SHARED CARE PRESCRIBING GUIDELINE

Azathioprine, Hydroxychloroquine, Leflunomide, Methotrexate, Mycophenolate, Sulfasalazine for the treatment of AUTOIMMUNE HEPATITIS, AUTOIMMUNE RHEUMATIC DISEASES, AND INFLAMMATORY BOWEL DISEASE in PAEDIATRICS (≤ 18 years of age)

SHARED CARE PROCESS FLOWCHART

Specialist clinician completes Shared Care Request Letter (Appendix 1) and sends to patient's GP via email.

GP considers shared care request, taking into account the following:

- Is the patient's condition predictable or stable?
- Whether they have the relevant knowledge, skills and access to equipment to allow them to monitor treatment as indicated in this shared care prescribing guideline?
- Whether they have been provided with relevant clinical details including monitoring data?

If YES to all the above, and after reading this shared care guideline then it is appropriate for GP to accept prescribing responsibility

If NO to any of these questions, GP should contact the requesting consultant or the local primary care Medicines Optimisation Team within 2 weeks of receipt to discuss

Issues resolved / details clarified

Complete Shared Care Agreement Letter (Appendix 2) and email back to the requesting clinician within 2 weeks of receipt

Complete Shared Care Refusal Letter (Appendix 3) and email back to the requesting clinician

NOTES

There may be implications for the patient where invitation to share care is declined. For example, the patient may need to be changed to an alternative treatment regimen. It would not normally be expected that shared care prescribing would be declined on the basis of cost.

Sharing of care assumes communication between the specialist, GP and patient. The intention to share care should be explained to the patient by the doctor initiating treatment. **It is important that patients are consulted about treatment and are in agreement with it.**

Prescribing should follow requirements in the South East London Interface Prescribing Policy.
The doctor who prescribes the medication legally assumes clinical responsibility for the drug and the consequences of its use. The patient's best interests are always paramount.

If the GP is not confident to undertake these roles, then he or she is under no obligation to do so. In such an event, the total clinical responsibility for the patient for the diagnosed condition remains with the specialist. If a specialist asks the GP to prescribe this drug, the GP should reply to this request as soon as practicable.

1. AREAS OF RESPONSIBILITY

Consultant / Specialist team responsibilities

- Ensuring appropriate use of the immunomodulatory drug(s) e.g. no contraindications, cautions, fits local or national agreement for use of the drug
- Undertake baseline investigations and initial monitoring
- Enter blood results in patient held monitoring book and issue to patient
- Prescribe treatment for a minimum of the first 3 months or until the patient is considered stable (whichever is longer) and shared care is agreed with GP.
- After initiation and stabilization of dose ensure that the patient is reviewed prior to requesting shared care with the GP.
- Discuss adverse effects and any practical issues related to the use of the immunomodulatory drugs with the patient
- Notify the GP when immunomodulatory drug therapy is initiated. The GP should be invited to share care once the patient is stable. Information provided to the GP should include:
    - A clinical summary of the patient including information on prescribed medication, initial response and any adverse effects experienced
    - A request that the GP continue prescribing and monitoring
    - A copy of the shared care guidelines outlining required ongoing monitoring
    - Information on when the patient will next be reviewed by Consultant/Specialist team
    - A letter following each shared care review with results of monitoring blood tests and any medication changes
- Review patient at the request of GP should any problems arise (side-effects / lack of efficacy).
- Communicate (within 2 weeks) with the GP if treatment is changed.
- Undertake serology test and administer Varicella-Zoster vaccines (VZV) for appropriate patients
- Report any suspected adverse effects to the MHRA: www.yellowcard.mhra.gov.uk

General Practitioner responsibilities

- To consider shared care protocol and respond to the GP decision form within 2 weeks of receipt. If agree to request to continue prescribing as detailed in shared care guideline. Confirmation to the requesting consultant or nurse specialist is required within 2 weeks of receipt of this guideline by completing and returning the letter in Appendix 2, pg 13.
- If you do not agree to shared care discuss with requesting consultant or the specialist team and local primary care medicines management team within 2 weeks of receipt of shared care request. Complete the letter in Appendix 3 pg 14.
- Provide ongoing prescriptions and adjust dose as advised by the specialist.
- Undertake ongoing monitoring as outlined in the monitoring information
- Enter blood results in patient held monitoring book or provide patient/carer with a copy of the most up to date results.
- Report and seek advice regarding any concerns, for example: side-effects, co-morbidities, pregnancy, or lack of efficacy to the specialist team
- Advise the specialist if non-compliance is suspected
- Refer back to specialist team if the patient's condition deteriorates
- Stop treatment on the advice of the specialist or immediately if an urgent need to stop treatment arises.
- Report any suspected adverse effects to the MHRA via the Yellow Card scheme: www.yellowcard.mhra.gov.uk

Patient's / Carer's responsibilities

- Read pre-treatment information leaflets and monitoring book
- Bring monitoring book and/or blood results to each appointment with GP/specialist and show the book to community pharmacist when having prescriptions dispensed
- Contact the specialist or GP if he or she does not have a clear understanding of any aspect of the treatment.
- Agree to attend all hospital and GP appointments
- For replacement or renewal of patient held monitoring book contact the specialist nurse helpline or ask patient to request at their next outpatient follow up appointment
- Inform GP and hospital of any changes in addresses or telephone contact numbers
- Report any adverse effects, new/worsening symptoms or pregnancy/breastfeeding to GP or hospital specialist
- Inform prescribing specialist, GP and other healthcare professionals of any other medication being taken, including over the counter products (including aspirin or non-steroidal anti-inflammatories), alternative therapies or recreational drugs.
- Inform community pharmacists of all prescribed medication before purchasing medicines over-the-counter
- Take medicines as agreed and take steps to ensure that no doses are missed and not to share medicines with others

2. CLINICAL INFORMATION

NOTE: The information here is not exhaustive. Please also consult the current Summary of Product Characteristics (SPC) for **Azathioprine, Hydroxychloroquine, Leflunomide, Methotrexate, Mycophenolate, Sulfasalazine** prior to prescribing for up to date prescribing information, including detailed information on adverse effects, drug interactions, cautions and contraindications (available via www.medicines.org.uk)

Immunomodulatory Drugs Licensing

O = 'off-label' but considered routine treatment option
X = unlicensed and not currently considered a routine option. These are not covered by this shared care guideline and therefore would not be transferred to primary care.

	Azathioprine Page. 16	**Hydroxychloroquine** Page. 18	**Leflunomide** Page. 20	**Methotrexate** Page. 22	**Mycophenolate** Page. 24	**Sulfasalazine** Page. 26
Behcets	**O**	***X***	***X***	**O**	**O**	***X***
Juvenile Dermatomyositis	**O**	**O**	***X***	**O**	**O**	***X***
Juvenile Idiopathic Arthritis	**O**	***Licensed***	**O**	**O**	***X***	**O**
Juvenile Psoriatic arthritis	**O**	**O**	**O**	**O**	***X***	**O**
Juvenile Systemic Lupus Erythematosus	**O**	***Licensed***	***X***	**O**	**O**	***X***
Scleroderma	**O**	**O**	***X***	**O**	**O**	***X***
Sjögren's Syndrome	**O**	**O**	***X***	**O**	***X***	***X***
Vasculitis (including EGPA, GPA, MPA & PAN)	**O**	**O**	***X***	***X***	**O**	**O**
Uveitis	***X***	***X***	***X***	**O**	**O**	***X***
Ulcerative Colitis	***Licensed***	***X***	***X***	**O**	***X***	***Licensed***
Crohn's Disease	***Licensed***	***X***	***X***	***Licensed***	***X***	***Licensed***
Inflammatory Bowel Disease	**O**	***X***	***X***	**O**	***X***	***O***
Autoimmune hepatitis	***Licensed***	***Not used in AIH***	***Not used in AIH***	**Not used in AIH**	***X***	***Not used in AIH***

Background and Place in Therapy

As the name implies, immunomodulators modify the activity of the immune system, in turn, decreasing the inflammatory response. Immunomodulators are most often used in organ transplantation to prevent rejection of the new organ as well as in autoimmune diseases such as rheumatoid arthritis. Since the late 1960s, they have also been used to treat people with IBD, where the normal regulation of the immune system is affected.

a) Medication use in autoimmune rheumatic diseases

Medical treatment for paediatric rheumatology has two main goals: achieving remission as soon as possible (control or resolution of inflammation) and then maintaining remission. The drugs work to reduce inflammation, to minimise or prevent joint/organ damage, and to preserve the structure and function of the joints/organs. Immunomodulatory drugs are initiated in secondary/tertiary care in order to induce remission. Examples include Methotrexate, Sulfasalazine, Leflunomide and Hydroxychloroquine. It may take up to three to six months to see an improvement in symptoms with medication, so on many occasions steroids may be commenced at the same time as immunomodulatory drugs to

produce a faster response. However, the main benefit of these immunomodulatory drugs is to reduce the long-term need for steroids and prevent recurring flares. For that reason, immunomodulatory drugs are sometimes referred to as "steroid-sparing" drugs. They also may be used in combination with other agents such as biologics for synergetic effect and also to help prevent antibody formation, which can result in loss of response to biologics.

Once patients are stabilised on their treatment it is feasible for the on-going prescribing of immunomodulatory drugs and monitoring to be undertaken in primary care with review in secondary/tertiary care.

b) Medication use in inflammatory bowel disease (IBD)

Medical treatment for Crohn's disease and ulcerative colitis has two main goals: achieving remission (control or resolution of inflammation leading to symptom resolution with healing of the inflamed tissue) and then maintaining remission. To accomplish these goals, treatment is aimed at controlling the ongoing inflammation in the intestine—the cause of IBD symptoms.

Immunomodulatory drugs, by themselves or with another agent, may be appropriate in the following treatment situations:
• Nonresponse or intolerance to aminosalicylates, antibiotics, or corticosteroids
• Steroid-dependent disease or frequent need for steroids
• Perianal (around the anus) disease that does not respond to antibiotics
• Fistulas (abnormal channels between two loops of intestine, or between the intestine and another structure—such as the skin)
• To bolster or optimise the effect of a biologic drug and prevent the development of resistance to biologic drugs
• To prevent recurrence after surgery

Because it can take up to three to six months to see an improvement in symptoms with immunomodulators, steroids may be started at the same time to produce a faster response. Lower doses of the steroid may be utilised in some cases, producing fewer side effects. However, the main benefit of these drugs is to decrease the long-term need for steroids and prevent recurring flares. For that reason, immunomodulators are sometimes referred to as "steroid-sparing" drugs. They also may be used in combination with other agents such as the biologics to help prevent antibody formation, which can result in loss of response to biologics

c) Medication use in autoimmune hepatitis/liver disease (AIH)

AIH is the prototype autoimmune liver disease in adults and children and is a progressive inflammatory hepatopathy which, if not treated, progresses to end stage liver disease requiring liver transplantation. Unless it is a sudden and severe presentation with encephalopathy, AIH responds satisfactorily to treatment with immunomodulatory drugs whatever the degree of liver damage, with remission rates reported up to 90%. AIH responds to immunomodulatory treatment in the majority of cases and treatment should be instituted promptly upon diagnosis.

Conventional treatment of AIH consists of prednisolone at a dosage of 2 mg/kg/day (maximum 60 mg/day), which is gradually decreased during a period of 4 to 8 weeks, adjusted according to the decline of transaminase levels, to a maintenance dose of 2.5 to 5 mg/day. It is reported that approximately 85% of patients will require addition of azathioprine as a steroid-sparing agent. The timing of adding in azathioprine will depend on the patient's symptoms, liver function, transaminase levels, tolerability of steroids and/or co-morbidities.

<table>
<tr><td>Initiation and ongoing dose regime

Note:
• Transfer of monitoring and prescribing to primary care is normally after the patient's dose has been optimised and with satisfactory investigation results for at least 4 weeks.
• The duration of treatment & frequency of review will be determined by the specialist, based on clinical response and tolerability.
• All dose or formulation adjustments will be the responsibility of the initiating specialist unless directions have been discussed and agreed with the primary care clinician.
• Termination of treatment will be the responsibility of the specialist.</td><td colspan="2"><u>Initial stabilisation:</u>
(The loading period must be prescribed by the initiating specialist)

3 months

<u>Maintenance dose (following initial stabilisation):</u>
(The initial maintenance dose must be prescribed by the initiating specialist)

Please see appendix 4

<u>Conditions requiring dose adjustment</u>

Please see appendix 4 and refer to the individual drug information.

General reasons that might require dose adjustment include
• Sub-therapeutic
• Mild side-effects i.e. headache
• Some patients may have more individualised parameters set out by their secondary care specialist which fall outside the normal range; these should be communicated to primary care in writing

<u>Duration of treatment</u>

Ongoing provided there is benefit, no reported intolerance and/or adverse effects.</td></tr>
<tr><td rowspan="4">Pharmaceutical aspects – refer to the SEL paediatric formulary for further detail</td><td>Route of administration</td><td>Enteral/Subcutaneous injection</td></tr>
<tr><td>Formulation</td><td>Tablets/Capsules/Liquid/Subcutaneous injection</td></tr>
<tr><td>Administration details</td><td>Please see appendix 4</td></tr>
<tr><td>Other important information</td><td>Please see appendix 4</td></tr>
<tr><td>Baseline investigations, initial monitoring and ongoing monitoring to be undertaken by specialist</td><td colspan="2"><u>Baseline investigations:</u>

Please see appendix 4

<u>Initial monitoring</u>

Monitoring at baseline and during initiation is the responsibility of the specialist, only once the patient is optimised on the chosen medication with no anticipated further changes expected in immediate future will prescribing and monitoring be transferred to the GP.

<u>Ongoing monitoring:</u>

Please see appendix 4</td></tr>
<tr><td rowspan="2">Ongoing monitoring requirements to be undertaken by primary care</td><td>Monitoring</td><td>Frequency</td></tr>
<tr><td>Please see appendix 4</td><td>Please see appendix 4</td></tr>
<tr><td rowspan="2">Adverse effects and management

Any serious adverse reactions should be reported to the MHRA via the Yellow Care scheme</td><td>Result</td><td>Action for GP</td></tr>
<tr><td>Please see appendix 4</td><td>Please see appendix 4</td></tr>
</table>

www.mhra.gov.uk/yellowcard		
Advice to patients and carers The specialist will counsel the patient with regard to the benefits and risks of treatment and will provide the patient with any relevant information and advice, including patient information leaflets on individual medicines.	**The patient should be advised to report any of the following signs or symptoms to their GP without delay:** Rashes, oral ulceration, bruising, bleeding, signs and symptoms of infection Please see appendix 4	
Criteria for stopping treatment e.g. poor response, adverse effects requiring cessation	Failure to respond to treatment or adverse effects necessitating withdrawal Patient request Please see appendix 4	
Follow up arrangements e.g. frequency of specialist clinic attendance	Request patient seen earlier if condition deterioration or adverse effects experienced between appointments It is the primary care prescriber's responsibility to ensure patients adhere to the monitoring schedule. It should be clearly communicated to the patient how often they are required to attend. Concerns that the patient is unable to adhere to the monitoring schedule should be discussed with the secondary care team. Patients must be informed that they will be unable to continue the medication unless they adhere to the monitoring requirements	
Pregnancy, paternal exposure and breast feeding It is the responsibility of the specialist to provide advice on the need for contraception to male and female patients on initiation and at each review but the ongoing responsibility for providing this advice rests with both the GP and the specialist.	Please see appendix 4	
Additional information	**Where patient care is transferred from one specialist service or GP practice to another, a new shared care agreement must be completed.** Some patients may have more individualised parameters set out by their secondary care specialist which fall outside the normal range; these should be communicated to primary care in writing. Please see appendix 4	
Information relating to vaccination and Varicella Zoster Virus (chicken pox)	**Vaccination** 1. All non-live vaccines are safe and recommended to continue on non-biologic immunomodulatory drugs, including the seasonal influenza vaccination (inactivated) and pneumococcal vaccine 2. COVID-19: Immunosuppressed children >5yrs old, due to disease or treatment are an 'at-risk' group and should be vaccinated against COVID-19 as stated by UK Health Security Agency (UKHSA – formerly known as PHE) Immunisation Against Infectious Disease (The Green Book). 3. Where possible vaccines should be administered at times of stable disease. 4. Live-vaccinations may be considered in patients with chronic inflammatory diseases treated with non-biologic immunomodulatory drugs. For the most uptodate advice please refer to ***The Green Book*: Immunisation against infectious diseases – Chapter 6: Contraindications and special considerations.**	

	5. **Please discuss with the specialist consultant/team if in any doubt about the degree of immunomodulation and whether a particular live-vaccination should be considered.** **Varicella Zoster Virus (chicken pox)** • The specialist centre will undertake serology testing. • Patients VZV IgG negative, should be considered to receive the varicella vaccines. Varicella vaccinations will be organised by the specialist centre. • Patients who are VZV IgG negative and have exposure to chicken-pox / shingles should receive passive immunisation with VZIG (varicella immunoglobulin), which will be provided by the specialist centre or aciclovir, which GPs may be asked to prescribe. • If patient develops chickenpox / shingles withhold azathioprine, treat with aciclovir and inform the medical team.
Evidence base for treatment and key references Include hyperlinks to original sources and access dates	1) Summary of product characteristics for individual drugs. Available online at https://www.medicines.org.uk/emc 2) British National Formulary for Children. Available online at BNFC (British National Formulary for Children) | NICE 3) South East London Paediatric Formulary. Available online at https://www.clinibee.com/ 4) Department of Health. Green Book. Available online: https://www.gov.uk/government/collections/immunisation-against-infectious-disease-the-green-book#the-green-book 5) NICE National Clinical Guideline NG129 Crohn's Disease: Management. Available online at https://www.nice.org.uk/guidance/ng129 6) NICE National Clinical Guideline NG130 2019 Ulcerative Colitis: Management. Available online at https://www.nice.org.uk/guidance/ng130 7) BSR/BHPR guideline for the prescription and monitoring of non-biologic disease-modifying anti-rheumatic drugs, *Rheumatology* volume 56, issue 6, June 2017. Available online at: https://academic.oup.com/rheumatology/article/56/6/865/3053478 8) The European Crohn's and Colitis Organisation (ECCO) Therapeutic Interventions. Available online at Interventions | ECCO E-Guide (ecco-ibd.eu) 9) 2018 Management of Paediatric Ulcerative Colitis, Part 1: Ambulatory Care – An Evidence-based Guideline From European Crohn's and Colitis Organisation and European Society of Paediatric Gastroenterology, Hepatology and Nutrition. Available online at Management of Paediatric Ulcerative Colitis, Part 1: Ambulat... : Journal of Pediatric Gastroenterology and Nutrition (lww.com) 10) 2020 The Medical Management of Paediatric Crohn's Disease: An ECCO-ESPGHAN Guideline Update. Available online at Medical Management of Paediatric Crohn's Disease: an ECCO-ESPGHAN Guideline Update | Journal of Crohn's and Colitis | Oxford Academic (oup.com) 11) The Royal College of Ophthalmologists. Hydroxychloroquine and Chloroquine Retinopathy Monitoring Guideline and Recommendations 2020. Available online at https://www.rcophth.ac.uk/resources-listing/2609/ 12) Juvenile idiopathic arthritis: management and therapeutic options. Ther Adv Musculoskelet Dis, 2012 Apr; 4(2): 99-110. Available online at https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3383518/ 13) Drugs in Pregnancy and Lactation. Accessed online via MedicinesComplete — Dashboard

To be read in conjunction with the following documents	South East London Paediatric Formulary. Available online at https://www.clinibee.com/
Local arrangements for referral Define the referral procedure from hospital to primary care prescriber & route of return should the patient's condition change.	Clinic letter/email request to GP for shared care consideration. Practice letter/email from GP to secondary care

3. COMMUNICATION AND SUPPORT FOR PAEDIATRIC RHEUMATOLOGY

King's College and Princess Royal/Orpington Hospitals switchboard: 020 3299 9000	
Consultant/Specialist team Paediatric Rheumatology Consultant Dr Sreena Das	Tel: via hospital switchboard
Medication – Prescribing advice, interactions, availability of medicines Women's and Children's Pharmacy Team	kch-tr.WomenandChildrenPharmacyTeam@nhs.net 0203 299 9000 ex: 39656
Evelina London Children's Hospital - Guy's & St. Thomas' Hospital switchboard: 020 7188 7188	
Consultant/Specialist team Consultant Paediatric Rheumatologists Dr Vinay Shivamurthy, Dr Theonymfi Doudouliak, Dr Nadia Rafiq Paediatric Rheumatology Specialist Registrar Rheumatology Specialist Nurse Helpline Dani Adams Department Email:	Tel: Secretary via hospital switchboard (or Consultant Paediatric Rheumatologist on call via switchboard) Tel: 07787 842692 (Mon to Fri 0900-1700) Tel: 07918 338768 (Mon to Fri 0900-1700) Email: gst-tr.rheve@nhs.net
Medication – Prescribing advice, interactions, availability of medicines Paediatric Rheumatology Specialist Pharmacist Soni Bhatt Medicines Information (GSTFT)	 Tel: 020 7188 9152 Tel: 020 7188 8748 Email: medicinesinformation@gstt.nhs.uk
Lewisham & Greenwich Hospitals switchboard Lewisham 0208 333 3000 Queen Elizabeth 020 8836 6000	
Consultant/specialist team Consultant Paediatrician with an interest in paediatric rheumatology Dr Alistair Lim	Tel: Lewisham - Secretary via hospital switchboard ext: 6401 Queen Elizabeth: Secretary via hospital switchboard ext 5286, 6222 or 4521.
Medication – Prescribing advice, interactions, availability of medicines	Email: LG.QE-MedInfo@nhs.net Tel: 0208 836 4900.

3. COMMUNICATION AND SUPPORT FOR PAEDIATRIC GASTROENTEROLOGY

King's College and Princess Royal/Orpington Hospitals switchboard: 020 3299 9000	
Consultant/Specialist team Consultant Paediatric Gastroenterologists Mr Ben Hope, Dr Babu Vadamalayan, Dr Huey Miin and Dr Matilde Pescarin Paediatric Gastroenterology Specialist Registrar Paediatric Gastroenterology Specialist Nurses Bukunola Kukoyi and Andrew Hubbert	Tel: Secretary: Denmark Hill site 020 3299 1674 (or Consultant Paediatric Gastroenterologist on call via switchboard) Bleep: 493 Tel: 020 3299 1897 Email: kch-tr.paedgastrocns@nhs.net
Medication – Prescribing advice, interactions, availability of medicines Women's and Children's Pharmacy Team	kch-tr.WomenandChildrenPharmacyTeam@nhs.net 0203 299 9000 ex: 39656
Evelina London Children's Hospital - Guy's & St. Thomas' Hospital switchboard: 020 7188 7188	
Consultant/Specialist team Consultant Paediatric Gastroenterologists Dr Mohamed Mutalib, Dr Jochen Kammermeier, Dr Rakesh Vora Paediatric Gastroenterology Fellow Paediatric Gastroenterology Specialist Nurses Helpline Gemma Lee, Christopher Rae Department email: gst-tr.ibdhelplineelch@nhs.net	Tel: Secretary via hospital switchboard (or Consultant Paediatric Gastroenterologist on call via switchboard) Bleep: 1996 (Mon to Fri 0900-1730) Tel: 07824 605001 (Mon to Fri 0900-1700) Email: gst-tr.ibdhelplineelch@nhs.net
Medication – Prescribing advice, interactions, availability of medicines Paediatric Gastroenterology Specialist Pharmacist Jaini Shah Medicines Information (GSTFT)	 Tel: 020 7188 9152 Tel: 020 7188 3849/ 3855/ 8750 Email: medicinesinformation@gstt.nhs.uk
Lewisham and Greenwich Hospitals switchboard Lewisham 0208 333 3000 Queen Elizabeth 020 8836 6000	
Consultant/specialist team Consultant Paediatric Gastroenterologists Dr Sarmad Kalamchi Paediatric Specialist Pharmacist Chew Phang	 Tel: Lewisham: 0208 333 3000 ext: 6760 Tel: Lewisham: 0208 333 3000 ext: 8820 Bleep: 7315
Medication – Prescribing advice, interactions, availability of medicines	Email: LG.QE-MedInfo@nhs.net Tel: 0208 836 4900.

3. COMMUNICATION AND SUPPORT FOR PAEDIATRIC HEPATOLOGY – Autoimmune Hepatitis Patients

King's College Hospital Denmark Hill switchboard: 020 3299 9000	
Consultant/Specialist team Consultant Paediatric Hepatologists: Professor Anil Dhawan, Professor Alastair Baker, Professor Dino Hadzic, Dr Tassos Grammatikopoulos, Dr Marianne Samyn, Dr Sanjay Bansal, Dr Jonathan Hind, Dr Vandana Jain, Dr Eirini (Serena) Kyrana	Secretaries: 0203 299 3214
Paediatric Hepatology Specialist Registrar	Via switchboard
Paediatric Gastroenterology Specialist Nurses: Louise Hair, Lucy-Claire Murphy, Natalie Bailey, Lisa Clay and Jenny Yerlett	Tel: 0203 299 3774 Email: kch-tr.livercns@nhs.net
Medication – Prescribing advice, interactions, availability of medicines **Paediatric Liver Pharmacy Team**	kch-tr.PaediatricLiverPharmacists@nhs.net Tel: 020 3299 9000 ext 39651

Note: King's College Hospital is a national hub providing a highly specialised service to children with liver disease. Other SEL trusts would defer to King's for advice on the management of these patients, hence their contact details only documented here.

Appendix 1: Shared Care Request letter (Specialist to Primary Care Prescriber)

Dear *[insert Primary Care Prescriber's name]*

Patient name: *[insert patient's name]*
Date of birth: *[insert date of birth]*
NHS Number*: [insert NHS Number]*
Diagnosis: *[insert diagnosis]*

As per the agreed South East London shared care prescribing guideline for *[insert medicine name]* for the treatment of *[insert indication],* this patient is now suitable for prescribing to move to primary care.

The patient fulfils criteria for shared care and I am therefore requesting your agreement to participate in shared care. Where baseline investigations are set out in the shared care protocol, I have carried these out.

I can confirm that the following has happened with regard to this treatment:

	Specialist to complete
The patient has been initiated on this therapy and has been on an optimised dose for the following period of time:	
Baseline investigation and monitoring as set out in the shared care documents have been completed and were satisfactory	*Yes / No*
The condition being treated has a predictable course of progression and the patient can be suitably maintained by primary care	*Yes / No*
The risks and benefits of treatment have been explained to the patient/parent/carer	*Yes / No*
The roles of the specialist/specialist team/ Primary Care Prescriber / Patient/Parent/Carer and pharmacist have been explained and agreed	*Yes / No*
The patient/parent/carer has agreed to this shared care arrangement, understands the need for ongoing monitoring, and has agreed to attend all necessary appointments	*Yes / No*
I have enclosed a copy of the shared care protocol which covers this treatment/the SCP can be found here (insert electronic/ web link)	*Yes / No*
I have included with the letter copies of the information the patient has received	*Yes / No*
I have provided the patient with sufficient medication to last until	*Insert date*
I have arranged a follow up with this patient in the following timeframe e.g. within 3 months / 6 months	*Please specify*

Treatment was started on *[insert date started]* and the current dose is *[insert dose and frequency]*.

If you agree, please undertake monitoring and treatment from *[insert date]* NB: date must be at least 1 month from initiation of treatment.

The next blood monitoring is due on *[insert date]* and should be continued in line with the shared care guideline.

Please could you reply to this request for shared care and initiation of the suggested medication to either accept or decline within 14 days.

Appendix 2: Shared Care Agreement Letter (Primary Care Prescriber to Specialist)

Primary Care Prescriber Response

Dear *[insert Doctor's name]*

Patient *[insert Patient's name]*

NHS Number *[insert NHS Number]*

Identifier *[insert patient's date of birth and/oraddress]*

Thank you for your request for me to accept prescribing responsibility for this patient under a shared care agreement and to provide the following treatment

Medicine	Route	Dose & frequency

I can confirm that I am willing to take on this responsibility from *[insert date]* and will complete the monitoring as set out in the shared care protocol for this medicine/condition.

Primary Care Prescriber signature: _____ Date: _____

Primary Care Prescriber address/practice stamp:

Appendix 3: Shared Care Refusal Letter (Primary Care Prescriber to Specialist)

Re*:*
Patient *[insert Patient's name]*

NHS Number *[insert NHS Number]*

Identifier *[insert patient's date of birth and/oraddress]*

Thank you for your request for me to accept prescribing responsibility for this patient.

In the interest of patient safety, the local NHS in South East London have classified *[insert medicine name]* as a Shared Care medicine, and requires a number of conditions to be met before transfer can be made to primary care.

I regret to inform you that in this instance I am unable to take on responsibility due to the following:

		Tick which apply
1.	**The prescriber does not feel clinically confident in managing this individual patient's condition, and there is a sound clinical basis for refusing to accept shared care** As the patient's primary care prescriber I do not feel clinically confident to manage this patient's condition because *[insert reason]*. I have consulted with other primary care prescribers in my practice who support my decision. This is not an issue which would be resolved through adequate and appropriate training of prescribers within my practice. **I have discussed my decision with the patient and request that prescribing for this individual remain with you as the specialist, due to the sound clinical basis given above.**	
2.	**The medicine or condition does not fall within the criteria defining suitability for inclusion in a shared care arrangement** As the medicine requested to be prescribed is not included on the national list of shared care drugs as identified by RMOC (Regional Medicines Optimisation Committees) or is not a locally agreed shared care medicine I am unable to accept clinical responsibility for prescribing this medication at this time. **Until this medicine is identified either nationally or locally as requiring shared care the responsibility for providing this patient with their medication remains with you**	
3.	**A minimum duration of supply by the initiating clinician** As the patient has not had the minimum supply of medication to be provided by the initiating specialist I am unable to take clinical responsibility for prescribing this medication at this time. Therefore, can you please contact the patient as soon as possible in order to provide them with the medication that you have recommended. ***Until the patient has had the appropriate length of supply the responsibility for providing the patient with their medication remains with you.***	
4.	**Initiation and optimisation by the initiating specialist** As the patient has not been optimised on this medication I am unable to take clinical responsibility for prescribing this medication at this time. Therefore, can you please contact the patient as soon as possible in order to provide them with the medication that you have recommended. ***Until the patient is optimised on this medication the responsibility for providing the patient with their medication remains with you.***	
5.	**Shared Care Protocol not received**	

	As legal responsibility for clinical care lies with the clinician who signs the prescription, I need to ensure that I am in possession of sufficient clinical information for me to be confident to prescribe this treatment for my patient and it is clear where each of our responsibilities lie to ensure the patient is safely managed**.** For this reason, I am unable to take clinical responsibility for prescribing this medication at this time, therefore would you please contact the patient as soon as possible in order to provide them with the medication that you have recommended. ***Until I receive the appropriate SCP, responsibility for providing the patient with their medication remains with you.***	
6.	**Other (Primary Care Prescriber to complete if there are other reasons why shared care cannot be accepted. NB: Capacity issues to be discussed with local primary care Medicines Optimisation Team prior to returning this form)**	

I would be willing to consider prescribing for this patient once the above criteria have been met for this treatment.

NHS England 'Responsibility for prescribing between Primary & Secondary/Tertiary care' guidance (2018) states that "when decisions are made to transfer clinical and prescribing responsibility for a patient between care settings, it is of the utmost importance that the GP feels clinically competent to prescribe the necessary medicines. It is therefore essential that a transfer involving medicines with which GPs would not normally be familiar should not take place without full local agreement, and the dissemination of sufficient, up-to-date information to individual GPs." In this case we would also see the term GP being interchangeable with the term Primary Care Prescriber.

Please do not hesitate to contact me if you wish to discuss any aspect of my letter in more detail and I hope to receive more information regarding this shared care agreement as soon as possible

Yours sincerely

Primary Care Prescriber signature: _____ Date: _____

Primary Care Prescriber address/practice stamp:

Appendix 4: Drug Prescribing and Monitoring Information

Azathioprine

Route, Dose, Duration	Monitoring Undertaken by Specialist before requesting shared care	Ongoing monitoring to be undertaken by GP	Stopping Criteria		Monitoring following dose increase	Follow Up
Enteral (administration via the oral or enteral tube route): Initially 0.5mg/kg - 2mg/kg daily increasing to a maximum of 3mg/kg daily. **Recommended formulations** 25mg and 50mg Tablet 50mg/5mL oral suspension – unlicensed special **refer to the SEL paediatric formulary for further detail** **Administration details** Doses should be rounded to the most appropriate tablet strength. Tablets should not be crushed due to the cytotoxic and immunosuppressive nature of the drug The oral suspension should be reserved for those children unable to swallow a whole tablet, or on a dose not equivalent to a tablet strength.	**Baseline** FBC, electrolytes, creatinine, LFT, ESR, CRP, TPMT assay, HIV, VZV, Measles and Hepatitis B & C status. Inform GP if patient is heterozygous for TPMT. If heterozygous, start on low dose and titrate slowly. **Ongoing** FBC, electrolytes, creatinine, LFT, ESR, CRP count at 1- 2 weeks, interval to be determined by the specialist team and dependent on factors such as dose titration, and control of underlying disease. Interval increased to monthly for up to 6 months. If stable increase interval to 2-3 monthly. In patients with an adverse TPMT profile, monitoring should continue at monthly intervals.	FBC, electrolytes, creatinine, LFT, ESR, CRP every 2-3 months once stable, unless in patients with an adverse TPMT profile, in whom monitoring should continue at monthly intervals. Ask patient/parent/carer about any rashes, oral ulceration, bruising or bleeding at each patient review. Monitor for signs and symptoms of infection	Failure to respond to treatment or adverse effects necessitating withdrawal. **Withhold and discuss with specialist consultant/team if any of the following occur:**		FBC, electrolytes, creatinine, LFT, ESR, CRP, 1-2 weeks after dose change then monthly for 3 months. If maintenance dose is achieved and stable for 3 months consider reducing monitoring to 2-3 monthly.	**Specialist:** Subject to individual patient response: 3 - 6 monthly if well controlled and disease activity stable. Ask patient/parent/carer about any new symptoms including rashes, oral ulceration, bruising or bleeding at each clinic appointment. Communicate to the GP after each clinic attendance indicating current dose, most recent blood tests and frequency of visits. Ensure the patient has access to their blood results and update their medicines monitoring book or the form of communication provided to the patient e.g. online access to patient records Advise GP on review, duration and or discontinuation of treatment when necessary. Inform GP of patients who do not attend clinic appointments **GP** Blood tests as outlined. **Please ensure the patient has access to their blood results and update their relevant form of communication**. Patients should be seen earlier if there is disease flare or adverse effects (including infection) experienced between appointments. If any concerns about adherence, lack of appropriate blood tests results o attendance to review appointments contact the consultant/specialist team
			Neutrophils < 1.50 x 10^9/L	Withhold until discussed with specialist consultant/team		
			Lymphocytes < 0.5 x 10^9/L	Withhold until discussed with specialist consultant/team		
			Platelets < 150 x 10^9/L	Withhold until discussed with specialist consultant/team		
			MCV > 105fL	Check folate., TSH, B12. If folate or B12 are low, please start the appropriate supplementation		
			AST,ALT > 120IU/L	Withhold until discussed with specialist consultant/team. Transaminase increase x3 normal is common within 2 days of drug administration and may be attributable to an asymptomatic viral infection. It may also be attributable to underlying condition, namely if being used to treat autoimmune hepatitis. Consider rechecking ALT at trough level (i.e. 0-2 days prior to administration).		
			Abnormal bruising or frequent abnormal mouth ulcers	Check FBC immediately and discuss severe sore throat or discuss with specialist consultant/team		
			Renal Impairment (GFR <20 ml/min) OR urea and creatinine are continually rising	Withhold until discussed with specialist consultant/team		

Azathioprine (cont)

Practical issues including adverse effects, interactions, other relevant advice and information (refer to SPC and/or BNFc for full list) **:**

1. **Abnormal laboratory parameters** - MCV> 105 fL check B12, folate and TSH. If abnormal treat any underlying abnormality. If normal discuss with specialist consultant/team.
2. **TPMT Deficiency** - Thiopurine methyl transferase (TPMT) deficiency (heterozygous state) may be associated with delayed (up to 6 months after starting azathioprine) haematological toxicity including bone marrow toxicity. Azathioprine is generally avoided in patients who are homozygous for TPMT. If considered for treatment they would be monitored closely for neutropenia.
3. **TGNs metabolites** - The accumulation of high levels of thiopurine metabolites is also responsible for some side effects of azathioprine and has been associated with leucopenia. Such patients would be monitored more closely.
4. **Adverse Effects** - Patients should be advised to use a sunscreen with a high protection factor and protective clothing to reduce sunlight exposure.
5. **Pregnancy and Breast Feeding** - Azathioprine can be prescribed to pregnant and breast-feeding patients. Any patient considering becoming pregnant or has discovered they are pregnant should be referred back to their consultant/team immediately and shared care will no longer apply for the duration of the pregnancy and while they continue to breast-feed.
6. **Renal impairment** - is not uncommon in diseases treated with azathioprine, poor renal function can indicate disease worsening and need to increase the dose rather than stop. Specialists may use this information to inform treatment decisions rather than as grounds to stop the drug.

Clinically Significant Drug Interactions refer to SPC and/or BNFc for full list

- **Allopurinol** – enhanced effects and increased toxicity of allopurinol – reduce azathioprine dose to 25% of the original dose. Discuss with Consultant Paediatric Gastroenterologist if allopurinol to be initiated.
- **Co-trimoxazole, trimethoprim, sulfamethoxazole** – avoid, increased risk of haematological toxicity
- **Coumarin anticoagulants** – reduced anticoagulant effect, monitor INR closely and increase maintenance dose if necessary

Hydroxychloroquine

Route, Dose, Duration	Monitoring Undertaken by Specialist before requesting shared care	Ongoing monitoring to be undertaken by GP	Stopping Criteria	Monitoring following dose changes	Follow Up
Enteral (administration via the oral or enteral tube route): Initially 4-6mg/kg in one or two divided doses to a maximum of 400mg daily. If the dose is < 200mg daily. Calculate the total weekly dose and divide over a set number of days to the nearest suitable whole or half tablet. Use ideal body weight to calculate dose. **Recommended formulations** 200mg Tablet **refer to the SEL paediatric formulary for further detail** **Administration details** If the dose is <200mg daily, it is advised to calculate the total weekly dose and divide over a set number of days to the nearest suitable whole or half a tablet. Tablets may be crushed and dispersed in water if necessary	**Baseline** FBC, electrolytes, creatinine, LFT, ESR, CRP. G6PD status should be considered in at risk ethnic groups. There are no reports of hydroxychloroquine induced retinopathy in patients under the age of 18 by The Royal College of Ophthalmologists. There are no reports of, or evidence for screening paediatric patients for drug toxicity. All patients will receive a baseline assessment to establish the health of their eye ideally within the first 6 months and definitely within the first year of starting hydroxychloroquine. **Ongoing** Nil	Specialist's responsibility to refer the patient for annual ophthalmology screening after the patients has been on therapy for 5 years. GP to prompt specialist if they are aware this referral has not been done. N.B. The risk of hydroxychloroquine retinopathy is low in the first five years. Any test results should be brought to the next appointment.	Failure to respond to treatment or adverse effects necessitating withdrawal. **Withhold and discuss with specialist consultant/team if any of the following occur:** Visual disturbances Renal impairment GFR <30mL/min	Nil	**Specialist:** Subject to individual patient response: 3 - 6 monthly if well controlled and disease activity stable. To refer patients for annual ophthalmology screening after 5 years of therapy Ask patient/parent/carer about any new symptoms including rashes, oral ulceration, bruising or bleeding at each clinic appointment. Communicate to the GP after each clinic attendance indicating current dose, most recent blood tests and frequency of visits. Ensure the patient has access to their blood results and update their medicines monitoring book or the form of communication provided to the patient e.g. online access to patient records Advise GP on review, duration and or discontinuation of treatment when necessary. Inform GP of patients who do not attend clinic appointments **GP:** Check patient has been referred for annual screening after five years of therapy and be reviewed annually thereafter whilst on therapy. Contact the specialist if this has not been done. **Please ensure the patient has access to these results**. Request patient seen earlier if disease flare or adverse effects (including infection) experienced between If any concerns about adherence, lack of appropriate blood tests results or attendance to review appointments contact the consultant/specialist team.

Hydroxychloroquine (cont)

Practical issues including adverse effects, interactions, other relevant advice and information (refer to SPC and/or BNFc for full list)**:**

1. **Adverse Effects** - G.I. disturbances, headache, rashes, pruritus, retinal damage.
2. **Psychiatric adverse effects** – Hydroxychloroquine has been previously associated with psychiatric reactions, including reports of depression, anxiety, hallucinations, and psychosis. Patients should be advised to notify a clinician if they become aware of any changes in their mental health. Refer to the SPC and/or MHRA Drug Safety Update for further information.
3. **Eye Checks** - Patients with renal impairment should have eye checks more frequently than once a year. Hydroxychloroquine is contraindicated in patients with pre-existing maculopathy.
4. **Pregnancy and Breast Feeding** - Hydroxychloroquine can be prescribed to pregnant and breast-feeding patients. Any patient considering becoming pregnant or has discovered they are pregnant should be referred back to their consultant/team immediately and shared care will no longer apply for the duration of the pregnancy and while they continue to breast-feed.
5. **If hydroxychloroquine is being used as monotherapy there is no need for a monitoring book**

Clinically Significant Drug Interactions refer to SPC and/or BNFc for full list

- **Macrolide Antibiotics may increase the risk of cardiovascular events –** consider the benefits and risks before prescribing, consult the MHRA Drug Safety Update for further information
- **Antacids** reduce absorption of hydroxychloroquine and should be avoided within 4 hours of dose
- **Amiodarone** avoid due to the increased risk of ventricular arrhythmias
- **Moxifloxacin** avoid due to the increased risk of ventricular arrhythmias)
- **Digoxin** may increase digoxin levels - check for signs of toxicity and monitor levels if appropriate
- **Ciclosporin** may increase ciclosporin levels - monitor levels and check for signs of toxicity)
- **Mefloquine** avoid due to increased risk of convulsions

Leflunomide

Route, Dose, Duration	Monitoring Undertaken by Specialist before requesting shared care	Ongoing monitoring to be undertaken by GP	Stopping Criteria	Monitoring following dose changes	Follow Up
Enteral (administration via the oral or enteral tube route): • <10kg: 5mg/day • 10-40 kg: 10mg/day • >40kg; 20mg/day **Recommended Formulations** 10mg and 20mg Tablet **refer to the SEL paediatric formulary for further detail** **Administration details** Tablets can be crushed and dispersed in water to achieve a dose of 5mg, or in those children who cannot swallow a whole tablet.	**Baseline** FBC, electrolytes, creatinine, LFT, ESR, CRP. Hepatitis B, Hepatitis C and HIV screening as clinically appropriate. Baseline blood pressure – ensure within the normal ranges for paediatric patients, see Appendix 5 Check blood pressure at each face to face visit. Recheck any blood pressures above 90th centile in 1 week. If above 95th centile for 3 consecutive weeks then discuss with specialist team. **Ongoing** FBC, electrolytes, creatinine, LFT, ESR, CRP count at 2 weeks then monthly for up to 6 months. If stable increase interval to 2-3 monthly.	FBC, electrolytes, creatinine, LFT, ESR, CRP every 2-3 months. Ask patient/parent/carer about any rashes, oral ulceration, bruising or bleeding at each patient review.	Failure to respond to treatment or adverse effects necessitating withdrawal. **Withhold and discuss with specialist consultant/team if any of the following occur** Neutrophils < 1.50 x 10^9/L — Withhold until discussed with specialist consultant/team Platelets < 150 x 10^9/L — Withhold until discussed with specialist consultant/team MCV > 105fL — Check folate. GGT, TSH, B12. If folate or B12 are low, please start the appropriate supplementation AST,ALT > 120 IU/L — Withhold until discussed with specialist consultant/team. Transaminase increase x3 normal is common within 2 days of drug administration and may be attributable to an asymptomatic viral infection. Consider rechecking ALT at trough level (i.e. 0-2 days prior to administration). Abnormal bruising or severe sore throat or frequent abnormal mouth ulcers — Check FBC immediately and discuss with specialist consultant/team Renal Impairment (GFR < 20 ml/min) — Consider alternative causes. Discuss with specialist consultant/team. as dose reduction may be required. **Washout procedure – The specialist consultant/ team will advise if a washout procedure is required**	FBC, electrolytes, creatinine, LFT, ESR, CRP, 2 weeks after dose change then monthly for 3 months. If maintenance dose is achieved and stable for 3 months consider reducing monitoring to 2-3 monthly.	**Specialist:** Subject to individual patient response: 3 - 6 monthly if well controlled and disease activity stable. Ask patient/parent/carer about any new symptoms including rashes, oral ulceration, bruising or bleeding at each clinic appointment. Communicate to the GP after each clinic attendance indicating current dose, most recent blood tests and frequency of visits. Ensure the patient has access to their blood results and update their medicines monitoring book or the form of communication provided to the patient e.g. online access to patient records Advise GP on review, duration and or discontinuation of treatment when necessary. Inform GP of patients who do not attend clinic appointments. **GP** Blood tests as outlined. **Please ensure the patient has access to their blood results and update their relevant form of communication**. Patient should be seen earlier if there is disease flare up or adverse effects (including infection) experienced between appointments. If any concerns about adherence, lack of appropriate blood tests results or attendance to review appointments contact the consultant/specialist team

Leflunomide (cont)

Practical issues including adverse effects, interactions, other relevant advice and information (refer to SPC and/or BNFc for full list)**:**

1. **Abnormal laboratory parameters** - MCV > 105 fl - if B12, folate and TSH abnormal treat any underlying abnormality. If B12, folate and TSH normal discuss with specialist consultant/team.
2. **Adverse effects** - G.I. disturbances, reversible alopecia, mild weight loss.
   Hepatotoxicity: Leflunomide can cause hepatotoxicity and caution is advised when patients are prescribed other hepatotoxic drugs or if there is evidence of current or recent hepatitis B or C infection. Most cases of hepatotoxicity have occurred in the first 6 months of treatment and in the presence of multiple risk factors. Contact the specialist consultant/team if there are any concerns over hepatotoxicity or co-prescribing with other drugs (see monitoring requirements above).
3. **Pregnancy, breastfeeding and contraception** - Leflunomide is contraindicated in pregnancy and breast feeding. Any patient considering family planning should be discussed with the specialist consultant/team. Pregnancy should be excluded prior to treatment and a serum or urine pregnancy test should be conducted in patients who are of child bearing age. Two forms of effective contraception should be used before commencing and whilst on mycophenolate and for 3 months after discontinuation of treatment. Women must wait 2 years between stopping the drug and becoming pregnant. This can be reduced to 3 months if patients are treated with a rapid washout under the supervision of a specialist consultant/team. Men should continue to use effective contraception for 3 months after stopping treatment. Breast feeding must be avoided.

Clinically Significant Drug Interactions refer to SPC and/or BNFc for full list

- **Coumarins** - Potential increase in INR, monitor INR closely and reduce maintenance dose if necessary
- **Methotrexate** – increased risk of hepatotoxicity. However, both drugs are used concomitantly in some circumstances. Closer monitoring may be required particularly around the neutrophil count and ALT.
- Note: Leflunomide has a very long half-life (2 weeks) therefore the interactions can be potentially serious and a drug wash out procedure may be required. Discuss with Consultant Paediatric Rheumatologist if necessary.

Methotrexate

Route, Dose, Duration	Monitoring Undertaken by Specialist before requesting shared care	Ongoing monitoring to be undertaken by GP	Stopping Criteria	Monitoring following dose changes	Follow Up
Enteral (administration via the oral or enteral tube route) **or subcutaneous injection** 10-20mg/m^2 to a maximum of 25mg per dose once a week. For body surface area dosing chart see Appendix 5. **Recommended formulations** • 2.5mg Tablet • 10mg in 5mL Oral solution • 7.5mg, 10mg, 12.5mg, 15mg, 17.5mg, 20mg, 22.5mg, 25mg, 27.5mg and 30mg Solution for injection in pre-filled syringe **refer to the SEL paediatric formulary for further detail** **Only prescribe** • 2.5mg tablets • the appropriate strength of pre-filled pen/syringe • the licensed sugar free oral solution 10mg/5mL **Administration details** Methotrexate is cytotoxic. Tablets can be dispersed in water but they CANNOT be crushed. Please ensure protective clothing is worn when handling this medication. For patients < 8 years of age the use of subcutaneous preparation reduces chances of dose duplication, e.g. if the patient spits out the tablet.	**Baseline** FBC, electrolytes, creatinine, LFT, ESR, CRP. Hepatitis B, Hepatitis C, HIV or VZV screening as considered clinically appropriate. T-Spot for diagnosis of tuberculosis. **Ongoing** FBC, electrolytes, creatinine, LFT, ESR, CRP count at 2 weeks then monthly for up to 6 months. If stable increase interval to 2-3 monthly.	FBC, electrolytes, creatinine, LFT, ESR, CRP every 2-3 months. Ask patient/parent/carer about any rashes, oral ulceration, bruising or bleeding at each patient review	Failure to respond to treatment or adverse effects necessitating withdrawal. **Withhold and discuss with specialist consultant/team if any of the following occur:** Neutrophils < 1.50 x 10^9/L — Withhold until discussed with specialist consultant/team Platelets < 150 x 10^9/L — Withhold until discussed with specialist consultant/team MCV > 105fL — Check folate. GGT, TSH, B12. If folate or B12 are low, please start the appropriate supplementation AST,ALT > 120 IU/L — Withhold until discussed with specialist consultant/team. Transaminase increase x3 normal is common within 2 days of drug administration and may be attributable to an asymptomatic viral infection. Consider rechecking ALT at trough level (i.e. 0-2 days prior to administration). Nausea & vomiting — Consider starting folic acid. Usual dosing 5mg once weekly (except on the day methotrexate is taken). Ondansetron may also be considered if nausea and vomiting is persistent. Usual dosing: <10kg 2mg 10-40kg 4mg >40kg 4-8mg 30 minutes before injection and up to 2 hrs post injection. Max dose 8mg in patients > 12 years of age Abnormal bruising or severe sore throat or frequent abnormal mouth ulcers — Check FBC immediately and discuss with specialist consultant/team. For persistent mouth ulcers folic acid may be helpful Unexplained acute widespread vasculitic rash — Look for alternative causes. Withhold until discussed with specialist consultant/team	FBC, electrolytes, creatinine, LFT, ESR, CRP, 2 weeks after dose change then monthly for 3 months. If maintenance dose is achieved and stable for 3 months consider reducing monitoring to 2-3 monthly.	**Specialist:** Subject to individual patient response: 3 - 6 monthly if well controlled and disease activity stable. Ask patient/parent/carer about any new symptoms including rashes, oral ulceration, bruising or bleeding at each clinic appointment. Communicate to the GP after each clinic attendance indicating current dose, most recent blood tests and frequency of visits. Ensure the patient has access to their blood results and update their medicines monitoring book or the form of communication provided to the patient e.g. online access to patient records Advise GP on review, duration and or discontinuation of treatment when necessary. Inform GP of patients who do not attend clinic appointments. **GP** Blood tests as outlined. **Please ensure the patient has access to their blood results and update their relevant form of communication.** Patient should

Concomitant folic acid 5mg once a week is not an absolute requirement however may be initiated if the patient is experiencing side effects. Folic acid is usually taken the day after methotrexate			Renal Impairment (GFR < 50 ml/min)	Consider alternative causes, reduce dose following discussion with Consultant specialist consultant/team		be seen earlier if there is disease flare up or adverse effects (including infection) experienced between appointments. If any concerns about adherence, lack of appropriate blood tests results or attendance to appointments contact the consultant/specialist team.

Methotrexate (cont)

Practical issues including adverse effects, interactions, other relevant advice and information (refer to SPC and/or BNFc for full list):

1. **Abnormal laboratory parameters -** if Hb < 90 g/L, B12, folate and TSH abnormal treat any underlying abnormality. If B12, folate and TSH normal discuss with specialist consultant/team.
2. **Pregnancy, breastfeeding and contraception** - methotrexate is contraindicated in pregnancy. Pregnancy should be excluded prior to treatment and a serum or urine pregnancy test should be conducted in patients who are of child bearing age. Two forms of effective contraception should be used before commencing and whilst on mycophenolate and for 3 months after discontinuation of treatment. Any patients planning pregnancy should be referred back to the specialist consultant/team. Breast feeding must be avoided. ***NOTE: Some manufacturers recommend using reliable contraception for 6 months after cessation of methotrexate therapy. Always consult the Summary of Product Characteristics for the product being prescribed (www.medicines.org.uk)** Methotrexate may be excreted in breast milk so breast feeding must be avoided.
3. ***NOTE: Some manufacturers recommend using reliable contraception for 6 months after cessation of methotrexate therapy. Always consult the Summary of Product Characteristics for the product being prescribed (www.medicines.org.uk)** Methotrexate may be excreted in breast milk so breast feeding must be avoided.
4. **Risk factors for hepatotoxicity** – obesity and diabetes increase the likelihood of methotrexate induced liver damage.
5. **Methotrexate injection** - follow local Trust procedures to ensure patient or carer is appropriately trained and can demonstrate competence on injection technique. Specialist team will initiate treatment and provide a suitable sharps bin. Guy's and St Thomas' protocol available on intranet and copies available from medicines information, via specialist paediatric nurse specialists. Nurses also hold copies of competency assessments (Trust specific). Check sharps bin and collection with local council.

Clinically Significant Drug Interactions refer to SPC and/or BNFc for full list

- **Co-trimoxazole, trimethoprim, sulphonamides** - May increase anti folate effect. Acute courses of treatment may be necessary.
- **NSAIDs** - concomitant use of NSAIDs and methotrexate are routine practice in paediatric rheumatology, unless the patient has pre-existing renal disease. The use of NSAIDs is not recommended in paediatric gastroenterology patients and such cases should be discussed with the specialist consultant/team.
- **Ciprofloxacin** - Although excretion of methotrexate may possibly be reduced, acute courses of treatment may be necessary
- **Doxycycline/tetracycline** - Although there is an increased risk of toxicity, doxycycline/tetracyclines may be used acutely in conjunction with methotrexate.
- **Penicillins** - Although there is an increased risk of toxicity, penicillins may be used acutely in conjunction with methotrexate.
- **Ciclosporin** - Although there is an increased risk of toxicity, ciclosporin may be used in conjunction with methotrexate.
- **Leflunomide** - Although there is an increased risk of toxicity, leflunomide may be used in conjunction with methotrexate.

Mycophenolate Mofetil

Route, Dose, Duration	Monitoring Undertaken by Specialist before requesting shared care	Ongoing monitoring to be undertaken by GP	Stopping Criteria	Monitoring following dose changes	Follow Up
Enteral (administration via the oral or enteral tube route): Maintenance dose: 300-600mg^2 or 15-30mg/kg twice daily to a maximum of 2g daily. The dose is usually titrated gradually to avoid GI side effects e.g. 300mg^2 once daily for one week, then 300mg2 twice daily for one week then 600mg^2 twice daily. In some patients > 50kg a dose of 1.5g twice daily may be required. For body surface area dosing chart see Appendix 5. **Recommended formulations** • 500mg Tablet • 250mg capsule • 1g/5mL oral suspension **refer to the SEL paediatric formulary for further detail** **Administration details** Where possible please round to the nearest solid dosage form. Where this is not possible please provide the oral suspension.	**Baseline** FBC, electrolytes, creatinine, LFT, ESR, CRP. Hepatitis B, Hepatitis C and HIV or VZV screening as considered clinically appropriate. In patients who are of child bearing age a serum or urine pregnancy test is recommended. **Ongoing** FBC, electrolytes, creatinine, LFT, ESR, CRP count at 2 weeks then monthly for up to 6 months. If stable increase interval to 2-3 monthly.	FBC, electrolytes, creatinine, LFT, ESR, CRP every 2-3 months.	Failure to respond to treatment or adverse effects necessitating withdrawal. **Withhold and discuss with specialist consultant/team if any of the following occur:** Neutrophils < 1.50 x 10^9/L — Withhold until discussed with specialist consultant/team Platelets < 150 x 10^9/L — Withhold until discussed with specialist consultant/team MCV > 105fL — Check folate. GGT, TSH, B12. If folate or B12 are low, please start the appropriate supplementation AST,ALT > 120 IU/L — Withhold until discussed with specialist consultant/team. Transaminase increase x3 normal is common within 2 days of drug administration and may be attributable to an asymptomatic viral infection. Consider rechecking ALT at trough level (i.e. 0-2 days prior to administration). Abnormal bruising or severe sore throat or frequent abnormal mouth ulcers — Check FBC immediately and discuss with specialist consultant/team	FBC, electrolytes, creatinine, LFT, ESR, CRP, 2 weeks after dose change then monthly for 3 months. If maintenance dose is achieved and stable for 3 months consider reducing monitoring to 2-3 monthly.	**Specialist:** Subject to individual patient response: 3 - 6 monthly if well controlled and disease activity stable. Ask patient/parent/carer about any new symptoms including rashes, oral ulceration, bruising or bleeding at each clinic appointment. Communicate to the GP after each clinic attendance indicating current dose, most recent blood tests and frequency of visits. Ensure the patient has access to their blood results and update their medicines monitoring book or the form of communication provided to the patient e.g. online access to patient records Advise GP on review, duration and or discontinuation of treatment when necessary. Inform GP of patients who do not attend clinic appointments. **GP** Blood tests as outlined. **Please ensure the patient has access to their blood results and update their relevant form of communication**. Patient should be seen earlier if there is disease flare up or adverse effects (including infection) experienced between appointments. If any concerns about adherence, lack of appropriate blood tests results or attendance to review appointments contact the consultant/specialist team for advice.

Mycophenolate Mofetil (cont)

Practical issues including adverse effects, interactions, other relevant advice and information (refer to SPC and/or BNFc for full list)**:**

1. **Abnormal laboratory parameters -** if Hb < 90 g/L, B12, folate and TSH abnormal treat any underlying abnormality. If B12, folate and TSH normal discuss with Consultant Paediatric Rheumatologist.
2. **Adverse Effects -** Diarrhoea, nausea, vomiting, abdominal cramps and dyspepsia. If intolerable discuss with specialist consultant/team. Patients should avoid exposure to sunlight by wearing protective clothing and a sunscreen with a high protection factor (minimum SPF 50).
3. **Pregnancy, breastfeeding and contraception** - mycophenolate is contraindicated in pregnancy. Pregnancy should be excluded prior to treatment and a serum or urine pregnancy test should be conducted in patients who are of child bearing age. Two forms of effective contraception should be used before commencing and whilst on mycophenolate and for 3 months after discontinuation of treatment. Any patients planning pregnancy should be referred back to the specialist consultant/team. Breast feeding must be avoided.
4. **Fertility** - mycophenolate does not affect long term fertility.

Clinically Significant Drug Interactions refer to SPC and/or BNFc for full list

- **Aciclovir** -Plasma concentration of the inactive metabolite mycophenolate increased although no action is required.
- **Co-amoxiclav** - plasma concentration of mycophenolate possibly reduced
- **Metronidazole** and **norfloxacin** - bioavailability of mycophenolate mofetil possibly reduced
- **Phenytoin** - Reduced absorption of phenytoin
- **Rifampicin** - plasma concentration of active metabolite of mycophenolate mofetil reduced

Sulfasalazine

Route, Dose, Duration	Monitoring Undertaken by Specialist before requesting shared care	Ongoing monitoring to be undertaken by GP	Stopping Criteria	Monitoring following dose changes	Follow Up
Enteral (administration via the oral or enteral tube route): **In patients with IBD** 6 months and above: 5-10mg/kg (maximum dose 1g) 4 times a day to a maximum of 60mg/kg/day **In patients with JIA** 2 years and above: 5mg/kg twice daily increasing to a maximum of 25mg/kg twice daily; maximum dose per day 2g. **Recommended formulations** 500mg Tablet 250mg in 5mL oral suspension **refer to the SEL paediatric formulary for further detail** **Administration details** Where possible please round to the nearest solid dosage form of the standard release tablets. Where this is not possible please provide the oral suspension. Patients with autoimmune rheumatic disease in children, and those treated over a long period with NSAIDs, may have sensitive stomachs and for this reason enteric-coated tablets may be a suitable option.	**Baseline** FBC, electrolytes, creatinine, LFT, ESR, CRP, G6PD deficiency. **Ongoing** FBC, electrolytes, creatinine, LFT, ESR, CRP count at 2 weeks then monthly for up to 6 months. If stable increase interval to 2-3 monthly.	FBC, electrolytes, creatinine, LFT, ESR, CRP every 2-3 months. After discussion with specialist consultant/team, the frequency of monitoring may be reduced after the first year providing the dose and blood results are stable to every 6 months. Ask patient/parent/carer about any rashes, oral ulceration, bruising or bleeding at each patient review	Failure to respond to treatment or adverse effects necessitating withdrawal. **Withhold and discuss with specialist consultant/team if any of the following occur:** Neutrophils < 1.50 x 10^9/L — Withhold until discussed with specialist consultant/team Platelets < 150 x 10^9/ — Withhold until discussed with MCV > 105fL — Check folate. GGT, TSH, B12. If folate or B12 are low, please start the appropriate supplementation. AST,ALT > 120 IU/L — Withhold until discussed with specialist consultant/team. Transaminase increase x3 normal is common within 2 days of drug administration and may be attributable to an asymptomatic viral infection. Consider rechecking ALT at trough level (i.e. 0-2 days prior to administration). Abnormal bruising or severe sore throat or frequent abnormal mouth ulcers — Check FBC immediately and discuss with specialist/clinical team GFR 10-20 ml/min — Use with caution and ensure high fluid intake GFR <10 ml/min — Withhold until discussed with specialist consultant/team	FBC, electrolytes, creatinine, LFT, ESR, CRP, 2 weeks after dose change then monthly for 3 months. If maintenance dose is achieved and stable for 3 months consider reducing monitoring to 2-3 monthly. After discussion with specialist consultant/team the frequency of monitoring may be reduced after the first year providing the dose and blood results are stable to every 6 months	**Specialist:** Subject to individual patient response: 3 - 6 monthly if well controlled and disease activity stable. Ask patient/parent/carer about any new symptoms including rashes, oral ulceration, bruising or bleeding at each clinic appointment. Communicate to the GP after each clinic attendance indicating current dose, most recent blood tests and frequency of visits. Ensure the patient has access to their blood results and update their medicines monitoring book or the form of communication provided to the patient e.g. online access to patient records Advise GP on review, duration and or discontinuation of treatment when necessary. Inform GP of patients who do not attend clinic appointments. **GP** Blood tests as outlined. **Please ensure the patient has access to their blood results and update their relevant form of communication**. Patient should be seen earlier if there is disease flare up or adverse effects (including infection) experienced between appointments. If any concerns about adherence, lack of appropriate blood tests results or attendance to review appointments contact the consultant/specialist team for advice.

Sulfasalazine (cont)

Practical issues including adverse effects, interactions, other relevant advice and information (refer to SPC and/or BNFc for full list)**:**

1. **Abnormal laboratory parameters** – MCV> 105 fl check B12, folate and TSH. If abnormal treat any underlying abnormality. If normal discuss with specialist consultant/team.
2. **Adverse effects** – nausea/dizziness/headache - if possible continue. Severe symptoms may require dose reduction or cessation of treatment. Discuss with specialist consultant/team.
3. **Infertility** – oligospermia and infertility may occur in men. Discontinuation appears to reverse these effects within 2 to 3 months. Discuss with specialist consultant/team.
4. **Pregnancy and breastfeeding** – sulfasalazine can be prescribed to pregnant patients. Any patient considering becoming pregnant or has discovered they are pregnant should be referred back to their consultant/team immediately and shared care will no longer apply for the duration of the pregnancy. . Sulfasalazine can be prescribed to breast-feeding patients however it should be avoided in very preterm jaundiced neonates - discuss with obstetrician and neonatologist.
5. **Prescription selection** – Due to risk of drug selection error ensure prescription reads SulfaSALAZINE NOT SulfaDIAZINE. For more information: https://www.gov.uk/drug-safety-update/recent-drug-name-confusion
6. **Discolouration of bodily fluids** – Reassure patients that yellow/orange discolouration of the skin, urine and body fluids is normal. Staining can occur to soft contact lenses.

Clinically Significant Drug Interactions refer to SPC and/or BNFc for full list
No clinically significant drug interactions

Appendix 5: Blood pressure levels for boys and girls by age and height percentile

Blood Pressure Levels for Boys by Age and Height Percentile

Age (Year)	BP Percentile ↓	Systolic BP (mmHg) ← Percentile of Height →							Diastolic BP (mmHg) ← Percentile of Height →						
		5th	10th	25th	50th	75th	90th	95th	5th	10th	25th	50th	75th	90th	95th
1	50th	80	81	83	85	87	88	89	34	35	36	37	38	39	39
	90th	94	95	97	99	100	102	103	49	50	51	52	53	53	54
	95th	98	99	101	103	104	106	106	54	54	55	56	57	58	58
	99th	105	106	108	110	112	113	114	61	62	63	64	65	66	66
2	50th	84	85	87	88	90	92	92	39	40	41	42	43	44	44
	90th	97	99	100	102	104	105	106	54	55	56	57	58	58	59
	95th	101	102	104	106	108	109	110	59	59	60	61	62	63	63
	99th	109	110	111	113	115	117	117	66	67	68	69	70	71	71
3	50th	86	87	89	91	93	94	95	44	44	45	46	47	48	48
	90th	100	101	103	105	107	108	109	59	59	60	61	62	63	63
	95th	104	105	107	109	110	112	113	63	63	64	65	66	67	67
	99th	111	112	114	116	118	119	120	71	71	72	73	74	75	75
4	50th	88	89	91	93	95	96	97	47	48	49	50	51	51	52
	90th	102	103	105	107	109	110	111	62	63	64	65	66	66	67
	95th	106	107	109	111	112	114	115	66	67	68	69	70	71	71
	99th	113	114	116	118	120	121	122	74	75	76	77	78	78	79
5	50th	90	91	93	95	96	98	98	50	51	52	53	54	55	55
	90th	104	105	106	108	110	111	112	65	66	67	68	69	69	70
	95th	108	109	110	112	114	115	116	69	70	71	72	73	74	74
	99th	115	116	118	120	121	123	123	77	78	79	80	81	81	82
6	50th	91	92	94	96	98	99	100	53	53	54	55	56	57	57
	90th	105	106	108	110	111	113	113	68	68	69	70	71	72	72
	95th	109	110	112	114	115	117	117	72	72	73	74	75	76	76
	99th	116	117	119	121	123	124	125	80	80	81	82	83	84	84
7	50th	92	94	95	97	99	100	101	55	55	56	57	58	59	59
	90th	106	107	109	111	113	114	115	70	70	71	72	73	74	74
	95th	110	111	113	115	117	118	119	74	74	75	76	77	78	78
	99th	117	118	120	122	124	125	126	82	82	83	84	85	86	86
8	50th	94	95	97	99	100	102	102	56	57	58	59	60	60	61
	90th	107	109	110	112	114	115	116	71	72	72	73	74	75	76
	95th	111	112	114	116	118	119	120	75	76	77	78	79	79	80
	99th	119	120	122	123	125	127	127	83	84	85	86	87	87	88
9	50th	95	96	98	100	102	103	104	57	58	59	60	61	61	62
	90th	109	110	112	114	115	117	118	72	73	74	75	76	76	77
	95th	113	114	116	118	119	121	121	76	77	78	79	80	81	81
	99th	120	121	123	125	127	128	129	84	85	86	87	88	88	89
10	50th	97	98	100	102	103	105	106	58	59	60	61	61	62	63
	90th	111	112	114	115	117	119	119	73	73	74	75	76	77	78
	95th	115	116	117	119	121	122	123	77	78	79	80	81	81	82
	99th	122	123	125	127	128	130	130	85	86	86	88	88	89	90

Blood Pressure Levels for Boys by Age and Height Percentile (Continued)

Age (Year)	BP Percentile ↓	Systolic BP (mmHg) ← Percentile of Height →							Diastolic BP (mmHg) ← Percentile of Height →						
		5th	10th	25th	50th	75th	90th	95th	5th	10th	25th	50th	75th	90th	95th
11	50th	99	100	102	104	105	107	107	59	59	60	61	62	63	63
	90th	113	114	115	117	119	120	121	74	74	75	76	77	78	78
	95th	117	118	119	121	123	124	125	78	78	79	80	81	82	82
	99th	124	125	127	129	130	132	132	86	86	87	88	89	90	90
12	50th	101	102	104	106	108	109	110	59	60	61	62	63	63	64
	90th	115	116	118	120	121	123	123	74	75	75	76	77	78	79
	95th	119	120	122	123	125	127	127	78	79	80	81	82	82	83
	99th	126	127	129	131	133	134	135	86	87	88	89	90	90	91
13	50th	104	105	106	108	110	111	112	60	60	61	62	63	64	64
	90th	117	118	120	122	124	125	126	75	75	76	77	78	79	79
	95th	121	122	124	126	128	129	130	79	79	80	81	82	83	83
	99th	128	130	131	133	135	136	137	87	87	88	89	90	91	91
14	50th	106	107	109	111	113	114	115	60	61	62	63	64	65	65
	90th	120	121	123	125	126	128	128	75	76	77	78	79	79	80
	95th	124	125	127	128	130	132	132	80	80	81	82	83	84	84
	99th	131	132	134	136	138	139	140	87	88	89	90	91	92	92
15	50th	109	110	112	113	115	117	117	61	62	63	64	65	66	66
	90th	122	124	125	127	129	130	131	76	77	78	79	80	80	81
	95th	126	127	129	131	133	134	135	81	81	82	83	84	85	85
	99th	134	135	136	138	140	142	142	88	89	90	91	92	93	93
16	50th	111	112	114	116	118	119	120	63	63	64	65	66	67	67
	90th	125	126	128	130	131	133	134	78	78	79	80	81	82	82
	95th	129	130	132	134	135	137	137	82	83	83	84	85	86	87
	99th	136	137	139	141	143	144	145	90	90	91	92	93	94	94
17	50th	114	115	116	118	120	121	122	65	66	66	67	68	69	70
	90th	127	128	130	132	134	135	136	80	80	81	82	83	84	84
	95th	131	132	134	136	138	139	140	84	85	86	87	87	88	89
	99th	139	140	141	143	145	146	147	92	93	93	94	95	96	97

BP, blood pressure

* The 90th percentile is 1.28 SD, 95th percentile is 1.645 SD, and the 99th percentile is 2.326 SD over the mean.

For research purposes, the standard deviations in Appendix Table B–1 allow one to compute BP Z-scores and percentiles for boys with height percentiles given in Table 3 (i.e., the 5th,10th, 25th, 50th, 75th, 90th, and 95th percentiles). These height percentiles must be converted to height Z-scores given by (5% = -1.645; 10% = -1.28; 25% = -0.68; 50% = 0; 75% = 0.68; 90% = 1.28%; 95% = 1.645) and then computed according to the methodology in steps 2–4 described in Appendix B. For children with height percentiles other than these, follow steps 1–4 as described in Appendix B.

Blood Pressure Levels for Girls by Age and Height Percentile

Age (Year)	BP Percentile ↓	Systolic BP (mmHg) ← Percentile of Height →							Diastolic BP (mmHg) ← Percentile of Height →						
		5th	10th	25th	50th	75th	90th	95th	5th	10th	25th	50th	75th	90th	95th
1	50th	83	84	85	86	88	89	90	38	39	39	40	41	41	42
	90th	97	97	98	100	101	102	103	52	53	53	54	55	55	56
	95th	100	101	102	104	105	106	107	56	57	57	58	59	59	60
	99th	108	108	109	111	112	113	114	64	64	65	65	66	67	67
2	50th	85	85	87	88	89	91	91	43	44	44	45	46	46	47
	90th	98	99	100	101	103	104	105	57	58	58	59	60	61	61
	95th	102	103	104	105	107	108	109	61	62	62	63	64	65	65
	99th	109	110	111	112	114	115	116	69	69	70	70	71	72	72
3	50th	86	87	88	89	91	92	93	47	48	48	49	50	50	51
	90th	100	100	102	103	104	106	106	61	62	62	63	64	64	65
	95th	104	104	105	107	108	109	110	65	66	66	67	68	68	69
	99th	111	111	113	114	115	116	117	73	73	74	74	75	76	76
4	50th	88	88	90	91	92	94	94	50	50	51	52	52	53	54
	90th	101	102	103	104	106	107	108	64	64	65	66	67	67	68
	95th	105	106	107	108	110	111	112	68	68	69	70	71	71	72
	99th	112	113	114	115	117	118	119	76	76	76	77	78	79	79
5	50th	89	90	91	93	94	95	96	52	53	53	54	55	55	56
	90th	103	103	105	106	107	109	109	66	67	67	68	69	69	70
	95th	107	107	108	110	111	112	113	70	71	71	72	73	73	74
	99th	114	114	116	117	118	120	120	78	78	79	79	80	81	81
6	50th	91	92	93	94	96	97	98	54	54	55	56	56	57	58
	90th	104	105	106	108	109	110	111	68	68	69	70	70	71	72
	95th	108	109	110	111	113	114	115	72	72	73	74	74	75	76
	99th	115	116	117	119	120	121	122	80	80	80	81	82	83	83
7	50th	93	93	95	96	97	99	99	55	56	56	57	58	58	59
	90th	106	107	108	109	111	112	113	69	70	70	71	72	72	73
	95th	110	111	112	113	115	116	116	73	74	74	75	76	76	77
	99th	117	118	119	120	122	123	124	81	81	82	82	83	84	84
8	50th	95	95	96	98	99	100	101	57	57	57	58	59	60	60
	90th	108	109	110	111	113	114	114	71	71	71	72	73	74	74
	95th	112	112	114	115	116	118	118	75	75	75	76	77	78	78
	99th	119	120	121	122	123	125	125	82	82	83	83	84	85	86
9	50th	96	97	98	100	101	102	103	58	58	58	59	60	61	61
	90th	110	110	112	113	114	116	116	72	72	72	73	74	75	75
	95th	114	114	115	117	118	119	120	76	76	76	77	78	79	79
	99th	121	121	123	124	125	127	127	83	83	84	84	85	86	87
10	50th	98	99	100	102	103	104	105	59	59	59	60	61	62	62
	90th	112	112	114	115	116	118	118	73	73	73	74	75	76	76
	95th	116	116	117	119	120	121	122	77	77	77	78	79	80	80
	99th	123	123	125	126	127	129	129	84	84	85	86	86	87	88

Blood Pressure Levels for Girls by Age and Height Percentile (Continued)

Age (Year)	BP Percentile ↓	Systolic BP (mmHg) ← Percentile of Height →							Diastolic BP (mmHg) ← Percentile of Height →						
		5th	10th	25th	50th	75th	90th	95th	5th	10th	25th	50th	75th	90th	95th
11	50th	100	101	102	103	105	106	107	60	60	60	61	62	63	63
	90th	114	114	116	117	118	119	120	74	74	74	75	76	77	77
	95th	118	118	119	121	122	123	124	78	78	78	79	80	81	81
	99th	125	125	126	128	129	130	131	85	85	86	87	87	88	89
12	50th	102	103	104	105	107	108	109	61	61	61	62	63	64	64
	90th	116	116	117	119	120	121	122	75	75	75	76	77	78	78
	95th	119	120	121	123	124	125	126	79	79	79	80	81	82	82
	99th	127	127	128	130	131	132	133	86	86	87	88	88	89	90
13	50th	104	105	106	107	109	110	110	62	62	62	63	64	65	65
	90th	117	118	119	121	122	123	124	76	76	76	77	78	79	79
	95th	121	122	123	124	126	127	128	80	80	80	81	82	83	83
	99th	128	129	130	132	133	134	135	87	87	88	89	89	90	91
14	50th	106	106	107	109	110	111	112	63	63	63	64	65	66	66
	90th	119	120	121	122	124	125	125	77	77	77	78	79	80	80
	95th	123	123	125	126	127	129	129	81	81	81	82	83	84	84
	99th	130	131	132	133	135	136	136	88	88	89	90	90	91	92
15	50th	107	108	109	110	111	113	113	64	64	64	65	66	67	67
	90th	120	121	122	123	125	126	127	78	78	78	79	80	81	81
	95th	124	125	126	127	129	130	131	82	82	82	83	84	85	85
	99th	131	132	133	134	136	137	138	89	89	90	91	91	92	93
16	50th	108	108	110	111	112	114	114	64	64	65	66	66	67	68
	90th	121	122	123	124	126	127	128	78	78	79	80	81	81	82
	95th	125	126	127	128	130	131	132	82	82	83	84	85	85	86
	99th	132	133	134	135	137	138	139	90	90	90	91	92	93	93
17	50th	108	109	110	111	113	114	115	64	65	65	66	67	67	68
	90th	122	122	123	125	126	127	128	78	79	79	80	81	81	82
	95th	125	126	127	129	130	131	132	82	83	83	84	85	85	86
	99th	133	133	134	136	137	138	139	90	90	91	91	92	93	93

BP, blood pressure

* The 90th percentile is 1.28 SD, 95th percentile is 1.645 SD, and the 99th percentile is 2.326 SD over the mean.

For research purposes, the standard deviations in Appendix Table B–1 allow one to compute BP Z-scores and percentiles for girls with height percentiles given in Table 4 (i.e., the 5th,10th, 25th, 50th, 75th, 90th, and 95th percentiles). These height percentiles must be converted to height Z-scores given by (5% = -1.645; 10% = -1.28; 25% = -0.68; 50% = 0; 75% = 0.68; 90% = 1.28%; 95% = 1.645) and then computed according to the methodology in steps 2–4 described in Appendix B. For children with height percentiles other than these, follow steps 1–4 as described in Appendix B.

(2004)The fourth report on the diagnosis, evaluation, and treatment of high blood pressure in children and adolescents. National High Blood Pressure Education Program Working Group on High Blood Pressure in Children and Adolescents.*Pediatrics*. Aug;114(2 Suppl 4th Report):p 555-76