NHS
Somerset
Clinical Commissioning Group

Service Specification No.	11X-04-V2
Service	Enhanced Drug Monitoring
Commissioner Lead	Sheryl Vincent, Commissioning Manager
Provider Lead	
Period	01 April 2018 – 31 March 2019
Date of Review	TBC

1. Population Needs

National/local context and evidence base

1.1 The treatment of several diseases within the fields of medicine, particularly in rheumatology, is increasingly reliant on drugs that, while clinically effective, need regular blood monitoring. This is due to the potentially serious side-effects that 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 well-organised way, close to the Service User's home.

1.2 Each different drug has different monitoring and safety requirements to ensure that the Service User takes the medication safely and effectively. Please see Appendix 1 to this specification for the individual drug monitoring requirements which are being commissioned.

1.3 Providers should note that the individual drugs SPCs and local shared care guidance may specify more intense drug monitoring than this enhanced service specification. The level of monitoring commissioned has been set upon what is deemed safe and practical for the overwhelming majority of Service Users prescribed one of the drugs specified.

1.4 Prescribers are recommended to take into account the individual Service Users co-morbidities and co-prescribed medication when deciding whether to monitor Service Users more frequently than set out in the enhanced service. Particular consideration should be given to increased monitoring in Service Users newly initiated, after a dose increase, with impaired renal function or on combinations of two drugs in the enhanced service or another drug likely to increase the need for monitoring

2. Outcomes

2.1 NHS Outcomes Framework Domains & 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 safe environment and protecting them from avoidable harm**	☑

2.2 Local defined outcomes

Not applicable

3. Scope

Aims and objectives of service

SERVICE AIMS

3.1 The Near Service User Testing Service is designed to be one in which:

- therapy is only started for recognised indications and for specified lengths of time
- maintenance of Service Users who have not first been stabilised in the secondary care setting can be under taken safely in primary care with a shared care approach between consultant and GP.
- the service to the Service User is convenient
- the need for continuation of therapy is reviewed regularly
- the therapy is discontinued when appropriate, including discussing any reported side-effects with the relevant secondary care department (e.g. rheumatology) if necessary
- any necessary monitoring is undertaken as commissioned, the GP gives due consideration to additional monitoring if recommended by the secondary care consultant or is clinically indicated, and
- the use of resources by the National Health Service is efficient.

Service description/care pathway

3.2 The Near Service User Testing Service shall include the provision of a shared care drug monitoring service in respect of the following specified drugs:

3.3 DMARDs

- Sulfasalazine
- Azathioprine
- Penicillamine
- Leflunomide
- Oral Methotrexate
- Sodium Aurothiomalate (Myocrisin)
- Sub-cutaneous Methotrexate injections
- Hydroxychloroquine
- Mercaptopurine

3.4 Other Drugs

- Dronedarone

3.5 Services not included in specification

- Monitoring of drugs not listed above such as chlorambucil, ciclosporin, etanercept, infliximab or other biological drugs

SERVICE REQUIREMENTS

3.6 The Provider shall ensure that the Near Service User Testing Service includes but is not limited to:

3.7 Service specification and criteria

- ensuring that all newly diagnosed Service Users (and/or their carers and support staff when appropriate) receive appropriate education and advice on management of, and prevention of, secondary complications of their condition including the provision of written information
- ensuring that the systematic call and recall of Service Users using the Near Service User Testing Service is taking place in primary medical services setting
- ensuring that all Service Users (and/or their carers and support staff when appropriate) are informed of how to access appropriate and relevant information
- preparing an individual management plan with the Service User, which gives the diagnosis, planned duration, the monitoring timetable and, if appropriate, the therapeutic range to be obtained
- referring Service Users promptly to other necessary services and to the relevant support agencies, when clinically appropriate, using locally agreed shared care guidelines where these exist and in line with any Summary of Product Characteristics datasheets available at www.medicines.org.uk
- working with other professionals when appropriate
- developing and maintaining an up-to-date register of all Service Users using the Near Service User Testing Service, indicating Service User name, date of birth, the indication for treatment, duration of treatment and last hospital appointment
- maintaining adequate records of the performance and result of the Near Service User Testing Service provided, incorporating appropriate known information, as appropriate. This shall include all known information relating to any significant events e.g. hospital admissions and death of which the provider has been notified.

Quality Assurance

3.8 The Provider acknowledges that:

- quality assurance must be carried out in accordance with relevant local and national guidance and protocols
- all significant events relating to the shared care drug monitoring service must be adequately identified, recorded and investigated both by the Provider in accordance with Section 8 of this specification
- all significant events resulting in death must be reported to the Somerset Clinical Commissioning Group within 72 hours

Health Record

3.9 The Provider should ensure that all clinical information related to this service is recorded in the Service User's own General Practitioner (GP) held lifelong record.

3.10 Where a Service User ceases to take drugs that are relevant to this service then the Service User record should be duly updated

Training and Accreditation

3.11 The Provider shall ensure that:

- all staff involved in providing any aspect of care under this Near Service User Testing Service have the necessary training and skills to do so
- the expertise of other professionals can be drawn on where necessary
- all staff involved in this service should be providing care in accordance to the shared care protocols developed by the secondary care provider. Please complete and return the form at Appendix 2 to the Somerset Clinical Commissioning Group.

INFECTION CONTROL

3.12 Providers must have infection control policies that are compliant with national guidelines , which include:

- disposal of clinical waste
- needle stick incidents
- environmental cleanliness, and
- standard precautions, including hand washing.

REVIEW AND AUDIT

3.13 The Provider shall perform an annual review, which includes:

- details of training and education relevant to the drug monitoring service;
- details of the standards used for the control of the relevant condition; and
- assurance that any staff member responsible for prescribing must have developed the necessary skills to prescribe safely.

SIGNIFICANT/ADVERSE EVENTS

3.14 The Department of Health emphasizes the importance of collected incidents nationally to ensure that lessons are learned across the NHS. A proactive approach to the prevention of recurrence is fundamental to making improvements in Service User safety.

3.15 The Provider should be aware of the various reporting systems such as:

- the National Service User Safety Agency National Reporting and Learning System
- the Medicines and Healthcare products Regulatory Agency reporting systems for adverse reactions to medication (yellow card system), and accidents involving medical devices, and
- the legal obligation to report certain incidents to the Health and Safety Executive under the Reporting of Injuries, Diseases and Dangerous Occurrences Regulations (RIDDOR).

3.16 In addition to any regulatory requirements the Somerset Clinical Commissioning Group (SCCG) wishes the Provider to use a Significant Event Audit system (agreed with the SCCG) to facilitate the dissemination of learning, minimising risk and improving Service User care and safety.

3.17 In addition to their statutory obligations, the Provider will give notification, within 72 hours of the information becoming known to him/her, of all emergency admissions or deaths of any Service User treated by the Provider under this enhanced service, where such admission or

death is or may be due to the Providers treatment of the relevant underlying medical condition covered by this specification. Notifications are to be sent to the Director of Quality, Safety and Governance with a copy to the Primary Care Commissioning Manager for the specific locality.

PRICING

3.18 Each practice contracted to provide this service will receive:

- Level 3 – Provider-funded phlebotomist, provider sample, laboratory test, provider dosing £****

3.19 Where a Service User is receiving combinations of two or more drugs covered by this specification, only one payment per Service User will be made.

3.20 In addition to the above fees, where sampling requires a domiciliary visit to a housebound Service User on or behalf of the provider and not by a member of staff employed by an NHS body to provide community health services, an additional fee would be paid for each separate address visited on that day, £***.

3.21 Community nursing services staff are only able to take samples for those housebound Service Users already on their caseload.

PAYMENT

3.22 Payment will be made on a monthly basis, pro rata for the number of Service Users monitored in the previous year.

3.23 Payments will be reconciled after the year end and will be made on the basis of the number of Service Users monitored each quarter.

CONSENT

3.24 In each case the Service User should be fully informed of the treatment options, risks and the treatment proposed.

3.25 National guidelines suggest that written consent should be obtained from Service Users. The Somerset Clinical Commissioning Group wishes the Providers to note that their interpretation of 'written consent' in this context is the recording of consent by Read Code where appropriate. Where the Provider Read Codes consent given, the Somerset Clinical Commissioning Group will take this to mean that the Service User has been fully informed of the treatment options and risks, has been offered written information and has given consent.

SERVICE USER AND PUBLIC INVOLVEMENT

3.26 The service will conform to professional and legal requirements especially clinical guidelines and standards of good practice issued by the National Institute for Clinical Excellence (NICE) and professional regulatory bodies, and legislation prohibiting discrimination. It is anticipated that for the majority of enhanced services translated information will be available via the Department of Health. If a Service User wishes to communicate via a language that is not covered via these leaflets please let the Somerset Clinical Commissioning Group Equality and Diversity Lead know and use the commissioned interpretation and translation service[1] to facilitate the consultation and provision of information to the Service User. Use of the interpretation/translation service should be recorded in the Service User's lifelong medical record including confirmation of the first language of the Service User.

[1] Somerset CCG Interpretation and Translation Service – the PIN for accessing this service has been given to each provider, for queries please email: translations@somerset.nhs.uk

3.27 Practices should encourage, consider and report any Service User feedback (positive and negative) on the service that they provide and use it to improve the care provided to Service Users, particularly if there are plans to alter the way a service is delivered or accessed.

REFERENCES

3.28 Individual drugs SPCs www.medicines.org.uk.

3.29 Somerset Shared care protocols: http://nww.somerset.nhs.uk/welcome/directorates/primary-care-development/prescribing-and-medicines-management/supporting-shared-care/

3.30 The Health Act 2006: Code of Practice for the Prevention and Control of Healthcare Associated Infections. The Stationary Office, 2006.

Population covered

3.31

Any acceptance and exclusion criteria and thresholds

3.32 Not applicable

Interdependence with other services/providers

3.33 Not applicable

4. Applicable Service Standards

4.1 Applicable national standards (e.g. NICE)

4.2 Applicable standards set out in Guidance and/or issued by a competent body (e.g. Royal Colleges)

Not applicable

4.3 Applicable local standards

Not applicable

5. Applicable quality requirements and CQUIN goals

5.1 Applicable quality requirements (See Schedule 4 Parts A-D)

5.2 Applicable CQUIN goals (See Schedule 4 Part E)

6. Location of Provider Premises

The Provider's Premises are located at:

As defined in Schedule 5 Part A of the Contract Particulars

7. Individual Service User Placement

Not applicable

APPENDIX 1

PROTOCOLS FOR DRUG MONITORING - DMARDs

Protocol 1 **Sulphasalazine**

Indication: Rheumatoid Arthritis (long term treatment, two preparations – Salazopyrin EN is considered to have less GI side effects)

Dosage Regimes: 500mg daily increasing by 500mg weekly increments to a maximum of 2.0 – 3.0g/day, if tolerated. Some Service Users may respond to a lower dose. Treatment may be continued indefinitely, the usual reason for stopping being loss of benefit. Sulphasalazine is sometimes co-prescribed with other anti-rheumatic agents. Dose adjustment usually initiated in secondary care.
Time to response: Minimum of 3 months

Monitoring prior to treatment (Consultant responsibility)
FBC, LFTs, U&Es and creatinine

Further monitoring required after initiation (GP responsibility)	
FBC	Monthly for the first 12 weeks, 3 monthly thereafter
U&Es and creatinine	Monthly for the first 12 weeks, 3 monthly thereafter, consider urinalysis if clinically indicated
LFTs	(incl. AST or ALT) Monthly for the first 12 weeks and then 3 monthly thereafter

Notes	• FBC should include differential WCC and platelets. • Repeat FBC and LFT one month after each dose increase. • If 3-monthly FBC & LFTs remain stable during first year, reduce to 6-monthly in second year. • If dose and results remain stable in second year no further FBC or LFT monitoring is required unless clinically indicated. • Ask about skin rash or oral ulceration on each visit
Renal impairment (moderate)	• May cause crystaluria, suggest high fluid intake, withhold in severe renal impairment.
G6PD deficiency	May cause haemolysis May reduce folate absorption
Pregnancy and breast feeding	Weigh up risk benefits, keep dose< 2 g od Men may have transient reversible oligospermia Small amounts in breast milk not thought to be harmful May cause a drug induced lupus like syndrome (especially in slow acetylators) Contraindicated in hypersensitivity to sulphonamides , septrin or aspirin

WB<3.5 x10^9 /l	withhold until discussed with rheumatologist
Neutrophil <2.0x10^9 /l	withhold until discussed with rheumatologist
Platelets < 150x10^9/l	withhold until discussed with rheumatologist
>2-fold rise in AST, ALT or Alk. Phos (from upper limit of reference range)	withhold until discussed with rheumatologist
Rash or oral ulceration	withhold until discussed with rheumatologist
MCV>105fl	investigate and if B12 or folate low start appropriate supplementation nausea/dizziness/ headache if possible continue, may have to reduce dose or stop if symptoms severe.
Abnormal bruising or sore throat	Withhold until FBC result available
Widespread acute rash	Withhold and seek advice
Oral ulceration	Withhold and seek advice

References:

- T&S DMARD monitoring http://www.tsft.nhs.uk/OurServices/Rheumatology/InformationforGPs/DMARDMonitoring/Sulphasalazine/tabid/1650/Default.aspx (last accessed 28/5/12)

- British Society for Rheumatology Quick reference guideline for monitoring of DMARD therapy http://www.rheumatology.org.uk/includes/documents/cm_docs/2009/d/dmard_grid_november_2009.pdf (last accessed 28/5/2012)

- EMC Salazopyrin SPC http://www.medicines.org.uk/EMC/medicine/10722/SPC/Salazopyrin+En-Tabs/#INTERACTIONS

Urgent FBC if Service User complains of intercurrent illness during initiation of treatment

Protocol 2 **Oral and sub cut Methotrexate**

N.B. The National Service User Safety Agency pink advice and monitoring booklets should now replace shared care monitoring cards and should be carried by all Service Users.
http://www.nrls.npsa.nhs.uk/resources/?EntryId45=59800

Indication: Rheumatoid Arthritis, Psoriasis (second-line drug – immunosuppressant and anti-inflammatory effects)

In most Service Users, subcutaneous methotrexate will replace current oral methotrexate and monitoring should be continued as already being done by the GP without any change.

Dosage Regimes: **Oral -** Initially 5mg to 7.5mg orally once weekly, increased every 2-6 weeks to a maximum maintenance dose of up to 25mg ONCE per week. However dosage should be set by a secondary care clinician responsible under shared care for the Service User - they may recommend exceptions to these restrictions. To limit the side effects of methotrexate, Folic Acid (5mg) should be taken **once a week** on the day before or the day after methotrexate.
Sub cut injection - The dose is usually titrated at regular intervals until target dose/response is achieved. Maximum weekly dose should not exceed 25mg unless prior agreement between consultant and GP. Methotrexate must be used with caution in renal failure or hepatic impairment; elderly Service Users should be given a smaller test dose and titrated at a slower rate. To limit the side effects of methotrexate, Folic Acid (5mg) should be taken **once a week** on the day before or the day after methotrexate.

CSM advice; in view of reports of blood dyscrasias (including fatalities) and liver cirrhosis with low-dose methotrexate, the CSM has advised:

- Full blood count; renal and liver function tests before starting treatment and repeated weekly until therapy stabilized, thereafter Service Users should be monitored every 2-3 months
- Service Users should be advised to report all symptoms and signs suggestive of infection, especially sore throat

Monitoring prior to treatment (Consultant responsibility)	
FBC, LFTs, U&Es, Creatinine, Urinalysis, CXR, Pulmonary function (only in selected Service Users, e.g. abnormal shadowing on CXR)	
Further monitoring required after initiation (GP responsibility)	
FBC	SPC (Maxtrex) recommends weekly tests until therapy is stabilised. Provided results are stable, monthly thereafter. If the dose and disease is stable for a year then, following a discussion with the specialist team, the frequency of monitoring may be reduced to every 2-3 months
LFTs (inc AST or ALT)	as for FBC above
U&Es and Renal function	As for FBC

U&Es and Renal function	As for FBC

CRP (RA only)	Check monthly at onset of disease and prior to hospital appointment with consultant/specialist nurse when notified. CRP testing is not required as part of routine disease monitoring.

Notes	• Any dosage increase should be followed by an FBC one week later. • Service Users should be advised to report any symptoms or signs of infection. • Cotrimoxazole or trimethoprim must be avoided in Service Users taking methotrexate (greatly increases risk of marrow aplasia)

Action to be taken:

WBC < 3.5 x10^9/l	withhold *until discussed* with rheumatologist
Neutrophils < 2.0 x10^9	withhold *until discussed* with rheumatologist
Platelets<150x10^9 /l	withhold *until discussed* with rheumatologist
>2-fold rise in AST, ALT	withhold *until discussed* with rheumatologist (*from upper limit of reference range)* **Raised liver enzymes - see below***
Unexplained fall in albumin	withhold *until discussed* with rheumatologist (in absence of active disease)
Rash or oral ulceration	withhold *until discussed* with rheumatologist
New or increasing dyspnoea or dry cough	withhold *until discussed* with rheumatologist
MCV >105 fl	investigate TFT and if B12 or folate low start appropriate supplementation
Mild to moderate deterioration in renal function	reduce dose or discontinue (eGFR < 45mls/min)
Abnormal bruising or severe sore throat	withhold until FBC result available

*Raised ALT and or ALK PHOS in a Service User taking Methotrexate?

Generally we allow up to 5 consecutive mildly raised ALTs (<100) without withholding MTX. If Service User also taking an NSAID, discontinue that, if Sulphasalazine stop that. If persistent Check alcohol intake (GGT) and perform non-invasive liver screen: If any clinical concern discuss with Service Users consultant.

Ferritin, Hep B and C, Autoimmune profile, a-1 anti-trypsin levels, copper studies, Liver U/S, and refer (if Methotrexate is to continue a liver biopsy will be needed).

If Alkaline phosphatase minimally raised without ALT, check GGT (it maybe boney) and reflect disease activity, so continue methotrexate.

References:

- T&S DMARD monitoring http://www.tsft.nhs.uk/OurServices/Rheumatology/InformationforGPs/DMARDMonitoring/MethotrexateMTX/tabid/1651/Default.aspx

- British Society for Rheumatology Quick reference guideline for monitoring of DMARD therapy http://www.rheumatology.org.uk/includes/documents/cm_docs/2009/d/dmard_grid_november_2009.pdf (last accessed 28/5/2012)

- EMC Methotrexate SPC
  http://www.medicines.org.uk/EMC/medicine/6003/SPC/Maxtrex+Tablets+2.5+mg/

Protocol 3 **Azathioprine**

Indication: Rheumatoid Arthritis (used for the long term treatment, usually prescribed for cases that have not responded to other disease modifying drugs. Service Users prescribed AZATHIOPRINE should avoid allopurinol and should avoid live vaccines.) Also used as a steroid sparing drug (e.g. in myaesthenia gravis) – initiated in secondary care.

Dosage Regimes: **A typical dose regimen may be:** 1mg/kg/day increasing after 4 to 6 weeks to 2-3mg/kg/day. Lower doses if there is significant renal or hepatic impairment. If allopurinol is co-prescribed the dose of azathioprine must be cut to 25% of the original dose or avoid. Live vaccines should be avoided in Service Users taking azathioprine.

Watch for signs of early toxicity. Nausea, vomiting and diarrhoea may occur, usually starting early during the course of treatment, and may necessitate withdrawal of the drug. Herpes zoster infection may also occur. Lower doses should be used in the elderly or if significant renal or hepatic impairment.

Pneumovax and annual 'flu vaccine should be given. Passive immunisation should be carried out using Varicella zoster immunoglobulin (VZIG) in non-immune Service Users if exposed to chickenpox or shingles.

Monitoring prior to treatment (Consultant responsibility)
FBC, LFTs, U&Es, Creatinine, TPMT assay

Further monitoring required after initiation (GP responsibility)	
FBC, LFTs	Weekly for 6 weeks and then every 2 weeks until dose stable for 6 weeks; thereafter monthly.
U&E, Creatinine	6 monthly

Notes	• FBC should include platelets • Following a change in dose, repeat FBC and LFTs after 2 weeks and then monthly. • Once maintenance dose stable for 6 months, consider monitoring FBC and LFTs 3-monthly unless Service User is heterozygote for TPMT.

<u>Urgent FBC if Service User complains of abnormal bruising, oral ulceration or sore throat.</u>

Action to be taken

WBC < 3.5 x10^9/l	withhold *<u>until discussed</u>* with rheumatologist
Neutrophils<2.0x10^9 /l	withhold *<u>until discussed</u>* with rheumatologist
Platelets<150x10^9 /l	withhold *<u>until discussed</u>* with rheumatologist
>2-fold rise in AST, ALT or Alk. Phos	withhold *<u>until discussed</u>* with rheumatologist *(from upper limit of reference range)*
Rash or oral ulceration	withhold *<u>until discussed</u>* with rheumatologist
MCV>105fl	investigate and if B12 or folate low start appropriate supplementation (macrocytosis is common with Aza)
Abnormal bruising or sore throat	withhold until FBC result available

Trends should be monitored regularly (ideally quarterly). A downward trend (in addition to a rapid fall) should prompt caution and may require referral. Service Users should be warned to report immediately any signs or symptoms of bone marrow suppression e.g. inexplicable bruising, bleeding or infection.

Notable Interactions:

Allopurinol	See above, probably best avoided
Warfarin	Inhibits AC effect, increase dose warfarin
Phenytoin, Sodium Valproate, Carbamazepine	Azathioprine reduces absorption
Aminosalicylates (mesalazine, Osalazaine or sulphasalazine)	May contribute to BM toxicity
Co-trimoxazole, trimethoprim	Haematoxicity
Ace inhibitors	May cause anaemia, if significant avoid

References:

- T&S DMARD monitoring http://www.tsft.nhs.uk/OurServices/Rheumatology/InformationforGPs/DMARDMonitoring/Azathioprine/tabid/1653/Default.aspx

- British Society for Rheumatology Quick reference guideline for monitoring of DMARD therapy http://www.rheumatology.org.uk/includes/documents/cm_docs/2009/d/dmard_grid_november_2009.pdf (last accessed 28/5/2012)

- EMC Azathioprine SPC http://www.medicines.org.uk/EMC/medicine/2882/SPC/Imuran+Tablets+50mg/

Protocol 4 **Penicillamine**

Indication: Rheumatoid Arthritis (second-line drug)

Dosage Regimes: 125mg daily, increasing by 125mg increments every 4 weeks to 500mg – 750mg daily (in divided doses) if tolerated. Some Service Users respond to a lower dose. Occasionally 1500mg a day (in divided doses) is required. If no response in one year then discontinue treatment. Not to be taken within two hours of food.

Monitoring prior to treatment (Consultant responsibility)
FBC, U&Es, Creatinine, Urinalysis, previously also LFTs

Further monitoring required after initiation (GP responsibility)	
FBC, Urinalysis	FBC and urinalysis 1 – 2 weekly until dose and monitoring stable for 2 months; monthly thereafter.

Notes	• FBC should include platelets

Ask about skin rash or oral ulceration at every visit

References

- British Society for Rheumatology Quick reference guideline for monitoring of DMARD therapy http://www.rheumatology.org.uk/includes/documents/cm_docs/2009/d/dmard_grid_november_2009.pdf (last accessed 28/5/2012)

- EMC Penicillamine SPC http://www.medicines.org.uk/EMC/medicine/26390/SPC/Penicillamine+250mg+Tablets/

Protocol 5 **Leflunomide**

Indication: Active Rheumatoid Arthritis (third-line use (after Methotrexate/Sulphasalazine treatment contra-indicated, not tolerated or ineffective). Shared care to commence after Service User has been prescribed by a consultant for at least one month and the response to treatment has been assessed. Also used in some other conditions (e.g. Wilson's disease (excessive copper deposition) and autoimmune hepatitis.

Dosage: Loading dose of 100mg once daily for three days (may be ignored at Rheumatologists discretion) Recommended maintenance dose is 10-20mg once daily. This can be reduced to 10mg daily if poorly tolerated.
Time to response: 8-12 weeks

At present it is recommended that Leflunomide should not be used in conjunction with other DMARDs in routine clinical practice. 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. Male and female Service Users should not procreate within 2 years of discontinuing leflunomide. Blood concentrations of its active metabolite should be measured up to 2 years after discontinuation before pregnancy occurs. A washout procedure can shorten this but levels must still be done.

Monitoring prior to treatment (Consultant responsibility)
FBC, U&Es, Creatinine LFTs inc. ALT, BP (<140/90 on 2 consecutive readings 2 weeks apart), and body weight. Exclude pregnancy.

Further monitoring required after initiation (GP responsibility)	
FBC, LFTs (inc. ALT)	Every 2 weeks during the first 6 months and, if stable, 2 monthly thereafter. If co-prescribed with another immunosuppressant or potential hepatotoxic agent then blood checks should be continued long term, at least once a month.
BP, Weight	Check monthly.

Notes	• FBC should include differential WCC and platelets

Action to be taken

WBC < 3.5x10^9/l	withhold *until discussed* with rheumatologist
Neutrophils < 2x10^9/l	withhold *until discussed* with rheumatologist
Platelets < 150x10^9/l > 2 fold rise in ALT or AST	Reduce dose to 10 mg per day, recheck weekly (*from upper limit of reference range*)
If remains elevated	withhold *until discussed* with rheumatologist
Rash, itch or mouth ulcers	reduce dose (+- antihistamine)

If severe rash	withhold *until discussed* with rheumatologist. Consider washout procedure
Hair loss	Dosage reduction, If severe stop, consider washout
Headache	Dosage reduction, if severe stop consider washout
Abnormal bruising, severe sore throat	Stop, check FBC
GI upset (nausea and diarrhoea)	Symptomatic treatment and consider dosage reduction. If severe or persistent, stop and consider washout
Weight loss	Monitor, if > 10% , no other cause, reduce dosage, stop and consider washout
Breathlessness	If increasing SOB, stop consider washout

References

- T&S DMARD monitoring http://www.tsft.nhs.uk/OurServices/Rheumatology/InformationforGPs/DMARDMonitoring/LeflunomideArava/tabid/1652/Default.aspx

- British Society for Rheumatology Quick reference guideline for monitoring of DMARD therapy http://www.rheumatology.org.uk/includes/documents/cm_docs/2009/d/dmard_grid_november_2009.pdf (last accessed 28/5/2012)

- EMC Leflunomide SPC http://www.medicines.org.uk/EMC/medicine/25437/SPC/Leflunomide+20+mg+Film-coated+Tablets/

Protocol 6 **Sodium Aurothiomalate (Myocrisin)**

Indication: Rheumatoid Arthritis (slow-acting drug, improvement can be expected after 2-3 months (400-600 mg total dose), and in the absence of toxicity, gold injections can be continued indefinitely.)

Dosage Regimes: **Gold** can be given as **sodium aurothiomalate** for active progressive rheumatoid arthritis; it must be given by deep intramuscular injection and the area gently massaged. A test dose of 10 mg (must be given in the clinic followed by 30 minutes observation) followed by doses of 50 mg at weekly intervals until there is definite evidence of remission. Benefit is not to be expected until about 300–500 mg has been given; it should be discontinued if there is no remission after 1 g has been given. In Service Users who do respond, the interval between injections is then gradually increased to 4 weeks and treatment is continued for up to 5 years after complete remission. If relapse occurs the dosage frequency may be immediately increased to 50 mg weekly and only once control has been obtained again should the dosage frequency be decreased; if no response is seen within 2 months, alternative treatment should be sought. It is important to avoid complete relapse since second courses of gold are not usually effective

Monitoring prior to treatment (Consultant responsibility)
FBC, LFTs, U&Es, Urinalysis, serum creatinine

Further monitoring required after initiation (GP responsibility)	
FBC, Urinalysis, skin inspection	Prior to each injection

Notes	• FBC should include platelets • Dose record cards available from hospital must be carefully maintained. • Check CRP monthly at onset of disease and prior to hospital appointment with consultant/specialist nurse when notified. CRP testing is not required as part of routine disease monitoring.

Service User should be requested to report abnormal bruising, oral ulceration or sore throat, breathlessness, or unexplained rashes, this requires urgent FBC.

Action to be taken:

WBC<4.0x10^9/l	withhold until discussed with rheumatologist
Neutrophils<2.0x 10^9/l	withhold until discussed with rheumatologist
Platelets<150x10 ^9/l	withhold until discussed with rheumatologis
>1+ proteinuria on >1 occasion	withhold until discussed with rheumatologist

Rash or oral ulceration	withhold until discussed with rheumatologist
Abnormal bruising or sore throat	withhold until FBC result available

References

- T&S DMARD monitoring http://www.tsft.nhs.uk/OurServices/Rheumatology/InformationforGPs/DMARDMonitoring/SodiumaurothiomalateMyocrisin/tabid/1655/Default.aspx

- BNF http://www.medicinescomplete.com/mc/bnf/current/5289.htm

- British Society for Rheumatology Quick reference guideline for monitoring of DMARD therapy http://www.rheumatology.org.uk/includes/documents/cm_docs/2009/d/dmard_grid_november_2009.pdf (last accessed 28/5/2012)

- EMC Myocrisin SPC http://www.medicines.org.uk/EMC/medicine/18616/SPC/Myocrisin+Injection+2/

Protocol 7 - Intentionally Blank

Protocol 8 **Mercaptopurine**

Indication: For the treatment inflammatory bowel disease (unlicensed use), rheumatoid arthritis (unlicensed use) and other auto immune diseases.

Dosage Regimes: Mercaptopurine is commenced at 25mg per day (half a 50mg tablet). The dose is gradually increased by 25mg per week to the target dose, if tolerated. The target dose is 1-1.5mg/kg daily. A clinical response is not usually expected for 4-12 weeks.

Monitoring prior to treatment (Consultant responsibility)	
FBC, LFTs, U&Es, Creatinine, TPMT assay, varicella status	
Further monitoring required after initiation (GP responsibility)	
FBC, LFTs, U&Es, creatinine	Every week for 6 weeks then every 2 weeks until dose stable for 6 weeks then monthly. If stable for 6 months then consultant may reduce the frequency of monitoring to every 3 months. After a dose increase monitor after 2 weeks and then again at 4 weeks

Monitoring action and advice for GP
If a GP has taken blood tests for the general medical management of the Service User and the blood test results fall into the category below, the following action should be considered:

Blood test results	**Action**
MCV > 105 fl	check B12 and folate if low start appropriate supplementation.

WITHOLD MERCAPTOPURINE and contact consultant if:

- *Neutrophils < 2.0 x109
- *Platelets < 150 x109
- *>2-fold rise in AST, ALT (from upper limit of reference range)
- *Significant reduction in renal function
- Oral ulceration/sore throat, unexplained rash or unusual bruising
- Abdominal bruising or bleeding
- Recurrent sore throats, infections, fever, chills
- Upper abdominal or back pain

*Note: a rapidly increasing or decreasing trend in any values should prompt caution and extra vigilance.
Service Users should be advised to report any signs of bone marrow suppression (thrombocytopenia,neutropenia, leucopenia) i.e., infection, fever, unexplained bruising or bleeding. Treatment should be stopped and FBC checked.

References

- BNF
  http://www.medicinescomplete.com/mc/bnf/current/4735.htm?q=mercaptopurine&t=search&ss=text&p=1#_hit

- Somerset Shared Care protocol
  http://nww.somerset.nhs.uk/welcome/directorates/primary-care-development/prescribing-and-medicines-management/supporting-shared-care/

- EMC mercaptopurine SPC
  http://www.medicines.org.uk/EMC/medicine/24688/SPC/PURI-NETHOL+50+mg+Tablets/

Protocol 9 **Hydroxychloroquine**

Indication: Active rheumatoid arthritis (including juvenile idiopathic arthritis), systemic and discoid lupus erythematosus; dermatological conditions caused or aggravated by sunlight

Dosage Regimes: Dose for RA is 400mg OD. Reduce after 2 months to 200mg per day. In Lupus bigger doses may be necessary i.e. 400mg and 200mg alternate days.

Monitoring prior to treatment (Consultant responsibility)	
FBC, LFTs, U&Es. Ask about visual acuity of each eye (with reading glasses if worn) using a test type or reading chart.	
Further monitoring required after initiation (GP responsibility)	
	No blood monitoring necessary
Visual symptoms	Annual review by an optometrist The examination should include testing visual acuity, careful ophthalmoscopy, fundoscopy, central visual field testing with a red target, and colour vision. Discuss with the ophthalmologist if on treatment for >5years

Service Users should also be advised to report any visual disturbance.

References

- British Society for Rheumatology Quick reference guideline for monitoring of DMARD therapy http://www.rheumatology.org.uk/includes/documents/cm_docs/2009/d/dmard_grid_november_2009.pdf (last accessed 28/5/2012)

- EMC Hydroxychloroquine SPC http://www.medicines.org.uk/EMC/medicine/6977/SPC/Plaquenil+Tablets/

PROTOCOLS FOR DRUG MONITORING – Other Drugs

Protocol 10 **Dronedarone**

Indication: To prevent recurrence of atrial fibrillation (AF), or to lower ventricular rate, in adult clinically stable Service Users with a history of, or current, non-permanent AF in line with NICE guidance.

Dosage Regimes: The recommended dose is 400 mg twice daily, and it should be taken with food. No dose adjustment is required in the elderly, or in mild to moderate hepatic or renal impairment.

Monitoring prior to treatment (Consultant responsibility)
LFTs, creatinine, cardiac function, U&Es, pulmonary function

Further monitoring required after initiation (GP responsibility)	
Creatinine	Measure 7 days after initiation of treatment. If an increase in creatinine is observed, thus value should be used as the new reference baseline. Any further increase in creatinine should lead to discontinuation of dronedarone.
LFTs	Measure 7 days after initiation of treatment Repeat LFTs at months 1, 2, 3, 4, 5, 6, 9, 12 and periodically thereafter
Cardiac examination	Service Users should receive regular cardiac examinations, including an ECG and evaluation for symptoms of heart failure at least every 6 months. Treatment should be discontinued if the Service User develops permanent AF.

Notes	• A blood form should be completed for the day 7 serum creatinine and given to the Service User by the initiating specialist who should also book an appointment with the GP surgery for this blood test. • LFTs should include ALT.

References

- BNF http://www.medicinescomplete.com/mc/bnf/current/206568.htm?q=dronedarone&t=search&ss=text&p=1#_hit
- MHRA – Risk of cardiac failure and risk of hepatotoxicity http://www.mhra.gov.uk/Safetyinformation/DrugSafetyUpdate/CON108677
- EMC Dronedarone SPC http://www.medicines.org.uk/EMC/medicine/22894/SPC/Multaq+400mg+tablets/

Please note that full shared care protocols will be made available via the Medicines Management section on the Somerset Clinical Commissioning Group intranet site in due course.

LIST OF NAMED PRACTITIONERS

Provider Name:

The below named general practitioners will be providing services under the Near Service User Testing (DMARD monitoring) Enhanced Service for Service Users registered with this provider. The practitioners are aware and have copies of the latest shared care protocols.

General Practitioner	Signature	Date	Sulphasalazine	Azathioprine	Penicillamine	Leflunomide	Methotrexate	Sodium Aurothiomalate (Myocrisin)	Mercaptopurine	Hydroxychloro-quine

Please add more lines if the practice has more than 4 general practitioners.

Shared care guidelines will be made available from the medicines management/shared care section on the Somerset Clinical Commissioning Group intranet site in due course.