Newcastle, Gateshead, North Tyneside and Northumberland Guidelines for the Monitoring of Immune Modifying Drugs (IMDs) in Stable Adult Patients (excluding post transplantation) in Primary and Secondary Care

Initial guideline date 15/1/14
Reviewed and amended July 2018
Next review July 2021

Approved on behalf of the:	
North of Tyne, Gateshead and North Cumbria Medicines Guidelines and Use Group	
North of Tyne, Gateshead and North Cumbria Area Prescribing Committee	
Review date:	July 2021
Organisations signed up to this guideline:	CCGs North of Tyne and Gateshead, Newcastle upon Tyne Hospitals NHS Foundation Trust, Northumbria Healthcare Foundation Trust, Gateshead Health NHS Foundation Trust
Name of amending author:	Anne Henry
Target audience:	All clinicians in the Newcastle, Gateshead, North Tyneside Northumberland areas involved in the management of patients taking IMDs
Consultation Process:	Guideline group was multidisciplinary from all representative organisations
Training Requirements	No specific training requirements
Distribution	Primary care, secondary care
Implementation	Implementation process in primary care required as appropriate
Monitoring Compliance	Through audit of referrals received in secondary care

CONTENTS

INTRODUCTION

This local guideline was originally developed after reviewing the draft North of Tyne IMD guidelines (2010), NHS Clinical Knowledge Summaries, and current national guidelines. The review group brought together clinicians (consultants and specialist nurses) from a wide range of specialties including rheumatology, gastroenterology, immunology, neurology, dermatology, respiratory and renal medicine as well as GPs, and pharmacists. The aim is to provide guidance to clinicians on the routine monitoring required for adults receiving a range of drugs referred to as Immune Modifying Drugs (IMDs) following dose stabilisation by the initiating specialist.

British Society for Rheumatology (BSR) and the British Health Professionals in Rheumatology (BHPR) guidance 2017

In 2017 the British Society for Rheumatology (BSR) and the British Health Professionals in Rheumatology (BHPR) have jointly revised their 2008 guidelines for the safe use of non-biologic DMARDs in adults. The 2017 guideline is accredited by NICE. This local guideline has been updated to reflect the changes.

Significant changes from the BSR and BHPR 2008 guideline include:

Harmonisation of monitoring schedules, recommending that all DMARDs that require laboratory monitoring follow the same frequency of testing once stabilised, i.e. every 12 weeks.
The only exceptions are tacrolimus, ciclosporin and methotrexate/leflunomide combinations – where extended monthly monitoring longer term is advocated.
More nuanced discussion of the use of methotrexate in lung disease is provided, drawing from the two large meta-analyses recently published. Background lung disease should not be considered an absolute contraindication to methotrexate use, although in patients with poor respiratory reserve (in whom an acute pneumonitis would be more hazardous), caution is advised.

The Royal College of Ophthalmologists 2018 guidance on screening recommends baseline examination, including optical coherence tomography (OCT) within 12 months of starting treatment, for patients intending to take hydroxychloroquine for over 5 years. Existing patients who have been taking hydroxychloroquine for more than 5 years should receive annual OCT.
Local implementation of this service is not currently in place. Guidance will be amended once agreement has been reached. Patients should be advised to have a formal annual optical eye test until local agreement is reached.

Biologic IMDs – for information only

A section on monitoring of biologic IMDs has been included (Appendix 2), based on the individual manufacturers' Summaries of Product Characteristics. **This is for information only.**

Scope of the guideline

This local guideline is intended for all clinicians in the North of Tyne and Gateshead areas involved in the management of patients taking IMDs for most conditions other than post transplantation. Where there are specific reasons to deviate from these guidelines then this should be with the specific agreement of local clinical governance committees.
Dermatology

This guideline does not give details of the various arrangements regarding which clinician is responsible for monitoring or prescribing the drugs but seeks to standardise monitoring of stable patients across specialities. Within the North of Tyne and Gateshead areas there are a range of models for ensuring that patients taking these drugs receive routine

monitoring (shared care, hospital only care, community based phlebotomy services). This guidance should be used to ensure consistent monitoring parameters regardless of who does the monitoring.

Monitoring should be offered to all people who are likely to benefit, irrespective of race, disability, gender, age, sexual orientation or religion. Information should be provided to patients in an accessible format and consideration should be given to mobility and communication issues, and being aware of sensitive and cultural issues.

The information given for each drug is not inclusive of all prescribing information and potential adverse effects. Please refer to full prescribing data in the SPC or the BNF.

MONITORING REQUIREMENTS

Tables of testing intervals and parameters are given for a range of IMDs in Appendix 1. Details are given on the recommended course of action if results are outside of the normal range. Clinical judgement should be used, taking into account a full knowledge of a patient's clinical condition and the adverse drug reactions associated with the drug in question, when advising that a drug is stopped or dose reduced. Specialist advice should be sought.

HIGH RISK PATIENTS

High risk patients should remain on indefinite monitoring / monthly monitoring i.e. those who have renal impairment, are on other drugs which may interact with the IMD, those who have had previous blood abnormalities either due to low grade IMD toxicity or other medical problems e.g. mild ITP, those who have known liver disease.

PATIENTS ON LEFLUNOMDE/METHOTREXATE COMBINATION

Patient on leflunomide/methotrexate combination would normally need to remain on indefinite monthly monitoring[1].

PRESCRIBING IMDs IN PATIENTS WITH KNOWN CO-MORBIDITIES

Pre-existing lung disease is not a specific contraindication to IMD therapy; however, caution is advised when using drugs associated with pneumonitis in patients with poor respiratory reserve.
In patients with deranged liver biochemistry, hepatotoxic IMDs should be used with caution, with careful attention to trends in test results.
In patients with impaired liver synthetic function (e.g. cirrhosis), IMD therapy should be used with extreme caution.
Patients with chronic viral hepatitis infection should be considered for anti-viral treatment prior to immunosuppressive IMD initiation.
IMDs must be used with caution in chronic kidney disease, with appropriate dose reduction and increased frequency of monitoring.
Cardiovascular disease and prior malignancy are not considered contraindications to IMD therapy.

[1] Patients attending QE hospital will remain on monthly monitoring. Specialists in other areas may advise two-monthly monitoring for some patients

VACCINATION

Patients receiving immunosuppressive therapy (which includes azathioprine, 6-mercaptopurine, ciclosporin, leflunomide, methotrexate, mycophenolate, and tacrolimus) are more likely to suffer clinically significant infections. In line with national guidance in the 'Green Book' these patients should be offered annual inactivated influenza vaccination. Patients should also be given pneumococcal vaccination. Re-immunisation with pneumococcal vaccine is recommended every 5 years for patients with no spleen, splenic dysfunction or CKD. For patients going onto biologics, if pneumococcal titres are low revaccination is recommended. The use of live vaccines (e.g., MMR, measles, mumps, oral polio, BCG, yellow fever, live oral typhoid, rubella, Fluenz® - live attenuated nasal influenza vaccine, varicella-zoster vaccine) is contra-indicated unless immunosuppressive drugs are stopped at least 6 months beforehand[2,3]. For individuals due to commence immunosuppressive treatments, inactivated vaccines should ideally be administered at least 2 weeks before commencement to ensure a good immune response. In some cases this will not be possible and therefore vaccination may be carried out at any time and re-immunisation considered after treatment is finished and recovery has occurred. If use of live vaccines is necessary administer at least 4 weeks before immunosuppressive therapy is commenced.

The zoster (shingles) vaccine (Zostavax) is a live vaccine which can be given to some patients at 70 years of age as part of the national vaccination programme where patients are eligible as defined in the 'Green Book'[4].
N.B. Therapy with low-doses of methotrexate (<0.4 mg/kg/week), azathioprine (<3.0 mg/kg/day), or 6-mercaptopurine (<1.5 mg/kg/day) for treatment of rheumatoid arthritis, psoriasis, polymyositis, sarcoidosis, inflammatory bowel disease, and other conditions are not considered sufficiently immunosuppressive and are not contraindications for administration of zoster vaccine[5]**.** The Green Book further states that more intensive immunosuppression is, however, considered to be a contra-indication to the use of Zostavax and the vaccine should, in general, be avoided in patients on potent immunosuppressants such as cyclophosphamide and biologic drugs.

CLOSE CONTACTS OF IMMUNOSUPPRESSED INDIVIDUALS

To minimise the risk of infection, close contacts of immunosuppressed individuals should be fully immunised according to the UK schedule, as a matter of priority. Close contacts of severely immunosuppressed individuals should also be offered inactivated vaccine against influenza (there is the potential for respiratory spread with the live intranasal influenza vaccine which should be avoided). This will reduce the risk of vulnerable individuals being exposed to the serious consequences of vaccine-preventable infections.
It is important to ensure that household contacts are immune to measles. Household contacts who have not received two doses of a measles containing vaccine should be offered MMR vaccine.

---

[2] The BSR/BHPR guideline (2017) advises that live vaccines are not recommended in patients on immunosuppression. This is relevant for patients seeking vaccination for foreign travel (e.g. yellow fever vaccination) and also the shingles vaccine. A shingles vaccine is currently recommended by the JCVI for people over the age of 69 years, reducing the risk of shingles by 50% in immunocompetent adults aged 60 years and older.
There are limited data on the vaccine efficacy in immuno-compromised populations. The vaccine is live and therefore relatively contraindicated in individuals who are immunosuppressed. Low levels of immunosuppression are not considered an absolute contraindication, and the JCVI Green Book addresses this, recommending that low-dose prednisolone (<20mg daily) and oral DMARD therapy at standard doses are not a contraindication in most patients, although clinician discretion is advised.

[3] The Newcastle Virology team advised 'live vaccines could be considered from 3 months after stopping treatment where there is good reason to vaccinate between 3 and 6 months post stopping medication'. This is supported by CDC guidance (MMWR 2011. Vol 60, no.2)' The justification for this should be clearly documented.

[4] Vaccination may be beneficial in younger patients (age > 50 years), but there are currently issues with respect to supply of the vaccine and uncertainty regarding need for / timing of booster doses.

[5]The Newcastle Virology team advised 'no guidance is currently provided for patients on other low dose immunosuppressive regimes and so the vaccine cannot currently be routinely recommended out with these criteria. If it is not possible to administer zoster vaccine to patients before initiation of therapy, assess the immune status of the recipient on a case-by-case basis to determine the relevant risks and benefits. Otherwise, defer vaccination for at least 6 months after discontinuation of such therapy (making it consistent with recommendations for other vaccines) (CDC – Guide to vaccine contraindications and precautions)'.

Varicella vaccination of children within the household who do not have a history of chickenpox should also be considered[6].

CHICKEN POX/SHINGLES/MEASLES EXPOSURE

Ninety percent of adults are already immune and do not require routine testing of immunity against varicella zoster (VZV)[7,8]. (Children starting immunosuppressive therapy should have their VZV immunity checked and immunised as appropriate prior to treatment.)

For patients who have significant contact with an individual with either chicken pox or shingles IgG testing should be arranged by contacting the local laboratory. Further advice is also available from Public Health England on 0191 282 1104, who will also organise VZ immunoglobulin (VZIG) if the patient is susceptible (VZV IgG negative). VZIG should be given within 7 days of contact. It is not completely effective and patients should be advised to obtain early treatment should any symptoms develop.

Significant contact as defined in the 'Green Book', is contact with an individual with chickenpox or disseminated shingles from 2 days before rash appearance until lesions are fully crusted, or an individual with localised zoster on an exposed area from the day of rash onset until lesions are fully crusted. Immunocompromised patients with shingles should be considered infectious even if lesions are covered. Contact in the same room (house, classroom, four-bedded bay) for over 15 minutes or face to face contact is considered significant.

There was a large measles outbreak in the North East in 2012/13. If an immunocompromised patient has been in contact with a case of possible measles, urgent measles IgG testing should be arranged by contacting the local laboratory. Further advice is available for patients testing IgG negative from the virologists at the Public Health England Laboratory on 0191 282 1104 as prophylaxis with immunoglobulin may be required.

INFECTIONS

Patients with rheumatoid arthritis have an increased incidence of infection compared with the general population. Increased disease severity, corticosteroid use and comorbidities are associated with an increased infection risk. However it was noted that low-dose methotrexate does not appear to increase infection risk in RA patients[9].
Recurrent confirmed bacterial infections and/or opportunist infection should be flagged as requiring further attention and investigation.
During a serious infection i.e. if treatment with antibiotics is required, methotrexate, leflunomide, azathioprine, mycophenolate, 6-mercaptopurine, cyclosporine, tacrolimus, baricitinib, and biologics should be withdrawn. Treatment can be restarted once off antibiotics and bloods are normal.

[6] There is a lot of experience and work with MMR and varicella vaccine (both live vaccines), and these are not contraindicated in household contacts of immuno-compromised patients (Green Book). There are no alternative vaccines and the benefits of vaccinating household contacts are considered to outweigh any potential risk.
[7] Prof Judith Breuer, Professor of Virology UCL advised possibly test for VZV IgG if adult patient from Indian subcontinent, Sri Lanka etc., because chickenpox is less common (can be around 40-50% adult seroprevalence) and so a history of chickenpox is less reliable
[8] The Newcastle Virology team advised 'Testing for immunity to varicella and measles prior to immunosuppression, with vaccination of those testing negative is not routinely recommended in adults (although children should be assessed for measles and varicella immunity and vaccinated appropriately)'. Rationale is that greater than 90% of adult will have immunity and current IgG assays may be negative despite immunity. Vaccine response is likely to be relatively poor in those with chronic illness and protection could not be assumed after vaccination, hence checking of immunity would still be required in the event of any contact.'
[9] Methotrexate, rheumatoid arthritis and infection risk—what is the evidence? Rheumatology 2009;48:867–871

This guidance refers to non-transplant patients only. If patient is on immunosuppressive treatment for transplant rejection the immunosuppressant should not be stopped and appropriate advice sought from the transplant centre. **This is for information only.**

PREGNANCY, BREASTFEEDING AND PATERNAL EXPOSURE

Patients planning pregnancy should discuss this well in advance with their specialist. Further guidance regarding individual drug safety is available in the relevant BSR guideline listed in the reference section.
Paternal exposure – there is guidance to suggest that all DMARDs are safe for paternal exposure at conception, though in some cases (including methotrexate), data remains limited. Sulfasalazine may affect fertility but is otherwise safe. Male patients planning conception should discuss with their specialist the risks and benefits of continuing treatment prior to conception.

SAFE ALCOHOL LIMITS

When taken with alcohol, both methotrexate and leflunomide may increase the risk of liver damage, but there was no consensus by the BSR guideline group to recommend that alcohol consumption should be lower than the national limit. Patients should be advised that there is uncertainty about what are safe levels, and that they should certainly ensure their consumption is within the recommended maximum limits[10].
Those on combinations of methotrexate and leflunomide have a 31% risk of developing LFT abnormalities and are at risk of hepatic failure which is much greater than when on either drug alone. Patients on this combination should be made aware of the risks/benefits and encouraged to be extremely cautious in relation to alcohol intake long term, or, where possible, abstain altogether.
Discussions regarding alcohol consumption with methotrexate and leflunomide alone or in combination should be carefully documented.

MONITORING RECORDS

All patients should have a hand held monitoring booklet to record details of results unless a suitable IT monitoring system is in place. All blood test results are available via ICE.

CONTACT DETAILS

Further advice is available from a consultant virologist, Health Protection Agency Laboratory, Newcastle upon Tyne. Telephone 0191 2821104.

[10] Patients attending QE hospital on leflunomide either as mono ,or combination therapy, are advised to avoid alcohol for the first 6 months of treatment

REFERENCES

BSR and BHPR guideline for the prescription and monitoring of non-biologic disease-modifying anti-rheumatic drugs. Rheumatology, June 2017, Vol 56, Issue 6.
https://academic.oup.com/rheumatology/article/3053478/BSR-and-BHPR-guideline-for-the-prescription-and?searchresult=1

BSR and BHPR guideline on prescribing drugs in pregnancy and breastfeeding—Part I: standard and biologic disease modifying anti-rheumatic drugs and corticosteroids
Rheumatology, Volume 55, Issue 9, 1 September 2016, Pages 1693–1697,
https://doi.org/10.1093/rheumatology/kev404

British National Formulary, Updated 1st June 2018
https://bnf.nice.org.uk/

Electronic Medicines Compendium
https://www.medicines.org.uk/emc/

Immunisation against infectious disease - The Green Book 2013 with more recent updates:
https://www.gov.uk/government/collections/immunisation-against-infectious-disease-the-green-book

NHS Clinical Knowledge Summaries
http://cks.nice.org.uk/dmards#!topicsummary

Royal College of Ophthalmologists guideline: Hydroxychloroquine and Chloroquine Retinopathy: recommendations on Screening. Feb 2018 (review date Feb 2021). Available from: https://www.rcophth.ac.uk/wp-content/uploads/2018/07/Hydroxychloroquine-and-Chloroquine-Retinopathy-Screening-Guideline-Recommendations.pdf

Oral tacrolimus products: prescribe and dispense by brand name only, to minimise the risk of inadvertent switching between products, which has been associated with reports of toxicity and graft rejection
https://www.gov.uk/drug-safety-update/oral-tacrolimus-products-prescribe-and-dispense-by-brand-name-only-to-minimise-the-risk-of-inadvertent-switching-between-products-which-has-been-associated-with-reports-of-toxicity-and-graft-rejection

APPENDIX 1. MONITORING REQUIREMENTS FOR INDIVIDUAL DRUGS

<table>
<tr><th colspan="6">AZATHIOPRINE and 6-MERCAPTOPURINE</th></tr>
<tr><th>FBC</th><th>U&Es Creatinine</th><th>LFTs</th><th>ESR/CRP</th><th>Other important warnings</th><th>Important interactions</th></tr>
<tr>
<td colspan="3">(Initially every 2 weeks until on stable dose for 6 weeks then monthly for 3 months)

Thereafter, at least every 12 weeks

Dose increases should be monitored every 2 weeks until stable for 6 weeks , then revert to previous schedule

In people heterozygous for thiopurine methyl transferase (TPMT), monitoring should continue at monthly intervals (TPMT status should be determined in secondary care before starting treatment — azathioprine should not be given to people who are TPMT-homozygote). Treatment dose should be adjusted appropriately in TPMT heterozygotes. [11] There is evidence to suggest that reduced doses (25-75mg daily) can be used in patients with low (but not absent) TMPT levels; however the studies are small and did not have safety as their end point.

High risk patients should remain on indefinite monitoring / monthly monitoring i.e. those who have renal impairment, are potentially on other drugs which may interact with the DMARD, those who have had previous blood abnormalities either due to low grade DMARD toxicity or other medical problems e.g. mild ITP, those who have known liver disease.</td>
<td>RHEUMATOLOGY AND GASTROENTEROLOGY PATIENTS ONLY (marker of disease activity) Following dose stabilisation check at same time as other monitoring tests</td>
<td>Hypersensitivity reactions (including malaise, dizziness, rigors, myalgias, rashes, fever, abnormal liver function, arrhythmias and hypotension) - STOP drug. Seek urgent advice. Supportive circulatory measures needed if severe.

Rash or oral ulceration – STOP drug and seek urgent advice

Abnormal bruising or severe sore throat – STOP and seek advice

Unexplained cough, dyspnoea - STOP drug and seek advice</td>
<td>The following drugs should not be started without discussion with the initiating specialist

ALLOPURINOL - risk of severe myelosuppression
:
WARFARIN - effect may be reduced requiring increased dose of warfarin

TRIMETHOPRIM or CO-TRIMOXAZOLE - potential risk of haematological toxicity

AMINOSALICYLIC ACID DERIVATIVES e.g. OLSALAZINE, MESALAZINE AND SULPHASALAZINE - risk of an increased myelosuppressive effect

RIBAVIRAN – possibly enhances myelosuppressive effects of azathioprine

FEBUXOSTAT – risk of severe myelosuppression</td>
</tr>
<tr>
<td>Leucopenia <3.5 x 10^9/L
Neutropenia <2.0 x 10^9/L

Sequential falls in WBC or neutrophils >10% on 3 occasions
Thrombocytopenia <150 x 10^9/L

STOP and seek advice

Sequential falls in platelets - STOP unless falls are from high level
Lymphocytes <0.5 x 10^9/L - Seek advice
Macrocytosis >105 fl Check B12 and folate, thyroid function have been checked within last 12 months and are normal</td>
<td></td>
<td>Elevation of ALT >2 x upper limit of reference range - seek advice; >3 upper limit of reference range - STOP. Repeat LFTs.

Mild transaminitis is common and normally settles</td>
<td></td>
<td></td>
<td></td>
</tr>
</table>

[11] Dr Bridget Griffiths advised that at NuTH they give a lower maximum dose i.e. 1.5 mg/kg instead of 2.5 mg/kg but all patients receive their monitoring at the same frequency

<table>
<tr><th colspan="8">CICLOSPORIN</th></tr>
<tr><th>FBC</th><th>U&Es
Creatinine</th><th>LFTs</th><th>ESR/CRP</th><th>Serum
Lipids</th><th>BP and
Glucose</th><th>Other
important
warnings</th><th>Important interactions</th></tr>
<tr><td colspan="3">(Initially every 2 weeks until on stable dose for 6 weeks then monthly for 3 months)

Thereafter, ONCE a month.

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

Dose increases should be monitored every 2 weeks until stable for 6 weeks , then revert to previous schedule

High risk patients should remain on indefinite monitoring / monthly monitoring i.e. those who have renal impairment, are potentially on other drugs which may interact with the DMARD, those who have had previous blood abnormalities either due to low grade DMARD toxicity or other medical problems e.g. mild ITP, those who have known liver disease.</td><td>RHEUMATOLOGY AND GASTROENTEROLOGY PATIENTS ONLY (marker of disease activity) Following dose stabilisation check at same time as other monitoring tests</td><td>Every 6 months</td><td>Following stabilisation monitor ONCE a month</td><td rowspan="2">Unexplained cough, dyspnoea, abnormal bruising or bleeding - STOP drug and seek advice

Ciclosporin levels – trough drug levels may be indicated/considered if there are concerns about toxicity or concordance</td><td rowspan="2">The following drugs should not be started without discussion with the initiating specialist:
ACE INHIBITORS & ARIIAs: increased risk of hyperkalaemia
ANTIBIOTICS: erythromycin, azithromycin and clarithromycin increase ciclosporin levels; rifampicin decrease ciclosporin levels
ANTIFUNGALS: fluconazole, itraconazole, and ketoconazole decrease ciclosporin levels
CALCIUM-CHANNEL BLOCKERS: diltiazem, nicardipine and verapamil increase ciclosporin levels
ANTIEPILEPTICS: carbamazepine, phenobarbital, and phenytoin decrease ciclosporin levels
ANTI-MALARIAL DRUGS: Hydroxycholoquine and chloroquine increase ciclosporin levels
ANTI-OBESITY DRUGS: orlistat decreases ciclosporin levels
NSAIDs (and other nephrotoxic drugs): increased risk of nephrotoxicity
STATINS: lower doses should be used to reduce risk of muscular toxicity, however there is still a risk of myopathy with lowered doses. Avoid simvastatin and rosuvastatin is contraindicated with ciclosporin
POTASSIUM_ SPARING DIURETICS: only initiate with regular monitoring of U&Es
HERBAL MEDICINES: Avoid
GRAPEFRUIT JUICE: Avoid as increases ciclosporin levels NUMEROUS OTHERS: check BNF for details</td></tr>
<tr><td>Leucopenia <3.5 x 10^9/L
Neutropenia <2.0 x 10^9/L
Sequential falls in WBC neutrophils >10% on 3 occasions
Thrombocytopenia <150 x 10^9/L
STOP and seek advice

Sequential falls in platelets - STOP unless falls are from high level
Lymphocytes <0.5 x 10^9/L - Seek advice
Macrocytosis >105 fl Check B12 and folate, thyroid function have been checked within last 12 months and are normal</td><td>Increase in creatinine - >30% from baseline – reduce dose by 50% - >50 % above baseline – STOP drug and seek advice</td><td>Elevation of ALT >3 x upper limit of reference range - STOP. Repeat LFTs. Mild transaminitis is common and normally settles</td><td></td><td>Significant rise in fasting lipids STOP and seek advice</td><td>BP >140/90 on 2 readings 2 weeks apart Treat BP before stopping drug (e.g. with amlodipine). If uncontrolled STOP and control BP before restarting ciclosporin. Seek advice</td></tr>
</table>

HYDROXYCHLOROQUINE

Eye Checks

The Royal College of Ophthalmologists 2018 guidance on screening recommends baseline examination, including optical coherence tomography (OCT) within 12 months of starting treatment, for patients intending to take hydroxychloroquine for over 5 years. Existing patients who have been taking hydroxychloroquine for more than 5 years should receive annual OCT

Local implementation of this service is not currently in place. Guidance will be amended once agreement has been reached.

Patients should be advised to have annual optical eye test until local agreement is reached

Patients should immediately report any visual disturbances, including abnormal colour vision, pigmentary abnormality or visual field defects

The RC Ophthalmologist guidance also highlights that certain groups of patients are at increased risk of retinopathy, and care should be taken when prescribing HCQ for them:

- Patients with impaired renal function eGFR <60ml/min (odds ratio 2.1)
- Patients on tamoxifen (odds ratio 4.6)
- Patients taking doses of HCQ> 5mg/kg (odds ratio 5.7)
- Patients on long term therapy (odds ratio 3.22 for >10 years treatment). Risk of toxicity was <2% for patients who took 4-5mg/kg for up to 10 years, but approached 20% after 20 years treatment.

Important interactions

Amiodarone - increased risk of ventricular arrhythmias
Moxifloxacin - increased risk of ventricular arrhythmias
Antimalarials – arthemether/lumefantrine, mefloquine
Droperidol - increased risk of ventricular arrhythmias
Digoxin – increased digoxin levels
Ciclosporin – increased ciclosporin levels (increased risk of toxicity)
Mefloquine - increased risk of convulsions
Tamoxifen – increased risk of retinopathy

<table>
<tr><th colspan="8">LEFLUNOMIDE</th></tr>
<tr><th>FBC</th><th>U&Es
Creatinine</th><th>LFTs</th><th>ESR/CRP</th><th>BP</th><th>Weight</th><th>Other important warnings</th><th>Important interactions</th></tr>
<tr><td colspan="3">(Initially every 2 weeks until on stable dose for 6 weeks then monthly for 3 months)

Thereafter, at least every 12 weeks

Dose increases should be monitored every 2 weeks until stable for 6 weeks , then revert to previous schedule

High risk patients should remain on indefinite monitoring / monthly monitoring i.e. those who have renal impairment, are potentially on other drugs which may interact with the DMARD, those who have had previous blood abnormalities either due to low grade DMARD toxicity or other medical problems e.g. mild ITP, those who have known liver disease.

Leflunomide and methotrexate combined
Patients on leflunomide/methotrexate combination need to remain on indefinite monthly monitoring, or two-monthly according to local specialist advice (patients attending QE hospital will remain on monthly monitoring when on this combination).</td><td>RHEUMATOLOGY AND GASTROENTEROLOGY PATIENTS ONLY (marker of disease activity)
Following dose stabilisation check at same time as other monitoring tests</td><td colspan="2">At each monitoring visit</td><td>Unexplained cough, dyspnoea, severe rash, excessive weight loss, severe or persistent GI upset, severe, persistent headache, abnormal bruising or severe sore throat, severe hair loss - STOP drug and seek advice – WASHOUT procedure may be required due to the long half- life of the drug – see below for details</td><td>Contraindicated in hypoproteinaemia or impairment of liver function

Cholestyramine - dramatically increases elimination (may be used if WASHOUT required – see below for details).

Care with phenytoin, warfarin and tolbutamide

METHOTREXATE – increased risk of toxicity. Patients on leflunomide and methotrexate in combination, need to remain on indefinite monthly monitoring, or two-monthly according to local specialist advice (patients attending QE hospital will remain on monthly monitoring when on this combination).</td></tr>
<tr><td>Leucopenia <3.5 x 10^9/L

Neutropenia <2.0 x 10^9/L STOP

Sequential falls in WBC or neutrophils >10% on 3 occasions and seek advice

Thrombocytopenia <150 x 10^9/L

Sequential falls in platelets - STOP unless falls are from high level

Lymphocytes <0.5 x 10^9/L - Seek advice

Macrocytosis >105 fl Check B12 and folate, thyroid function have been checked within last 12 months and are normal</td><td></td><td>Elevation of ALT>2 x upper limit of reference range - seek advice

Elevation of ALT >3 x upper limit of reference range - STOP. Repeat LFTs.
Mild transaminitis is common and normally settles.

Repeat LFTs. Early sign of liver toxicity</td><td></td><td>>140/90 Mild rises seen in 10% of patients. Reduce dose if marked increase. Consider anti-hypertensives. STOP drug if refractory to these measures.</td><td>If > 10% weight loss with no other cause identified – seek advice</td><td></td><td></td></tr>
</table>

WASHOUT procedure (Product Literature): To aid drug elimination in case of serious adverse event, or before starting another IMD, or before conception (but see introduction section on preconception advice) – STOP treatment and give either cholestyramine 8g three times daily for 11 days or activated charcoal 50g four times daily for 11 days; the concentration of active metabolite should be less than 20 micrograms/litre (measured on 2 occasions 14 days apart) in men and women before conception – consult product literature. Procedure may be repeated as necessary.

METHOTREXATE

Folic Acid supplementation at a minimal dose of 5mg once weekly should be co-prescribed (usually 3-4 days after the methotrexate dose)

<table>
<tr><th>FBC</th><th>U&Es
Creatinine</th><th>LFTs</th><th>ESR/CRP</th><th>Other important warnings</th><th>Important interactions</th></tr>
<tr><td colspan="3">(Initially every 2 weeks until on stable dose for 6 weeks then monthly for 3 months)

Once stabilised, at least every 12 weeks[12].

Dose increases should be monitored every 2 weeks until stable for 6 weeks, then revert to previous schedule.

High risk patients should remain on indefinite monitoring / monthly monitoring i.e. those who have renal impairment, are potentially on other drugs which may interact with the DMARD, those who have had previous blood abnormalities either due to low grade DMARD toxicity or other medical problems e.g. mild ITP, those who have known liver disease.

Methotrexate and leflumomide combined
Patient on methotrexate/leflumomide combination need to remain on indefinite monthly monitoring, or two-monthly according to local specialist advice (patients attending QE hospital will remain on monthly monitoring when on this combination).</td><td>RHEUMATOLOGY AND GASTROENTEROLOGY PATIENTS ONLY (marker of disease activity) Following dose stabilisation check at same time as other monitoring tests</td><td rowspan="2">Unexplained cough, dyspnoea, rash, severe, oral ulceration, severe nausea/vomiting/ diarrhoea, abnormal bruising or bleeding , or severe sore throat, - STOP drug and seek advice

Advise patients to stay well within the national recommendations for alcohol intake</td><td rowspan="2">Numerous - check BNF; important ones include
ANTIBIOTICS - avoid trimethoprim and co-trimoxazole

Phenytoin - antifolate effect of methotrexate increased by phenytoin retinoids - plasma concentration of methotrexate increased by acitretin (also increased risk of hepatotoxicity)

NSAIDs are routinely co-prescribed for inflammatory arthritis (although they elevate serum levels) - adherence to monitoring schedule is advised.

HERBAL PREPARATIONS - may increase risk of toxicity and include Echinacea, Bishop's weed, Kava, Black cohosh and Borage

Probenecid - increased risk of toxicity
Clozapine - Avoid concomitant use increased risk of agranulocytosis

LEFLUNOMIDE – increased risk of toxicity. Increased monitoring vigilance advised when used in combination.</td></tr>
<tr><td>Leucopenia <3.5 x 10^9/L
Neutropenia <2.0 x 10^9/L STOP

Sequential falls in WBC or neutrophils >10% on 3 occasions and seek advice

Thrombocytopenia <150 x 10^9/L

Sequential falls in platelets - STOP unless falls are from high level

Lymphocytes <0.5 x 10^9/L - Seek advice

Macrocytosis >105 fl Check B12 and folate, thyroid function have been checked within last 12 months and are normal</td><td>Worsening renal function should be discussed with the specialist – Methotrexate is renaly excreted and any reduction in renal function (e.g. as a consequence dehydration or co-prescription of diuretics/ACEIs) may cause serious toxicity</td><td>Elevation of ALT >2 x upper limit of reference range - seek advice; >3 x upper limit of reference range - STOP. Repeat LFTs. Mild transaminitis is common and normally settles.

Albumin- unexplained fall (in absence of active disease) - Withhold until discussed with specialist team</td><td></td></tr>
</table>

[12] Dermatology clinics may follow less frequent monitoring schedules at initiation, in keeping with British Association of Dermatologists' guidelines for the safe and effective prescribing of methotrexate for skin disease 2016: http://www.bad.org.uk/shared/get-file.ashx?id=4020&itemtype=document.

<table>
<tr><th colspan="6">MINOCYCLINE – UNLICENSED USE</th></tr>
<tr><th>FBC</th><th>U&Es
Creatinine</th><th>LFTs</th><th>ESR/CRP</th><th>Other important warnings</th><th>Important interactions</th></tr>
<tr><td colspan="3">No routine laboratory monitoring</td><td>RHEUMATOLOGY PATIENTS ONLY (marker of disease activity)
Following dose stabilisation check at same time as other monitoring tests</td><td rowspan="2">Patients will be screened pre-treatment for presence of ANA autoantibodies: a significant titre of these will be taken as a relative contraindication to minocycline treatment.

Rare cases of auto-immune hepatotoxicity and isolated cases of SLE and also exacerbation of pre-existing SLE have been reported. If patients develop signs or symptoms of SLE or hepatotoxicity minocycline should be discontinued.

Advise patients to stay well within the national recommendations for alcohol intake

Patients should be advised to report any unusual pigmentation without delay - seek advice</td><td rowspan="2">Warfarin - possibly enhance anticoagulant effect

Retinoids - possible increased risk of benign intracranial hypertension when tetracyclines given with retinoids (avoid concomitant use)</td></tr>
<tr><td>Neutropenia <2.0 x 10^9/L

Sequential falls in WBC or neutrophils >10% on 3 occasions
Thrombocytopenia <150 x 10^9/L

STOP and seek advice

Sequential falls in platelets - STOP unless falls are from high level
Lymphocytes <0.5 x 10^9/L - Seek advice
Macrocytosis >105 fl Check B12 and folate, thyroid function have been checked within last 12 months and are normal</td><td></td><td>Elevation of ALT >2 x upper limit of reference range - seek advice; >3 upper limit of reference range - STOP. Repeat LFTs.

Mild transaminitis is common and normally settles</td><td></td></tr>
</table>

<table>
<tr><th colspan="6">MYCOPHENOLATE - UNLICENSED USE</th></tr>
<tr><th>FBC</th><th>U&Es
Creatinine</th><th>LFTs</th><th>ESR/CRP</th><th>Other important warnings</th><th>Important interactions</th></tr>
<tr><td colspan="3">(Initially every 2 weeks until on stable dose for 6 weeks then monthly for 3 months)

Thereafter, at least every 12 week

Dose increases should be monitored every 2 weeks until stable for 6 weeks , then revert to previous schedule

High risk patients should remain on indefinite monitoring / monthly monitoring i.e. those who have renal impairment, are potentially on other drugs which may interact with the DMARD, those who have had previous blood abnormalities either due to low grade DMARD toxicity or other medical problems e.g. mild ITP, those who have known liver disease.</td><td>RHEUMATOLOGY PATIENTS ONLY (marker of disease activity) Following dose stabilisation check at same time as other monitoring tests</td><td rowspan="2">Unexplained cough, dyspnoea, abnormal bruising or bleeding, severe sore throat - STOP drug and seek advice</td><td rowspan="2">Rifampicin Reduces levels of active metabolite of mycophenolate

Antacids may reduce absorption of mycophenolate

Cholestyramine may reduce absorption and bioavailability of mycophenolate by 40%
.
Probenecid increases plasma concentration of mycophenolate.

Aciclovir
causes significant increase in plasma concentration of mycophenolate in patients who have renal impairment</td></tr>
<tr><td>Leucopenia <3.5 x 10^9/L

Neutropenia <2.0 x 10^9/L
Sequential falls in WBC or neutrophils >10% on 3 occasions
Thrombocytopenia <150 x 10^9/ — STOP and seek advice

Sequential falls in platelets - STOP unless falls are from high level

Lymphocytes <0.5 x 10^9/L - Seek advice

Macrocytosis >105 fl Check B12 and folate, thyroid function have been checked within last 12 months and are normal</td><td>Increase in creatinine - > 140 micromol. STOP, repeat U&Es and seek advice</td><td>Elevation of ALT >2 x upper limit of reference range - seek advice; >3 x upper limit of reference range - STOP. Repeat LFTs. Mild transaminitis is common and normally settles.</td><td></td></tr>
</table>

SODIUM AUROTHIOMALATE I.M. - GOLD

FBC	U&Es Creatinine	LFTs	ESR/CRP	Urinalysis	Other important warnings	Important interactions
(Initially every 2 weeks until on stable dose for 6 weeks then monthly for 3 months) Thereafter, at least every 12 weeks Dose increases should be monitored every 2 weeks until stable for 6 weeks , then revert to previous schedule High risk patients should remain on indefinite monitoring / monthly monitoring i.e. those who have renal impairment, are potentially on other drugs which may interact with the DMARD, those who have had previous blood abnormalities either due to low grade DMARD toxicity or other medical problems e.g. mild ITP, those who have known liver disease.			RHEUMATOLOGY PATIENTS ONLY (marker of disease activity) Following dose stabilisation check at same time as other monitoring tests	Urinalysis for blood and protein prior to each injection	Severe rash, severe mouth ulcers, unexplained cough, dyspnoea, abnormal bruising or bleeding, severe sore throat, nitroid reaction (dizziness, nausea, vomiting, sweating, flushing, hypotension), visual disturbances, severe alopecia, severe diarrhoea - **STOP** drug and seek advice There is a risk of risk of prolonged/permanent hypogammaglobulinaemia	Increased toxicity with other **myelotoxic** and **nephrotoxic** drugs. ACEIs – increased risk of nitroid reactions
Leucopenia <3.5 x 10^9/L Neutropenia <2.0 x 10^9/L Sequential falls in WBC or neutrophils >10% on 3 occasions Thrombocytopenia <150 x 10^9/L **STOP** and seek advice Sequential falls in platelets - **STOP** unless falls are from high level Lymphocytes <0.5 x 10^9/L - Seek advice Macrocytosis >105 fl Check B12 and folate, thyroid function have been checked within last 12 months and are normal Sequential falls in platelets **STOP** unless falls are from high level Eosinophilia – rising trend – reduce dose; advance warning of likely adverse reaction – watch carefully		Elevation of ALT >3x upper limit of reference range – STOP and seek advice. Consider other causes. Rare late side effect. Fall in albumin >5g/L - seek advice; <25g/L – STOP, dipstick urine and send for albumin/creatinine ratio. May be an indication of renal damage (see recommendations for urinalysis)		**Haematuria** - Trace or + - Check MSU. Continue drug. ++ or +++ check ACR and seek advice. If evidence of symptomatic UTI check MSU and treat as appropriate. **Proteinuria** - Trace or + - Check MSU. Continue drug. ++ or +++ check albumin/creatinine Ratios (ACR) and seek advice. If evidence of symptomatic UTI check MSU and treat as appropriate		

<table>
<tr><th colspan="6">SULFASALAZINE</th></tr>
<tr><th>FBC</th><th>U&Es
Creatinine</th><th>LFTs</th><th>ESR/CRP</th><th>Other important warnings</th><th>Important interactions</th></tr>
<tr><td colspan="3">(Initially every 2 weeks until on stable dose for 6 weeks then monthly for 3 months)

Thereafter, at least every 12 week

No routine monitoring needed after 12 months

High risk patients should remain on indefinite monitoring / monthly monitoring i.e. those who have renal impairment, are potentially on other drugs which may interact with the DMARD, those who have had previous blood abnormalities either due to low grade DMARD toxicity or other medical problems e.g. mild ITP, those who have known liver disease.</td><td>RHEUMATOLOGY PATIENTS ONLY (marker of disease activity)
Following dose stabilisation check at same time as other monitoring tests</td><td rowspan="2">Unexplained cough, dyspnoea, abnormal bruising or bleeding, severe sore throat,, severe nausea/ dizziness/ headache , unexplained acute, widespread rash, oral ulceration - STOP drug and seek advice</td><td rowspan="2"></td></tr>
<tr><td>Leucopenia <3.5 x 109/L

Neutropenia <2.0 x 109/L

Sequential falls in WBC or neutrophils >10% on 3 occasions

Thrombocytopenia <150 x 109/L

STOP and seek advice

Sequential falls in platelets - STOP unless falls are from high level

Sequential falls in platelets STOP unless falls are from high level

Lymphocytes <0.5 x 109/L Seek advice

Macrocytosis - >105 fl – check B12 and folate, , thyroid function have been checked within last 12 months and are normal</td><td></td><td>Elevation of ALT >2 x upper limit of reference range - seek advice; >3 x upper limit of reference range - STOP. Repeat LFTs.
Mild transaminitis is common and normally settles.</td><td></td></tr>
</table>

TACROLIMUS – UNLICENSED USE							
FBC	**U&Es Creatinine**	**LFTs**	**ESR/CRP**	**Lipids**	**BP and Glucose**	**Other important warnings**	**Important interactions**
(Initially every 2 weeks until on stable dose for 6 weeks then monthly for 3 months) Once stabilised, ONCE a month Patients who have been stable for 12 months can be considered for reduced frequency monitoring on an individual patient basis Dose increases should be monitored every 2 weeks until stable for 6 weeks , then revert to previous schedule High risk patients should remain on indefinite monitoring / monthly monitoring i.e. those who have renal impairment, are potentially on other drugs which may interact with the DMARD, those who have had previous blood abnormalities either due to low grade DMARD toxicity or other medical problems e.g. mild ITP, those who have known liver disease.			RHEUMATOLOGY AND GASTROENTEROLOGY PATIENTS ONLY (marker of disease activity) Following dose stabilisation check at same time as other monitoring tests	Every 6 months	Following stabilisation monitor ONCE a month	Unexplained cough, dyspnoea, abnormal bruising or bleeding - **STOP** drug and seek advice **Ciclosporin levels** – trough drug levels may be indicated/considered if there are concerns about toxicity or concordance	**ANALGESICS** – possible increased nephrotoxicity with NSAIDS and especially **Ibuprofen** **ANTIBACTERIALS –** increased levels with clarithromycin, erythromycin, chloramphenicol and quinupristin/dalfopristin; reduced levels with rifampicin; increased nephrotoxicity with aminoglycosides, vancomycin **ANTIDEPRESSANTS –** Increased levels with St John's Wort **ANTEPILEPTICS** - carbamazepine phenobarbital and phenytoin decrease tacrolimus level, **ANTIFUNGALS –** Increased levels with fluconazole, itraconazole, ketoconazole and voriconazole **AMPHOTERICIN** - increased risk of nephrotoxicity with **ANTIPSYCHOTICS –** Droperidol **ANTIVIRALS –** Increased risk of nephrotoxicity with aciclovir, ganciclovir; **CALCIUM CHANNEL BLOCKERS** _ increased levels with felodipine, nicardipine, verampimil, diltiazem and nifedipine **CICLOSOPRIN –** Increased CyCA levels **DABIGATRAN** - tacrolimus possibly increases plasma concentration of dabigatran avoid concomitant use **DIURETICS and K SALTS– increased risk of hyperkalaemia** **GRAPEFRUIT JUICE –** increased levels
Leucopenia <3.5 x 10^9/L Neutropenia <2.0 x 10^9/L Sequential falls in WBC neutrophils >10% on 3 occasions Thrombocytopenia <150 x 10^9/L **STOP** and seek advice Sequential falls in platelets - **STOP** unless falls are from high level Lymphocytes <0.5 x 10^9/L - Seek advice Macrocytosis >105 fl Check B12 and folate, thyroid function have been checked within last 12 months and are normal	Increase in creatinine - >30% from baseline – reduce dose by 50% - >50 % above baseline – **STOP** drug and seek advice	Elevation of ALT >2 x upper limit of reference range - seek advice; >3 x upper limit of reference range - **STOP**. Repeat LFTs. Mild transaminitis is common and normally settles.		Significant rise in fasting lipids **STOP** and seek advice	BP> 140/90 on 2 readings 2 weeks apart – treat BP before stopping drug (e.g. with amlodipine). If uncontrolled **STOP** and control BP before restarting tacrolimus – seek advice		

Appendix 2 BIOLOGICS – for information only

<table>
<tr><th colspan="7">ADALIMUMAB, CERTOLIZOMAB PEGOL, ETANERCEPT, GOLIMUMAB, ANAKINRA, BELIMUMAB,</th></tr>
<tr><th>FBC</th><th>U&Es Creatinine</th><th>LFTs</th><th>ESR/CRP</th><th>Hepatitis B</th><th>Other important warnings</th><th>Important interactions</th></tr>
<tr><td colspan="4">Every 3 – 6 months</td><td>Periodically for those at risk</td><td rowspan="2">Infections — risk is greatest during the first 6 months of treatment. Serious infections — treat promptly, withhold biologic until discussed with specialist team.

Periodic skin examination for non-melanoma skin cancer for patients at increased risk (history of psoriasis or PUVA therapy).- if concerned, withhold until discussed with specialist team

Signs and symptoms of tuberculosis — during treatment and for 6 months after treatment has stopped - discuss with specialist team.

Signs and symptoms of heart failure or worsening heart failure - withhold until discussed with specialist team.

Shortness of breath or dry cough (symptoms of interstitial lung disease) - withhold until discussed with specialist team.</td><td rowspan="2">SULFASALAZINE with etanercept - caution - risk of decrease in mean white blood cell counts

Live vaccines/therapeutic infectious agents should not be given concurrently

CYP450 substrates with a narrow therapeutic index (e.g. warfarin and phenytoin) and anakinra - consider therapeutic monitoring of the effect or concentration upon start or end of anakinra treatment</td></tr>
<tr><td>WBC < 3.5 x 10^9/L
Neutrophils < 2 x 10^9/L
Platelets < 150 x 10^9/L
STOP and seek specialist advice</td><td>Any abnormal value - use clinical judgement; if in doubt discuss with specialist team</td><td>ALT twice the normal range – discuss with specialist team</td><td>An increase from baseline - discuss with specialist team</td><td>Any abnormal value - discuss with specialist team</td></tr>
</table>

For information only

ABATACEPT INFLIXIMAB, RITUXIMAB						
FBC	**U&Es Creatinine**	**LFTs**	**ESR/CRP**	**Hepatitis B**	**Other important warnings**	**Important interactions**
As advised by hospital				Periodically for those at risk	Infections — risk is greatest during the first 6 months of treatment. Serious infections — treat promptly, withhold biologic until discussed with specialist team. Periodic skin examination for non-melanoma skin cancer for patients at increased risk (history of psoriasis or PUVA therapy).- if concerned, withhold until discussed with specialist team Signs and symptoms of tuberculosis — during treatment and for 6 months after treatment has stopped - discuss with specialist team. Signs and symptoms of heart failure or worsening heart failure - withhold until discussed with specialist team. Shortness of breath or dry cough (symptoms of interstitial lung disease) - withhold until discussed with specialist team.	**Live vaccines/therapeutic infectious agents** should not be given concurrently
WBC < 3.5 x 10^9/L Neutrophils < 2 x 10^9/L Platelets < 150 x 10^9/L STOP and seek specialist advice	Any abnormal value - use clinical judgement; if in doubt discuss with specialist team	ALT twice the normal range – discuss with specialist team	An increase from baseline - discuss with specialist team	Any abnormal value - discuss with specialist team		

For information only

TOCILIZUMAB

See NoT&G website: http://www.northoftyneapc.nhs.uk/wp-content/uploads/sites/6/2018/07/Tocilizumab-monitoring-shared-care-guidance-June-18.doc

APPENDIX 3 – CIRCULATION LIST FOR COMMENT

Dr S Bourke	Consultant Respiratory Physician	The Newcastle upon Tyne Hospitals NHS FT
Dr S Bourke	Consultant Respiratory Physician	Northumbria Healthcare NHS FT
Mr I Campbell	Assistant Director of Pharmacy	The Newcastle upon Tyne Hospitals NHS FT
Dr D Coady	Consultant Rheumatologist	City Hospitals Sunderland
Dr H Coundon	GP	North Tyneside CCG
Dr A De Soyza	Consultant Respiratory Physician	The Newcastle upon Tyne Hospitals NHS FT
Dr C Dipper	Consultant Gastroenterologist	The Newcastle upon Tyne Hospitals NHS FT
Dr R Fielding	Consultant Nephrologist	The Newcastle upon Tyne Hospitals NHS FT
Dr I Forrest	Consultant Respiratory Physician	The Newcastle upon Tyne Hospitals NHS FT
Dr A Gall	GP and Prescribing Lead	Newcastle Gateshead CCG
Mr N Gammack	Chief Pharmacist	Gateshead Health NHS FT
Dr B Griffiths	Consultant Rheumatologist	The Newcastle upon Tyne Hospitals NHS FT
Dr M Grove	Consultant Rheumatologist	Northumbria Healthcare NHS FT
Dr J Hamilton	Consultant Rheumatologist	Gateshead Health NHS FT
Dr P Hamilton	Consultant Dermatologist	The Newcastle upon Tyne Hospitals NHS FT
Dr M Hudson	Consultant Hepatologist	The Newcastle upon Tyne Hospitals NHS FT
Dr W Innes	Consultant Ophthalmologist	The Newcastle upon Tyne Hospitals NHS FT
Dr C Jewitt	GP and Prescribing Lead	Newcastle Gateshead CCG
Dr L Kay	Consultant Rheumatologist	The Newcastle upon Tyne Hospitals NHS FT
Dr S Leech	Consultant Dermatologist	The Newcastle upon Tyne Hospitals NHS FT
Dr J Lordan	Consultant Respiratory Physician	The Newcastle upon Tyne Hospitals NHS FT
Mr M Lowery	Formulary Pharmacist	The Newcastle upon Tyne Hospitals NHS FT
Dr J Mansfield	Consultant Gastroenterologist	The Newcastle upon Tyne Hospitals NHS FT
Dr J Matthews	GP	North Tyneside
Dr S Meggitt	Consultant Dermatologist	The Newcastle upon Tyne Hospitals NHS FT
Dr J Miller	Consultant Neurologist	The Newcastle upon Tyne Hospitals NHS FT
Dr J Moore	Consultant Microbiologist	Gateshead Health NHS FT
Mr B Moulder	Head of Commissioning for	Northumberland CCG

	Planned Care	
Ms J Murphy	Lower Gastroenterology Nurse Specialist	Northumbria Healthcare NHS FT
Dr E Phillips	Consultant Gastroenterologist	Northumbria Healthcare NHS FT
Ms A Rodway	Chronic Disease Monitoring Lead	The Newcastle upon Tyne Hospitals NHS FT
Dr V Saravanan	Consultant Rheumatologist.	Gateshead Health NHS FT
Mr M Scott	GP	Newcastle upon Tyne
Dr D Shovlin	GP	Northumberland
Dr G Spickett	Consultant Immunologist	The Newcastle upon Tyne Hospitals NHS FT
Dr B Thompson	Consultant Rheumatologist. Head of Rheumatology	The Newcastle upon Tyne Hospitals NHS FT
Dr S Tulip	Pharmacist	Newcastle Gateshead CCG
Dr S Waugh	Consultant Virologist	The Newcastle upon Tyne Hospitals NHS FT
Dr J Warrington	Director for planned care	Northumberland CCG

Declared conflicts of interest
None declared

Date of reviewed guideline
July 2018

Date of review
July 2021