SHARED CARE PRESCRIBING GUIDELINE

Immunomodulatory Drugs: Azathioprine, Hydroxychloroquine, Leflunomide, Methotrexate, Mycophenolate and Sulfasalazine for the treatment of autoimmune rheumatic diseases in children (≤ 18 years of age)

Immunomodulatory Drugs: Azathioprine, Methotrexate and Sulfasalazine for the treatment of inflammatory bowel disease in children (≤ 18 years of age)

NOTES to the GP

The information in the shared care guideline has been developed in consultation with CCGs in South East London and it has been agreed that it is suitable for shared care.

This document should provide sufficient information to enable you to make an informed decision regarding the clinical and legal responsibility for prescribing immunomodulatory drugs for:

- The treatment of autoimmune rheumatic diseases in children (≤ 18 years of age)
- Inflammatory bowel disease in children (≤ 18 years of age)

The questions below will help you confirm this:

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

If you can answer YES to all these questions (after reading this shared care guideline), then it is appropriate for you to accept prescribing responsibility.

If the answer is NO to any of these questions you should contact the requesting consultant or your local CCG Medicines Management Team. There may be implications for the patient/carer where the invitation to share care is declined. For example, the patient may need to be changed to an alternative treatment regimen or attend hospital more frequently for prescriptions. 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 team, 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.

Once you have read the shared care guideline and considered the information above, please complete the GP decision form on the next page and email (via secure email) back to the requesting clinician if you are in agreement to participate in shared care.

GP DECISION FORM – Immunomodulatory drugs for the treatment of autoimmune rheumatic diseases in children

This shared care agreement outlines suggested ways in which the responsibilities for managing the prescribing of:

- **Immunomodulatory drugs: Azathioprine, Hydroxychloroquine, Leflunomide, Methotrexate, Mycophenolate and Sulfasalazine for the treatment of autoimmune rheumatic diseases in in children (≤ 18 years of age)**
- **Immunomodulatory drugs: Azathioprine, Methotrexate and Sulfasalazine for the treatment of inflammatory bowel disease in children (≤ 18 years of age)**
  These can be shared between the specialist and general practitioner (GP). GPs are invited to participate. 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 within 2 weeks.
- The term patient implies that they are of a suitable age (16 year of age and above) to take full responsibility of their care. Those who are under the age of 16, the term patient implies parents or carers.

Autoimmune Rheumatic Conditions and Immunomodulatory Drugs Licensing

Note some patients may have overlap syndromes with clinical features of multiple diseases

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	Hydroxychloroquine	Leflunomide	Methotrexate	Mycophenolate	Sulfasalazine
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*

DECISION FORM: AGREEMENT TO PARTICIPATE IN SHARED CARE for Immunomodulatory Drugs: [*Azathioprine, Hydroxychloroquine, Leflunomide, Methotrexate, Mycophenolate, Sulfasalazine*] in Autoimmune Rheumatic Diseases in children (≤ 18 years of age)

Consultant/Specialist Name:	**Patient name:**
Consultant/Specialist signature:	**Patient Hospital Number:** **Patient NHS Number:**
Date completed:	**Patient Agreement:**
Hospital requesting shared care:	Patient agrees to shared care ☐ Patient does not agree to shared care ☐
GP Name:	

This is to confirm that I agree/do not {delete as appropriate} to participate in shared care for immunomodulatory drug(s): (tick as appropriate)

Azathioprine ☐ **Hydroxychloroquine** ☐ **Leflunomide** ☐ **Methotrexate** ☐ **Mycophenolate** ☐

Sulfasalazine ☐

☐ **Please note that the patient is on more than one immunomodulatory drug**

for the treatment of autoimmune rheumatic diseases in children (≤ 18 years of age) for this patient as outlined in this shared care document.

If using electronically sent format of shared care agreement please refer to cover letter for consultant and hospital details.

Date GP is expected to take on prescribing _____

GP Signature:

Date signed:

ACTION

1. **HOSPITAL CONSULTANT/TEAM*** **Tick to confirm**

- Explain shared care to patient and obtain agreement Date agreement obtained: _____ ☐
- Indicate requesting hospital ☐
- Complete and sign agreement ☐
- Specialist team will call/write to GP to arrange shared care ☐
- Email full shared care guideline including signed agreement to GP (See section 4 – Communication and support for contact details) ☐
- Place original in patient's notes ☐

2. **GP PRACTICE**

- If **in agreement** to participate in shared care, sign and email (via secure NHS.net) this sheet back **within 2 weeks** of receipt **of request from specialist** (see contact numbers page 22)

Email address (via secure nhs.net): …….. **[TRUST to ADD email address]**

- If **do not agree** to participate in shared care, contact consultant and local Primary Care CCG Medicines Management Team within 2 weeks of receipt to discuss. If after discussion it is agreed not to undertake shared care for this patient, both the consultant and the local Primary Care CCG Medicines Management team should be informed.
- Once decision reached file a copy in the Patient's medical notes.
- *If using electronically sent copy of shared care agreement please refer to cover letter from hospital

GP DECISION FORM – Immunomodulatory drugs for the treatment of Inflammatory bowel disease in children

This shared care agreement outlines suggested ways in which the responsibilities for managing the prescribing of:

- **Immunomodulatory drugs: Azathioprine, Hydroxychloroquine, Leflunomide, Methotrexate, Mycophenolate and Sulfasalazine for the treatment of autoimmune rheumatic diseases in in children (≤ 18 years of age)**
- **Immunomodulatory drugs: Azathioprine, Methotrexate and Sulfasalazine for the treatment of inflammatory bowel disease in children (≤ 18 years of age)**
  These can be shared between the specialist and general practitioner (GP). GPs are invited to participate. 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 within 2 weeks.
- The term patient implies that they are of a suitable age (16 year of age and above) to take full responsibility of their care. Those who are under the age of 16, the term patient implies parents or carers.

Inflammatory Bowel Disease and Immunomodulatory Drugs Licensing

Note some patients may have overlap syndromes with clinical features of multiple diseases

O = 'off-label' but considered routine treatment option
X = unlicensed and not currently considered a routine option

	Azathioprine	Methotrexate	Sulfasalazine
Ulcerative Colitis	***Licensed***	**O**	***Licensed***
Crohn's Disease	***Licensed***	***Licensed***	***Licensed***
Inflammatory Bowel Disease	**O**	**O**	**O**

DECISION FORM: AGREEMENT TO PARTICIPATE IN SHARED CARE

Of Immunomodulatory Drugs:
[*Azathioprine, Methotrexate, Sulfasalazine*]
in Inflammatory Bowel Disease in children (≤ 18 years of age)

Consultant/Specialist Name:	**Patient name:**
Consultant/Specialist signature:	**Patient Hospital Number:** **Patient NHS Number:**
Date completed:	**Patient Agreement:**
Hospital requesting shared care:	Patient agrees to shared care ☐ Patient does not agree to shared care ☐
GP Name:	

This is to confirm that I agree/do not {delete as appropriate} to participate in shared care for immunomodulatory drug(s): (tick as appropriate)

Azathioprine ☐ **Methotrexate** ☐ **Sulfasalazine** ☐

☐ **Please note that the patient is on more than one immunomodulatory drug**

for the treatment of inflammatory bowel disease in children (≤ 18 years of age) for this patient as outlined in this shared care document.

If using electronically sent format of shared care agreement please refer to cover letter for consultant and hospital details.

Date GP is expected to take on prescribing _____

GP Signature:

Date signed:

ACTION

1. **HOSPITAL CONSULTANT/TEAM*** **Tick to confirm**

- Explain shared care to patient and obtain agreement Date agreement obtained: _____ ☐
- Indicate requesting hospital ☐
- Complete and sign agreement ☐
- Specialist team will call/write to GP to arrange shared care ☐
- Email full shared care guideline including signed agreement to GP (See section 4 – Communication and support for contact details) ☐
- Place original in patient's notes ☐

2. **GP PRACTICE**

- If **in agreement** to participate in shared care, sign and email (via secure NHS.net) this sheet back **within 2 weeks** of receipt **of request from specialist** (see contact numbers page 23)

Email address (via secure nhs.net): …….. **[TRUST to ADD email address]**

- If **do not agree** to participate in shared care, contact consultant and local Primary Care CCG Medicines Management Team within 2 weeks of receipt to discuss. If after discussion it is agreed not to undertake shared care for this patient, both the consultant and the local Primary Care CCG Medicines Management team should be informed.
- Once decision reached file a copy in the Patient's medical notes.
- *If using electronically sent copy of shared care agreement please refer to cover letter from hospital

CIRCUMSTANCES WHEN SHARED CARE IS APPROPRIATE

- Prescribing responsibility will only be transferred when the consultant and the GP are in agreement that the patient's condition is stable or predictable.
- The hospital will provide the patient with **a minimum of three** month's supply of therapy.
- **The choice of treatment/place in therapy is tailored to the individual patient circumstances and those patients who are stable from a disease point of view may need more frequent follow-up to facilitate support for the family in dealing with social or educational issues which arise from the disease.**

2. 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.
- 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
- 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 GP Decision Form (page 2 or 4 - depending on speciality)
- Add READ CODE #8BM5 to indicate share care prescribing
- 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
- 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

3. CLINICAL INFORMATION

NOTE: The information in these tables is not exhaustive. Please also consult the current Summary of Product Characteristics (SPC) for the respective immunomodulatory drugs 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). (FBC = full blood count, LFT = liver function tests, ESR = erythrocyte sedimentation rate, CRP = c-reactive protein, TMPT = thiopurine methyl transferase (TPMT) assay, ALT = Alanine aminotransferase, AST = Aspartate transaminase MCV Mean corpuscular volume, GFR = glomerular filtration rate, VZV = Varicella-Zoster vaccine)

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
Oral: Initially 2mg/kg daily increasing to a maximum of 3mg/kg daily. In general, doses should be rounded to the most appropriate tablet strength or if clinically required the suspension can be prescribed. If a liquid preparation is required, please prescribe the most cost-effective unlicensed specials e.g. Azathioprine 50mg/5ml oral suspension to reduce error in prescribing and dispensing **Duration of Treatment** Indefinitely if patient is responding well to treatment and in absence of significant side effects.	**Baseline** FBC, electrolytes, creatinine, LFT, ESR, CRP, TPMT assay, HIV, VZV, and Hepatitis B & C status. Measles 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 2 weeks then 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, monitoring should continue at monthly intervals. Ask patient about any rashes, oral ulceration, bruising or bleeding at each face to face visit.	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 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. 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) OR urea and creatinine are continually rising — 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 response to treatment: 3 monthly to 6 if well controlled and stable. Send a letter/results notification to the GP after each clinic attendance indicating current dose, most recent blood tests and frequency of visits. Update patient held monitoring book with most recent blood results. 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 medicines monitoring book**. Patient should be seen earlier if there is disease flare up or adverse effects (including infection) experienced between appointments.

Azathioprine (cont)

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

1. **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.
2. **TGNs metabolites** - The accumulation of high levels of thiopurine metabolites is also responsible for some side effects of azathipoprine and has been associated with leucopenia. Such patients would be monitored more closely.
3. **Abnormal laboratory parameters** - MCV> 105 fl check B12, folate and TSH. If abnormal treat any underlying abnormality. If normal discuss with specialist consultant/team.
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. **Vaccinations** -
   - All non-live vaccines are safe and recommended to continue on non-biologic immunomodulatory drugs, including the seasonal influenza vaccination (inactivated) and pneumococcal vaccine
   - Where possible vaccines should be administered at times of stable disease.
   - Live-vaccinations may be considered in patients with chronic inflammatory diseases treated with non-biologic immunomodulatory drugs. This is in line with ***The Green Book*: Immunisation against infectious diseases – Chapter 6: Contraindications and special considerations.**
     - *Long term stable low dose corticosteroid therapy, either alone or in combination with low dose **non-biological** oral immune modulating drugs (e.g. methotrexate 25mg per week in adults or up to 15mg/m^2 in children, azathioprine 3.0mg/kg/day or 6-mercaptopurine 1.5mg/kg/day), are **not** considered sufficiently immunosuppressive and these patients **can** receive live vaccines.*
     - *Live vaccinations are **not** recommended in patients who have received in the past 3 months immunosuppressive therapy including: Adults and children on high-dose corticosteroids (>40mg prednisolone per day or 2mg/kg/day in children under 20kg) for more than 1 week or adults and children on lower dose corticosteroids (>20mg prednisolone per day or 1mg/kg/day in children under 20kg) for more than 14 days.*
   - **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.**
7. **Chicken pox -**
   - Specialist centre will undertake serology testing.
   - Patients VZV IgG negative, should be considered to receive the varicella vaccines. Varicella vaccinations will be administered 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.
8. **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 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
Oral: 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 a tablet. Use ideal body weight to calculate maximum dose. **Duration of Treatment** Indefinitely if patient is responding well to treatment and in absence of significant side effects.	**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. https://www.rcophth.ac.uk/wp-content/uploads/2018/03/Hydroxychloroquine-and-Chloroquine-Retinopathy-Screening-Guideline-and-Recommendations.pdf 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	GP to ensure that the patient has been referred by the specialist for annual screening after 5 years on treatment. The risk of hydroxychloroquine retinopathy is low in the first five years. Any test results should be brought to the next appointment. Ask patient about any rashes, oral ulceration, bruising or bleeding at each face to face visit.	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 to 6 monthly if well controlled and disease activity stable. Send a letter/results notification to the GP after each clinic attendance indicating current dose, most recent blood tests and frequency of visits. Update patient held monitoring book with most recent blood results. **(not applicable if patient is on hydroxychloroquine monotherapy).** Advise GP on review, duration and or discontinuation of treatment when necessary. Inform GP of patients who do not attend clinic appointments. Long-term users of hydroxychloroquine under the age of 18 who otherwise satisfy the screening criteria should be referred for screening to the specialist in house ophthalmology team. **GP:** Check patient has been referred for annual screening after five years of therapy and be reviewed annually thereafter whilst on therapy. **Please ensure the patient has access to these results**. Request patient seen earlier if disease flare or adverse effects (including infection) experienced between appointments.

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. **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.
3. **Pregnancy and Breast Feeding** - Hydroxychloroquine can be prescribed to pregnant patients. Any patient considering becoming pregnant or has discovered they are pregnant should be referred back to their specialist consultant/team immediately and shared care will no longer apply for the duration of the pregnancy and while breast feeding.
4. **Vaccinations** -
   - All non-live vaccines are safe and recommended to continue on non-biologic immunomodulatory drugs, including the seasonal influenza vaccination (inactivated) and pneumococcal vaccine
   - Where possible vaccines should be administered at times of stable disease.
   - Live-vaccinations may be considered in patients with chronic inflammatory diseases treated with non-biologic immunomodulatory drugs. This is in line with ***The Green Book*: Immunisation against infectious diseases – Chapter 6: Contraindications and special considerations.**
     - *Long term stable low dose corticosteroid therapy, either alone or in combination with low dose **non-biological** oral immune modulating drugs (e.g. methotrexate 25mg per week in adults or up to 15mg/m^2 in children, azathioprine 3.0mg/kg/day or 6-mercaptopurine 1.5mg/kg/day), are **not** considered sufficiently immunosuppressive and these patients **can** receive live vaccines.*
     - *Live vaccinations are **not** recommended in patients who have received in the past 3 months immunosuppressive therapy including: Adults and children on high-dose corticosteroids (>40mg prednisolone per day or 2mg/kg/day in children under 20kg) for more than 1 week or adults and children on lower dose corticosteroids (>20mg prednisolone per day or 1mg/kg/day in children under 20kg) for more than 14 days.*
   - **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.**
5. **Chicken pox -**
   - Specialist centre will undertake serology testing.
   - Patients VZV IgG negative, should be considered to receive the varicella vaccines. Varicella vaccinations will be administered 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 hydroxychloroquine, treat with aciclovir and inform the medical team.
6. **If hydroxychloroquine is being used as monotherapy there is nil need for a monitoring book**

Clinically Significant Drug Interactions (refer to BNFc for full list)

- **Antacids** (reduce absorption of hydroxychloroquine and should be avoided within 4 hours of dose)
- **Amiodarone** (avoid - increased risk of ventricular arrhythmias)
- **Moxifloxacin** (avoid - increased risk of ventricular arrhythmias)
- **Digoxin** (may increase digoxin levels - check for signs of toxicity and monitor levels if appropriate)
- **Ciclosporin** (increased ciclosporin levels - monitor levels and check for signs of toxicity)
- **Mefloquine** (avoid - 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
Oral*: <10kg 5mg/day 10-40 kg 10mg/day >40kg 20mg **Duration of Treatment** Indefinitely if patient is responding well to treatment and in absence of significant side effects *Off-label for under 18 years of age but considered routine treatment option, dosing information is from Foeldvari & Wierk, 2010; Silverman et al 2005a; Silverman et al, 2005b.	**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 (Appendix A). 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 about any rashes, oral ulceration, bruising or bleeding at each face to face visit.	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 response to treatment: 3 monthly to 6 if well controlled and stable. Send a letter/results notification to the GP after each clinic attendance indicating current dose, most recent blood tests and frequency of visits. Update patient held monitoring book with most recent blood results. 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 medicines monitoring book**. Patient should be seen earlier if there is disease flare up or adverse effects (including infection) experienced between appointments.

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** - Any patient considering family planning should be discussed with the specialist consultant/team. Leflunomide is contraindicated in pregnancy and breast feeding. Men and women taking Leflunomide must use reliable contraceptives. 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.
4. **Vaccinations** -
   - All non-live vaccines are safe and recommended to continue on non-biologic immunomodulatory drugs, including the seasonal influenza vaccination (inactivated) and pneumococcal vaccine
   - Where possible vaccines should be administered at times of stable disease.
   - Live-vaccinations may be considered in patients with chronic inflammatory diseases treated with non-biologic immunomodulatory drugs. This is in line with ***The Green Book*: Immunisation against infectious diseases – Chapter 6: Contraindications and special considerations.**
     - *Long term stable low dose corticosteroid therapy, either alone or in combination with low dose **non-biological** oral immune modulating drugs (e.g. methotrexate 25mg per week in adults or up to 15mg/m^2 in children, azathioprine 3.0mg/kg/day or 6-mercaptopurine 1.5mg/kg/day), are **not** considered sufficiently immunosuppressive and these patients **can** receive live vaccines.*
     - *Live vaccinations are **not** recommended in patients who have received in the past 3 months immunosuppressive therapy including: Adults and children on high-dose corticosteroids (>40mg prednisolone per day or 2mg/kg/day in children under 20kg) for more than 1 week or adults and children on lower dose corticosteroids (>20mg prednisolone per day or 1mg/kg/day in children under 20kg) for more than 14 days.*
   - **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.**
5. **Chicken pox -**
   - Specialist centre will undertake serology testing.
   - Patients VZV IgG negative, should be considered to receive the varicella vaccines. Varicella vaccinations will be administered 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 leflunomide, treat with aciclovir and inform the medical team.

Clinically Significant Drug Interactions (refer to 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
Oral or subcutaneous injection: 10-20mg/m^2 to a maximum of 25mg per dose once a week Only prescribe 2.5mg tablets or the appropriate strength of pre-filled pen/syringe or the licensed sugar free oral solution 2mg/ml For patients < 8 years of age the use of subcutaneous preparation reduces chances of dose duplication, if the patient spits out the tablet. 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 and not on the same day as methotrexate. **Duration of Treatment** Indefinitely if patient is responding well to treatment and in absence of significant side effects.	**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 about any rashes, oral ulceration, bruising or bleeding at each face to face visit.	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 vomitting is persistant. Usual dosing: <10kg 2mg 10-40kg 4mg >40kg 4-8mg 30 minutes before injection and upto 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 Renal Impairment (GFR < 50 ml/min) — Consider alternative causes, reduce dose following discussion with Consultant 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 response to treatment: 3 monthly to 6 if well controlled and stable. Send a letter/results notification to the GP after each clinic attendance indicating current dose, most recent blood tests and frequency of visits. Update patient held monitoring book with most recent blood results. 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 medicines monitoring book**. Patient should be seen earlier if there is disease flare up or adverse effects (including infection) experienced between appointments.

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 and breast feeding. Whilst taking methotrexate and for at least 3* months stopping, both men and women must use reliable contraception. For patients considering family planning, discuss with Consultant Paediatric Rheumatologist. Women must wait at least 3 full menstrual cycles (or 3* months) after stopping methotrexate before conceiving. Men should continue to use contraceptives for 3* months after stopping methotrexate. ***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. **Vaccinations** -
   - All non-live vaccines are safe and recommended to continue on non-biologic immunomodulatory drugs, including the seasonal influenza vaccination (inactivated) and pneumococcal vaccine
   - Where possible vaccines should be administered at times of stable disease.
   - Live-vaccinations may be considered in patients with chronic inflammatory diseases treated with non-biologic immunomodulatory drugs. This is in line with ***The Green Book*: Immunisation against infectious diseases – Chapter 6: Contraindications and special considerations.**
     - *Long term stable low dose corticosteroid therapy, either alone or in combination with low dose **non-biological** oral immune modulating drugs (e.g. methotrexate 25mg per week in adults or up to 15mg/m^2 in children, azathioprine 3.0mg/kg/day or 6-mercaptopurine 1.5mg/kg/day), are **not** considered sufficiently immunosuppressive and these patients **can** receive live vaccines.*
     - *Live vaccinations are **not** recommended in patients who have received in the past 3 months immunosuppressive therapy including: Adults and children on high-dose corticosteroids (>40mg prednisolone per day or 2mg/kg/day in children under 20kg) for more than 1 week or adults and children on lower dose corticosteroids (>20mg prednisolone per day or 1mg/kg/day in children under 20kg) for more than 14 days.*
   - **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.**
4. **Chicken pox -**
   - Specialist centre will undertake serology testing.
   - Patients VZV IgG negative, should be considered to receive the varicella vaccines. Varicella vaccinations will be administered 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 methotrexate, treat with aciclovir and inform the medical team.
5. **Risk factors for hepatotoxicity** – obesity and diabetes increase the likelihood of methotrexate induced liver damage.
6. **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 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 recommend 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

<table>
<tr><th>Route, Dose, Duration</th><th>Monitoring Undertaken by Specialist before requesting shared care</th><th>Ongoing monitoring to be undertaken by GP</th><th>Stopping Criteria</th><th>Monitoring following dose changes</th><th>Follow Up</th></tr>
<tr>
<td>Oral:

300-600mg^2 or 15-30mg/kg twice daily to a maximum of 2g daily
Some circumstances in patients > 50kg a dose of 1.5g twice daily may be required.

Where possible please round to the nearest solid dosage form. Where this is not possible please provide the oral suspension.

Duration of Treatment
Indefinitely if patient is responding well to treatment and in absence of significant side effects</td>
<td>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.</td>
<td>FBC, electrolytes, creatinine, LFT, ESR, CRP every 2-3 months.</td>
<td>Failure to respond to treatment or adverse effects necessitating withdrawal.

Withhold and discuss with specialist consultant/team if any of the following occur:

<table>
<tr><td>Neutrophils < 1.50 x 10^9/L</td><td>Withhold until discussed with specialist consultant/team</td></tr>
<tr><td>Platelets < 150 x 10^9/L</td><td>Withhold until discussed with specialist consultant/team</td></tr>
<tr><td>MCV > 105fL</td><td>Check folate. GGT, TSH, B12. If folate or B12 are low, please start the appropriate supplementation</td></tr>
<tr><td>AST,ALT > 120 IU/L</td><td>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).</td></tr>
<tr><td>Abnormal bruising or severe sore throat or frequent abnormal mouth ulcers</td><td>Check FBC immediately and discuss with specialist consultant/team</td></tr>
</table>
</td>
<td>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.</td>
<td>Specialist:
Subject to response to treatment: 3 monthly to 6 if well controlled and stable.

Send a letter/results notification to the GP after each clinic attendance indicating current dose, most recent blood tests and frequency of visits. Update patient held monitoring book with most recent blood results.

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 medicines monitoring book. Patient should be seen earlier if there is disease flare up or adverse effects (including infection) experienced between appointments..</td>
</tr>
</table>

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.
5. **Vaccinations** -
   - All non-live vaccines are safe and recommended to continue on non-biologic immunomodulatory drugs, including the seasonal influenza vaccination (inactivated) and pneumococcal vaccine
   - Where possible vaccines should be administered at times of stable disease.
   - Live-vaccinations may be considered in patients with chronic inflammatory diseases treated with non-biologic immunomodulatory drugs. This is in line with ***The Green Book*: Immunisation against infectious diseases – Chapter 6: Contraindications and special considerations.**
     - *Long term stable low dose corticosteroid therapy, either alone or in combination with low dose **non-biological** oral immune modulating drugs (e.g. methotrexate 25mg per week in adults or up to 15mg/m^2 in children, azathioprine 3.0mg/kg/day or 6-mercaptopurine 1.5mg/kg/day), are **not** considered sufficiently immunosuppressive and these patients **can** receive live vaccines.*
     - *Live vaccinations are **not** recommended in patients who have received in the past 3 months immunosuppressive therapy including: Adults and children on high-dose corticosteroids (>40mg prednisolone per day or 2mg/kg/day in children under 20kg) for more than 1 week or adults and children on lower dose corticosteroids (>20mg prednisolone per day or 1mg/kg/day in children under 20kg) for more than 14 days.*
   - **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.**
6. **Chicken pox -**
   - Specialist centre will undertake serology testing.
   - Patients VZV IgG negative, should be considered to receive the varicella vaccines. Varicella vaccinations will be administered 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 mycophenolate mofetil, treat with aciclovir and inform the medical team.
7. **Renal impairment** - it is not uncommon in diseases treated with mycophenolate mofetil, 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.
8. **Malignancy** - considered to be an association. Risk especially small particularly with the doses used above. However if the patient experiences significant weight loss then please discuss with specialist consultant/team

Clinically Significant Drug Interactions (refer to 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
Oral: In patients 6 months and above: 10mg/kg in 2-4 divided doses to a maximum of 60mg/kg/day in 2-4 divided doses. 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. **Duration of Treatment** Indefinitely if patient is responding well to treatment and in absence of significant side effects.	**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 about any rashes, oral ulceration, bruising or bleeding at each face to face visit.	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 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 response to treatment: 3 monthly to 6 if well controlled and stable. Send a letter/results notification to the GP after each clinic attendance indicating current dose, most recent blood tests and frequency of visits. Update patient held monitoring book with most recent blood results. 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 medicines monitoring book**. Patient should be seen earlier if there is disease flare up or adverse effects (including infection) experienced between appointments.

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** - patients considering family planning should be referred to their specialist consultant/team. An assessment of risk/benefit should be discussed with the specialist consultant/team. Avoid breastfeeding 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.
7. **Vaccinations** -
   - All non-live vaccines are safe and recommended to continue on non-biologic immunomodulatory drugs, including the seasonal influenza vaccination (inactivated) and pneumococcal vaccine
   - Where possible vaccines should be administered at times of stable disease.
   - Live-vaccinations may be considered in patients with chronic inflammatory diseases treated with non-biologic immunomodulatory drugs. This is in line with ***The Green Book*: Immunisation against infectious diseases – Chapter 6: Contraindications and special considerations.**
     - *Long term stable low dose corticosteroid therapy, either alone or in combination with low dose **non-biological** oral immune modulating drugs (e.g. methotrexate 25mg per week in adults or up to 15mg/m^2 in children, azathioprine 3.0mg/kg/day or 6-mercaptopurine 1.5mg/kg/day), are **not** considered sufficiently immunosuppressive and these patients **can** receive live vaccines.*
     - *Live vaccinations are **not** recommended in patients who have received in the past 3 months immunosuppressive therapy including: Adults and children on high-dose corticosteroids (>40mg prednisolone per day or 2mg/kg/day in children under 20kg) for more than 1 week or adults and children on lower dose corticosteroids (>20mg prednisolone per day or 1mg/kg/day in children under 20kg) for more than 14 days.*
   - **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.**
8. **Chicken pox -**
   - Specialist centre will undertake serology testing.
   - Patients VZV IgG negative, should be considered to receive the varicella vaccines. Varicella vaccinations will be administered 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 sulfasalazine, treat with aciclovir and inform the medical team.

Clinically Significant Drug Interactions (refer to BNFc for full list)

- No clinically significant drug interactions

Evidence base for treatment and key references:

The evidence base for the autoimmune rheumatic diseases covered by this guideline has been reviewed by the South East London Area Prescribing Committee. It is available on request from the medicine management team. Key references are listed below:

- NICE National Clinical Guideline 152: Crohn's Disease Management
- NICE National Clinical Guideline 166: Ulcerative Colitis Management
- BSR/BHPR guideline for the prescription and monitoring of non-biologic disease-modifying anti-rheumatic drugs, Rheumatology 2017
- The European Crohn's and Colitis Organisation (ECCO) Therapeutic Interventions
- Consensus guidelines of ECCO/ESPGHAN on the medical management of pediatric Crohn's disease 2014
- The Royal College of Ophthalmologists Clinical Guidelines: Hydroxychloroquine and Chloroquine Retinopathy: Recommendations on screening, February 2018.
- Summary of product characteristics for individual drugs: www.medicines.org.uk
- British National Formulary for Children – April 2018
- Evelina London Paediatric Formulary
- Previous Shared care guidance DMARDs (individual drugs) Guy's & St Thomas' NHS Foundation Trust and King's College Hospital NHS Foundation Trust, April 2018.

4. 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	Via Medicines Information (Guy's and St Thomas') Tel: 020 7188 8748
Evelina London Children's Hospital - Guy's & St. Thomas' Hospital switchboard: 020 7188 7188	
Consultant/Specialist team Consultant Paediatric Rheumatologists Dr Nadia Rafiq, Dr Vinay Shivamurthy, Dr Nick Wilkinson Paediatric Rheumatology Specialist Registrar Rheumatology Specialist Nurse Helpline Dani Adams, Eunice Godbold 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 Jiten Modha 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 Charlotte Daman-Willems	 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	As above or via Medicines Information (Guy's and St Thomas')

5. 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 Paediatric Gastroenterology Specialist Registrar Paediatric Gastroenterology Specialist Nurses Helpline Tracee Reid Department Email:	 Tel: Secretary: Denmark Hill site 020 3299 8979 (or Consultant Paediatric Gastroenterologist on call via switchboard) Secretary: Orpington 016 8986 5232 or 016 8986 5233 (please contact secretary to speak to Consultant Paediatric Gastroenterologist) Bleep: 473 Tel: 020 3299 1897 Email: tracee.reid@nhs.net
Medication – Prescribing advice, interactions, availability of medicines	As above or via Medicines Information (Guy's and St Thomas') Tel: 020 3299 9000 ext 1897
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 Jiten Modha 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 Paediatric Specialist Pharmacist Aman Siddu	 Tel: Lewisham: 0208 333 3000 ext: 6760 Tel: Lewisham: 0208 333 3000 ext: 8820 Bleep: 7315 Tel: 020 8836 6000 ext: 4930 Bleep: 743
Medication – Prescribing advice, interactions, availability of medicines	As above or via Medicines Information (Guy's and St Thomas') 020 8836 4900

APPENDIX A

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