LEFLUNOMIDE FOR USE IN ADULT & PAEDIATRIC RHEUMATOLOGY
Shared Care Protocol

This protocol provides prescribing and monitoring guidance for leflunomide therapy. It should be read in conjunction with the Summary of Product Characteristics (SPC) available on www.medicines.org.uk/emc and the BNF

Shared Care Protocol – Responsibilities

Shared care assumes communication between the rheumatology specialist, GP and patient. The intention to share care should be explained to the patient and accepted by them. Patients are under regular follow-up and this provides an opportunity to discuss drug therapy.

Rheumatology Specialist Team

At the start of treatment:

- Complete pre-treatment assessments, including baseline tests, in accordance to the specific shared care protocol
- Initiate treatment by prescribing the first 56 days
- Supply the patient with 3 blood cards (for FBC, U&E and LFTs) and inform patients to book and attend blood tests at 2, 4 and 6 weeks after starting treatment
- Ensure that patients understand the nature and complications of drug therapy and their role in reporting adverse effects promptly, as part of obtaining informed agreement to shared care
- Provide a copy of the drug-specific patient information leaflet (or direct patient to Versus Arthritis website https://www.versusarthritis.org/about-arthritis/treatments/drugs/)
- Provide a copy of OUHFT 'Rheumatology Shared Care Monitoring Card' to the patient and/or carer, which includes contact details for the rheumatology advice line
- Send a letter to the GP requesting shared care once dose is stable, confirming the above has been completed. Include any results from pre-treatment assessments if appropriate. Provide details of the dose to be continued. Outline shared care protocol criteria and/or direct them to the relevant document on the Oxfordshire CCG website

After 2-6 weeks of treatment:

- Check blood test results from week 2, week 4 and week 6 (available on EPR for Oxfordshire patients/contact GP practice for blood results if patient's GP practice is not in Oxfordshire)
- Ensure any abnormal results are acted upon promptly

After 4- 6 weeks of treatment:

- Conduct a consultation with the patient and/or to check that the patient is not experiencing any issues or side effects.
- Confirm that the patient is stable (no side effects, tolerating the drug and established on monthly blood tests). Communicate this information in a shared care handover letter to the GP. Shared care can now commence.
- If the patient is not stable requiring change in the treatment regime, the patient will remain under the care of the specialist until they become stable, as above.

Unless any concerns are raised by the GP within 14 days, shared care will be assumed and the patient will collect the next prescription from the GP. [10]

During treatment:

- Liaise with GP regarding changes in disease management, drug dose, missed clinic appointments
- Be available to give advice to GP and patient
- If the dose is increased, patient's bloods will be monitored as above
- If dose is decreased, additional monitoring may not be required at discretion of the rheumatology specialist - this will be clearly communicated in the clinic letter and the existing monitoring schedule should continue

GP

- Ensure that provision has been made for the patient to have blood monitoring as per local arrangements
- Prescribe medication once the dose is stable or shared care is agreed
- Ensure all monitoring is completed in accordance to 'Recommended monitoring schedule for patients taking disease-modifying anti-rheumatic drugs (DMARDs)'
- Check results then advise the specialist of any deteriorations or abnormal results. Results should be recorded on the monitoring card if the GP practice is outside of Oxfordshire.
- Notify the specialist to any changes in patient's condition, any adverse drug reactions or failure to attend tests
- If a patient fails to attend for monitoring:
  - Only issue a 28 day prescription and book them in for the next available appointment for a blood test
  - If they fail to attend a second blood test then contact the specialist team for advice and to discuss suitability for continuing treatment before supplying further prescriptions

Patient and/or carer

- Agree to treatment and monitoring after making an informed decision
- Agree to being under the shared care of the GP and specialist
- Ensure that they are booked in for blood test monitoring as per local arrangements and attend as required
- Attend all hospital and GP appointments as scheduled
- Ensure monitoring card is kept up to date and is brought to all appointments (especially patients whose GPs are out of Oxfordshire)
- Report any side effects to the GP or a member of the specialist team

BACKGROUND FOR USE

Leflunomide is a disease modifying anti-rheumatic drug (DMARD) which should only be initiated by a rheumatologist. It is used for:

- Rheumatoid arthritis either as monotherapy or in combination with another DMARD (licensed)[1]
- Psoriatic arthritis (licensed)[1]
- Juvenile idiopathic arthritis (unlicensed)

In paediatrics, the optimum therapeutic dose of DMARDs should be achieved to minimise disease progression and joint erosions. Leflunomide is typically used to treat patients who are unable to tolerate methotrexate.
It can also be used simultaneously with other medications including methotrexate and sulfasalazine to gain optimum control of disease if monotherapy is ineffective. Studies of children and young people aged 3 to 18 years have shown leflunomide to be a safe and effective alternative to methotrexate, resulting in substantial improvements in joint mobility and function in children with juvenile idiopathic arthritis.[2,3,4]

DOSAGE

Adult Indications:

- Typical dosage is 10 - 20 mg daily[1,5].
- A dose of 10 mg daily is usually recommended if leflunomide is used in combination with another potentially hepatotoxic DMARD, e.g. methotrexate.
- There is no dose adjustment in patients over 65 years of age or those with mild renal insufficiency.
- Time to response is 8 to 12 weeks. Symptoms may further improve after several months.

Paediatric Indications:

- Leflunomide is prescribed according to weight, in patients over 3 years[6]:
  - 10-40kg – 10mg once a day
  - Greater than 40kg – 10-20mg once a day
- Frequency of treatment may need to be escalated over 1-2 weeks to minimise gastrointestinal side effects (e.g. 10mg alternate days up to 10mg daily)
- Benefit is seen after 6 to 8 weeks and improvement may continue over a further 4 to 6 months.

Leflunomide is taken in tablet form and should be ideally swallowed whole; however in young children or patients with swallowing difficulties, tablets can be dispersed in water.[7] Tablets are available as 10mg, 15mg and 20mg strengths.

PRE-TREATMENT ASSESSMENT BY SPECIALIST

- FBC, LFT, U&Es and CRP[8]
- Blood pressure.[8] In adults, if greater than 140/90 on two consecutive readings at least two weeks apart, refer back to GP for treatment of hypertension before commencing leflunomide. In paediatrics, see Appendix for normal blood pressures in children.[9]
- Weight (to allow assessment of weight loss which may be attributable to leflunomide).
- Exclude possibility of pregnancy
- A baseline chest X-Ray is not required unless pre-existing fibrotic or interstitial lung disease.

ONGOING MONITORING

More information available in separate guideline; 'Recommended Monitoring Schedule for patients taking disease-modifying anti-rheumatic drugs (DMARDs)'

Baseline assessments should include height, weight, blood pressure, FBC, U&Es, LFTs and CRP.

Standard Monitoring Schedule as per British Society of Rheumatology Guidelines[8]:

- Following initiation or dose change: Check FBC, U+Es and LFTs **every 2 weeks** until on stable dose for **6 weeks**
- Once on stable dose, check FBC, U+Es and LFTs **monthly** for **3 months**
- Thereafter, check FBC, U+Es and LFTs **every 3 months**.
- More frequent monitoring is appropriate in patients at higher risk of toxicity (extremes of body weight, CKD3 or above, pre-existing liver disease, significant other medical co-morbidity, age over 80 years and previous DMARD toxicity)

British Society of Paediatric & Adolescent Rheumatology monitoring guidelines are currently under review and will be added in when available.

Exceptions and Additions to the Monitoring Schedule:

Drug	Laboratory monitoring	Other monitoring
Leflunomide	Standard monitoring schedule	BP and weight at each monitoring visit
Methotrexate/Leflunomide combined	Extend monthly monitoring longer term (at least 12 months)	BP and weight at each monitoring visit. In women of childbearing age: pregnancy testing should be repeated as clinically required (e.g. after any gap of contraception is reported)

Abnormal Laboratory Results and Action to be Taken:

Please note that in addition to absolute values for haematological indices a rapid fall or consistent downward trend in any value should prompt caution and extra vigilance.
Some patients may have abnormal baseline values; specialist will advise if so. e.g. some patients with cirrhosis will have pre-existing pancytopenia and lupus patients may have leucopenia because of lymphopenia.

Laboratory Result	**Action**
WBC less than 3 x 10^9/l	Withhold and discuss with Rheumatology. Bone marrow suppression can occur abruptly.
Neutrophils less than 1.6 x 10^9/l	Withhold and discuss with Rheumatology. Bone marrow suppression can occur abruptly.
Platelets less than 140 x 10^9/l	Withhold and discuss with Rheumatology. Bone marrow suppression can occur abruptly.
MCV greater than 110 fl	Withhold and discuss with Rheumatology. May be able to continue if chronic increase. Check folate and $B_{12.}$ If level low, start appropriate supplementation.
Creatinine increase greater than 30% over 12 months and/or calculated GFR less than 60ml/min/1.73m^2	Discuss with Rheumatology as dose adjustments or further investigations may be required.
Adult liver function ALT greater than 2.5 x upper limit of normal or over 100U/l	Withhold and discuss with adult rheumatology.
Paediatric liver function ALT or AST greater than 120U/l	Withhold until discussed with paediatric rheumatology. Transaminase increase 3 times the upper limit of 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 dose) If LFT derangement occurs more than once, contact the paediatric rheumatology team before discontinuing.

CONTRAINDICATIONS AND PRECAUTIONS

Contraindications	
Impaired liver function due to any cause	Avoid
Moderate to severe renal impairment	Avoid

Precautions	
Infection	Vigilance required in detection and treatment.
Alcohol	Limit alcohol intake to 4 - 8 units per week.
Pulmonary infiltration /reactions	Acute allergic reactions can occur. Added risk when used in combination with methotrexate. Patients should be made aware of this rare complication.

SIDE EFFECTS AND ACTIONS TO BE TAKEN

Side effects	**Actions**
Hypertension	Adults: If BP greater than 140/90 treat according to NICE guidance. If BP remains uncontrolled, discontinue drug. Discuss with rheumatology team if patient not responding to treatment. Paediatrics: Refer to Appendix. Recheck any blood pressures above 90th centile in 1 week. If above 95th centile for 3 consecutive weeks, discuss with paediatric rheumatology team.
Rash or severe mouth ulcers	Adults: Consider dose reduction with or without antihistamines. If severe stop and consider washout procedure, Paediatrics: Look for alternative causes. Discuss with paediatric rheumatology team regarding discontinuing treatment. Rechallenge with lower doses once symptoms settle.
Severe sore throat, abnormal bruising	Immediate FBC and withhold until result of FBC available
GI upset/nausea, diarrhoea	Not uncommon, usually settles, but if severe may require reduction in dose/discontinuation of the drug with or without washout procedure. Monitor to ensure caused by leflunomide and not gastroenteritis. Discuss with specialist team if continues to be a problem.
Weight loss	If greater than 10% with no identified cause, reduce or discontinue with or without washout. Discuss with the specialist team.
Headache	If severe consider dosage reduction
Alopecia	Most cases are mild/ moderate and resolve during treatment. If severe consider dosage reduction. Usually reversible if attributable to leflunomide.
Tenosynovitis and rarely tendon rupture.	Discuss with specialist team.

- Leflunomide can be withheld for 2-3 weeks without inducing a flare.

WASHOUT PROCEDURE

This is used to aid drug elimination in the event of significant adverse effect, or before starting another DMARD or before conception (for both men and women planning a pregnancy). Stop Leflunomide, then refer back to Rheumatology for washout.

NOTABLE DRUG INTERACTIONS

(Please note that this is not an extensive list. Refer to BNF and SPC for any specific drug interaction queries)

Leflunomide has an extremely long elimination half-life and interactions with some drugs may continue for at least eight weeks after leflunomide has been discontinued.

Drug	Interaction
Warfarin	Plasma levels may be increased by leflunomide. Monitor INR closely.
Phenytoin	Plasma levels may be increased by leflunomide. Monitor phenytoin plasma levels of leflunomide treated patients.
Rifampicin	Increases leflunomide plasma levels, please monitor closely.
Haematotoxic and hepatotoxic drugs, e.g. methotrexate	Reduce monitoring intervals.
NSAIDs	May be used.
Tolbutamide	Hypoglycaemic effects may be increased by leflunomide.

FAMILY PLANNING

Females: Avoid in pregnancy. Avoid in breastfeeding. Seek specialist advice for women planning to conceive or in the case of accidental pregnancy.

Males: For advice on paternal exposure, please discuss with secondary care.

VACCINATIONS

Check Department of Health Green Book guidance and if not covered, discuss with secondary care

BACK-UP INFORMATION AND ADVICE

Contact Details	Oxford University Hospitals NHS Foundation Trust	
Rheumatology	Rheumatology Helpline (Adult and Paediatric) Adult - Option 1 (Monday to Friday 8am - 2pm, answerphone service) Paediatric - Option 2 (Monday to Friday, answerphone service) Closed on weekends and bank holidays Rheumatology Registrar/Consultant on call Registrar on site Monday to Friday 9am-8pm Weekends and bank holidays 9am-5pm	Tel: 01865 737656 Email: Adult - rheumatology.noc@nhs.net Paediatric - cnspaedrheumatology@ouh.nhs.uk OUH switchboard number: 0300 304 7777**,** ask for Rheumatology on call
Medicines Information	Tel: 01865 221505 (Monday to Friday 9am - 5pm) Email: Medicines.information@ouh.nhs.uk	

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APPENDIX

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)							Diastolic BP (mmHg)						
		← Percentile of Height →							← 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