creatinine/calculated GFR, ALT and/or AST and albumin every 2 weeks until on stable dose for 6 weeks then revert to previous schedule.

New or increasing dyspnoea or dry cough – withhold and discuss urgently with the specialist team.

Urgent Action to be Taken

Contact rheumatology team urgently and consider interruption in treatment if any of the following develop:

- White cell count <3.5 x 10^9/l
- Mean cell volume >105 fl
- Neutrophils <1.6 x 10^9/l
- Creatinine increase >30% over 12 months and/or calculated GFR <60ml/min
- Unexplained eosinophilia >0.5 x 10^9/l
- ALT and/or AST >100 U/l
- Platelet count <140 x 10^9/l
- Unexplained reduction in albumin <30g/l2x upper limit of normal Alk phos/γ GT
  withhold until discussed with patient's consultant or team (unless abnormal at pre-assessment – follow guidance given by secondary care – see above)
- Rash or oral ulceration withhold until discussed with patient's consultant team
- Abnormal bruising or sore throat withhold until discussed with patient's consultant team
- Symptoms of pneumonitis (dyspnoea, cough, fever) withhold until discussed with patient's consultant team

During a serious infection, Methotrexate should be temporarily discontinued until the patient has recovered from the infection.

Do not give live vaccines to patients taking methotrexate

Annual flu vaccine should be given

Contraception should be used and conception delayed for 3 months after treatment has stopped.

Patients should be advised to stay well within national recommendations for alcohol e.g. dermatology guidelines recommend no more than 6 units/week.

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

Protocol number: 9

Sodium Aurothiomalate (Myocrisin)

1. General guidance

This protocol outlines the shared care arrangements for patients taking SODIUM AUROTHIOMALATE. The full Shared Care Agreement is available from **www.shropshireccg.nhs.uk**

2. Background

Sodium aurothiomalate is a slow-acting drug effective in controlling disease activity in 60-70% of patients with rheumatoid arthritis. Improvement can be expected after 2-3 months (400-600 mg total dose), and in the absence of toxicity gold injections may be continued indefinitely.

3. Pre-treatment assessment

Check height, weight, blood pressure, FBC, urinalysis (for blood and protein), creatinine/calculated GFR, ALT and/or AST and albumin.

4. Dosing

Sodium aurothiomalate should be administered only by deep intramuscular (IM) injection followed by gentle massage of the area.

A typical dose regimen may be: 10mg test dose (with 30 minutes observation to look for any signs of allergic reaction) followed by 20 - 50mg weekly until there is a significant response (If no significant response is seen after a total cumulative dose of 1000mg has been given the efficacy should be questioned and alternative medicines considered.)

In patients who respond, the interval between doses may be increased by stages from 50mg per week to 50mg every 4 weeks.

Sodium aurothiomalate is available as: injection 10mg/0.5ml, 50mg/0.5ml

5. Monitoring

Urinalysis (for blood and protein) shall be done immediately before each injection.

Check FBC, creatinine/calculated GFR, ALT and/or AST and albumin every 2 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.

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

Ensure GP has sanctioned the dose. Complete nurse documentation and only give dose if all monitoring is within the limits outlined below.

Increases in dose should lead to a repeat of FBC, creatinine/calculated GFR, ALT and/or AST and albumin every 2 weeks until on stable dose for 6 weeks then revert to previous schedule.

Ask about oral ulceration/sore throat; unexplained rash or unusual bruising at every consultation.

Urgent Action to be Taken

Contact rheumatology team urgently and consider interruption in treatment if any of the following develop:

- White cell count <3.5 x 10^9/l
- Mean cell volume >105 fl
- Neutrophils <1.6 x 10^9/l
- Creatinine increase >30% over 12 months and/or calculated GFR <60ml/min
- Unexplained eosinophilia >0.5 x 10^9/l
- ALT and/or AST >100 U/l
- Platelet count <140 x 10^9/l
- Unexplained reduction in albumin <30g/l

• ≥1+ proteinuria on >1 occasion	withhold. Do MSSU. If positive – treat. Following treatment or if MSSU negative, continue to withhold until discussed with consultant team.
• Rash or oral ulceration	withhold until discussed with consultant team
• Abnormal bruising or sore throat	withhold until discussed with consultant team
• Flushing (possible nitritoid reaction)	withhold until discussed with consultant team

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

Protocol number: 10

Sulfasalazine

1. General guidance

This protocol outlines the shared care arrangements for patients taking SULFASALAZINE. The full Shared Care Agreement is available from **www.shropshireccg.nhs.uk**

2. Background

Sulfasalazine (*Salazopyrin / previously Sulphasalazine*) is widely use for the long term treatment of rheumatoid arthritis, and inflammatory bowel disease. The licensed indications for the different formulations indicate which is best for each condition e.g. EC for rheumatological conditions, non EC for ulcerative colitis).

3. Pre-treatment assessment

Check height, weight, blood pressure, FBC, creatinine/calculated GFR, ALT and/or AST and albumin.

4. Dosing

Dose and up-titration shall be at the recommendation of the specialist should be recorded within the practice.

5. Monitoring

Ensure result from tests, performed within relevant time period, are available at time of signing prescription.

Repeat FBC, creatinine/calculated GFR, ALT and/or AST and albumin every 2 weeks until on stable dose for 6 weeks.

Once on stable dose repeat FBC, creatinine/calculated GFR, ALT and/or AST and albumin monthly for 3 months. If dose and bloods stable for 3 months, then repeat at least every 12 weeks for remainder of the year. More frequent monitoring is required in patients at higher risk of toxicity.

Increases in dose should lead to a repeat of FBC, creatinine/calculated GFR, ALT and/or AST and albumin every 2 weeks until on stable dose for 6 weeks then if result stable, revert to previous schedule.

Ask about skin rashes or oral ulceration at every visit

After 12 months of therapy blood monitoring can be discontinued if results are normal and doses stable.

Urgent Action to be Taken

Contact rheumatology team urgently and consider interruption in treatment if any of the following develop:

• White cell count	<3.5 x 10^9/l
• Mean cell volume	>105 fl
• Neutrophils	<1.6 x 10^9/l
• Creatinine increase	>30% over 12 months and/or calculated GFR <60ml/min
• Unexplained eosinophilia	>0.5 x 10^9/l
• ALT and/or AST	>100 U/l
• Platelet count	<140 x 10^9/l
• Unexplained reduction in albumin	<30g/l
• 2x upper limit of normal Alk phos/γ GT	withhold until discussed with patient's consultant or team (unless abnormal at pre-assessment – follow guidance given by secondary care – see above)
• Rash or oral ulceration	withhold until discussed with patient's consultant or team
• Abnormal bruising or sore throat	withhold until discussed with patient's consultant or team
• Nausea/dizziness/headache	if possible, continue. May have to reduce dose if symptoms severe

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

During a serious infection, Sulfasalazine should be temporarily discontinued until the patient has recovered from the infection.