

The Newcastle upon Tyne Hospitals NHS Foundation Trust

Protocol for the initiation of Angiotensin Converting Enzyme Inhibitors (ACEi) in Paediatric Heart Failure

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Ratified By:	Dr Abbas Khushnood - Consultant Paediatric Cardiologist

1 Introduction

Angiotensin Converting Enzyme Inhibitors (ACEi) are used for multiple indications including the management of paediatric heart failure. In addition to effects on blood pressure, patients require renal function and electrolyte monitoring during careful dose titration to monitor for any signs of adverse effects.

2 Scope

This protocol is for use within Paediatric Heart Failure at The Newcastle upon Tyne Hospitals NHS Foundation Trust when recommended by a consultant. It covers the initial dosing, dose titration and monitoring requirements when starting treatment in an inpatient or outpatient setting. This does not apply to neonatal patients and dosing can be discussed with the cardiologist/pharmacist.

3 Aim

The aim of this protocol is to standardise the process of ACEi initiation. This will allow for better planning around elective admissions and increase the safety of dose titration. Clinical audit will be used to determine its effectiveness.

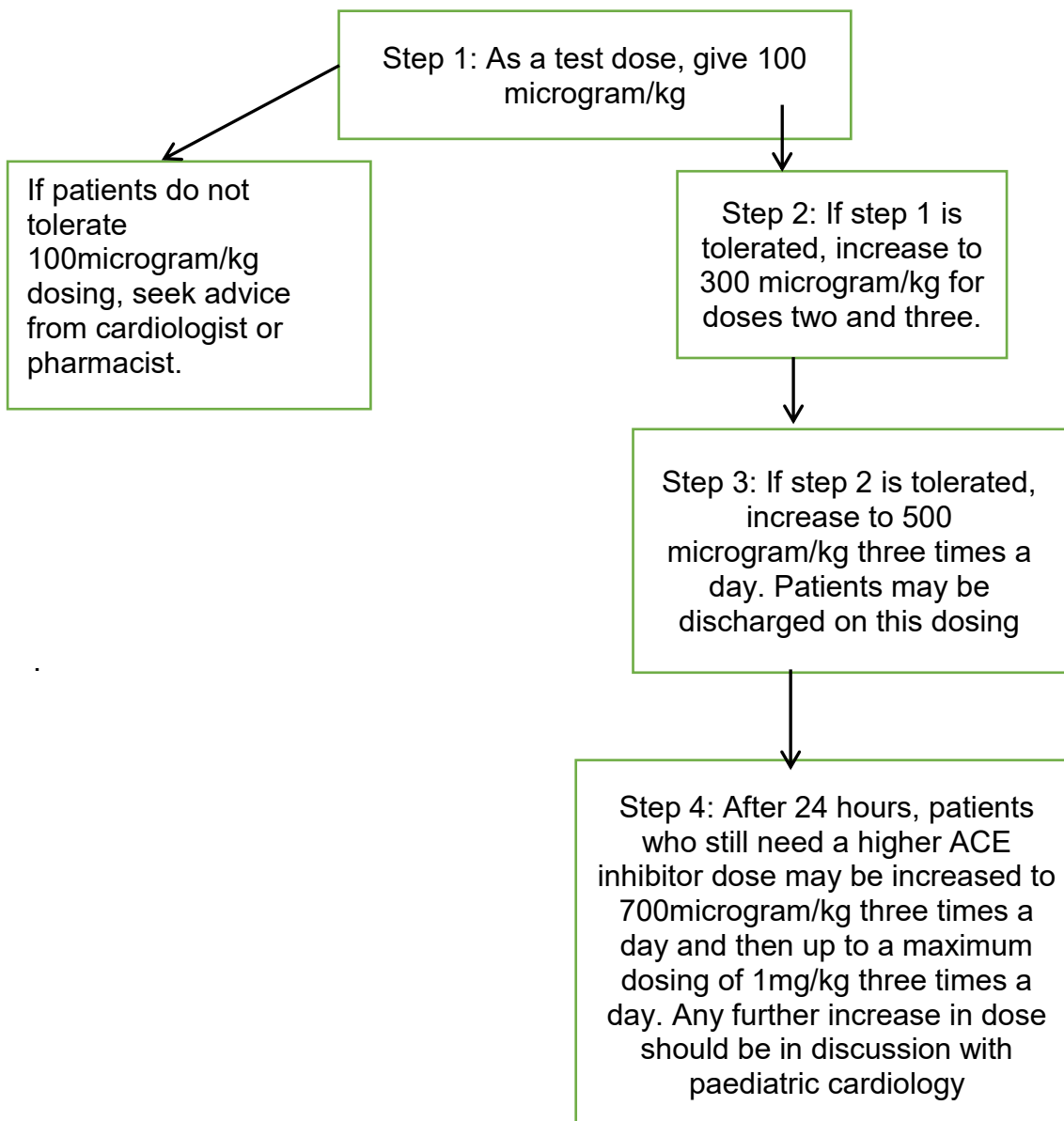
4 Recommendations

4.1 Captopril

- Captopril is available in the trust as 5mg/5ml liquid and also 12.5mg/25mg tablets, which can be crushed and dispersed for larger dosing. This can be given via an enteral tube.
- Captopril is given three times a day, generally on the ward this would be given at 6am, 2pm and 10pm.
Test dose should be given in the supine position for inpatients started on captopril.

4.1.2 Captopril dose initiation and titration:

For children up to 11 years and <20kg

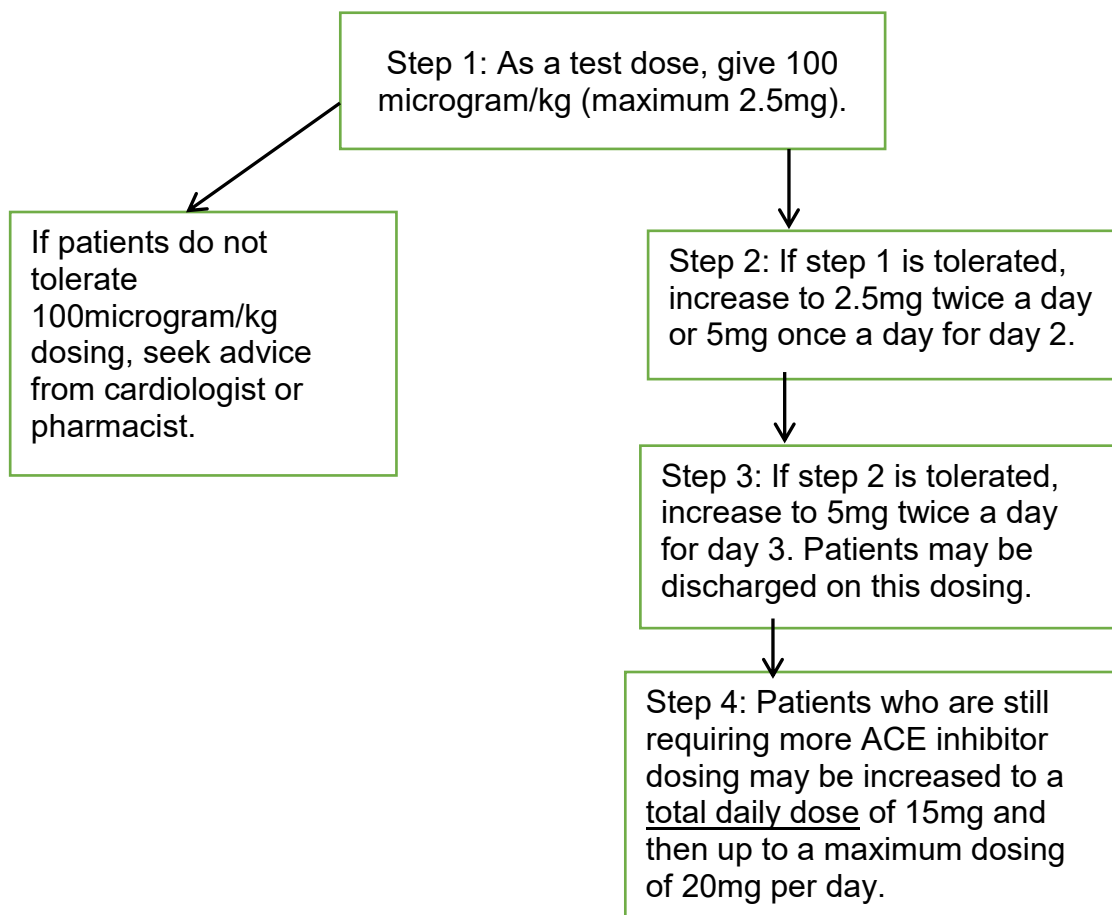


4.2 Enalapril

- Enalapril is available in the trust as 2.5mg, 5mg, 10mg and 20mg tablets and also as a 5mg/5ml liquid.
 - Tablets may be crushed and dispersed in water for administration to children who cannot swallow whole tablets, or those with an enteral tube. N.B. dispersion of tablets may take up to 5 minutes
 - Oro-dispersible tablets (Aqumeldi) are now available and can be used instead of liquid suspension or using tablets that need to be crushed and dispersed in water.
- Enalapril can be given in 1-2 divided doses.
- While SPC states that Enalapril is not recommended in neonates and in paediatric patients with glomerular filtration rate <30 ml/min/1.73 m, there is no data available to support this. Our suggestion is that the primary clinician makes an informed decision (risks vs. benefits) to use the medication in this situation.

4.2.1 Enalapril dose initiation and titration (tablets) :

For children up to 11 years and >20kg



For children <20kg, start with Captopril – can be converted to Enalapril using table below if achieved max. dose @ 1mg/kg/dose

4.2.2 Enalapril (orodispersible tablets – Aqumeldi)

This tablet is available in 0.25mg and 1mg orodispersible tablets.

- Aqumeldi is licenced in children with heart failure and can be used in much smaller doses compared to standard Enalapril preparations. This will allow the use of Enalapril as first line drug instead of Captopril.
- Aqumeldi® may be administered via enteral feeding tubes,
 - Remove the plunger from the syringe you use with the feeding tube and place the required number of orodispersible tablets in the barrel of the syringe.
 - Note: a maximum of four orodispersible tablets can be dispersed in 1 mL at any one time. The following procedure may need to be repeated to achieve recommended dose
 - Replace the plunger and draw up 1 mL of water. Sterile water should be used in children under 6 months of age.
 - Cap the syringe and carefully roll or mix for 3 minutes for the orodispersible tablets to disperse
 - Remove the cap and give the dose via the feeding tube.
 - Flush the feeding tube with at least 3 mL of water after giving the medicine.
 - The solution should be given immediately, do not store.

4.2.2.1 Enalapril orodispersible tablets (Aqumeldi) dose initiation and titration

Under 10kg –

Please follow captopril titration until 1mg/kg/TDS and then can convert to Aqumeldi as per Table. (Appendix 1) If cannot tolerate 1mg/kg TDS of captopril, please seek advice from cardiologist/pharmacist.

To ease administration and allow for dose rounding please see Appendix 2.

Over 10kg – starting dosing

Dose number	10-15kg	16-20kg
1	250 microgram	500 microgram
2	500 microgram	1mg
3	1mg	2mg

Maintenance dose in 1-2 divided doses

4	2mg	4mg
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Can be increased if needed up to 300microgram/kg in 1-2 divided doses, see administration table (appendix 2)

4.3 – Lisinopril

- Lisinopril is available in the trust as 2.5mg, 5mg, 10mg and 20mg tablets and also as a 5mg/5ml liquid.
 - Lisinopril oral solution is absorbed to a lesser extent than lisinopril tablets; absorption of oral solution may produce a different plasma concentration than tablets. Clinical effect should be monitored when switching between dosage forms.
- Lisinopril is generally given once a day;

4.3.1 Lisinopril dose initiation and titration

For children > 12 years (can be done as outpatient)

Heart failure:

Initially 2.5 mg once daily; increased in steps of up to 10 mg at least every 2 weeks; maximum 35 mg per day.

If patients are tolerating large doses of Enalapril, switching to Lisinopril may be appropriate using the table below to allow once a day dosing.

4.4 ACEi conversion

Converting from Captopril to Enalapril tablets– 1mg of Enalapril may be equivalent 7.5mg Captopril (total daily dose)

Converting from Captopril to Lisinopril – 1mg of Lisinopril may be equivalent to 5mg of Captopril (total daily dose).

Converting between Enalapril tablets to Lisinopril – dosing should be converted to total daily Captopril dosing and then converted to Lisinopril.

Drug	Captopril	Enalapril	Lisinopril
Equivalent total daily dosing	30mg	4mg	6mg

Converting from Captopril to Enalapril Aquumeldi – see table (**Appendix 1**)

4.5 Monitoring see Appendix 3

4.5.1 Inpatient – dose to be given as sitting or supine

- Blood pressure to be checked:
 - Before first dose (baseline)
 - At 30, 60 and 120 minutes after first dose
 - At 30, 60 and 120 minutes after each dose increase

Target blood pressures can be found in Appendix 1.

- Bloods to be taken:
 - Within the week before the first dose (baseline)
 - After 48 hours or before discharge

As a minimum this must include U&Es, LFTs and FBC.

4.5.2 Outpatient

- Blood pressure to be checked:
 - In clinic at the time of prescribing (baseline)
 - At GP practice one week after initiation of treatment

Target blood pressures can be found in Appendix 1.

- Bloods to be taken:
 - In clinic at the time of prescribing (baseline)
 - At Next clinic/GP practice one week after initiation of treatment

As a minimum, this must include U&Es, LFTs and FBC.

Repeat bloods annually, specifically if change in dosage.

In the event of hypotension, renal dysfunction or hyperkalaemia, discuss with a cardiologist, renal team or pharmacist for advice before starting or increasing the dose.

4.6 Contraindications

- Bilateral renovascular disease – this remains a relative contra-indication, and should be discussed with the renal and medical teams about the appropriateness of the drug and dosage along with monitoring.
- Severe stenosis in a single kidney
- Hereditary or Idiopathic angioedema
- History of hypersensitivity or angioedema with previous ACEi
- Pregnancy
- Concomitant use with sacubitril/valsartan therapy. ACE inhibitors must not be initiated earlier than 36 hours after the last dose of sacubitril/ valsartan (Entresto)

4.7 Cautions

- Aortic or Mitral Valve Stenosis/Hypertrophic Cardiomyopathy
- Concomitant medications known to increase the risk of hyperkalaemia e.g. co-trimoxazole, potassium sparing diuretics and potassium supplements and nephrotoxic medication e.g. NSAIDs and ciclosporin.
- Co-administration of medications known to cause hypotension
- Afro-Caribbean patients may respond less well to ACEi
- Renal impairment
- Diabetes
- Collagen vascular disease, immunosuppressant therapy or treatment with allopurinol or procainamide (especially if there is pre-existing impaired renal function) due to risk of neutropenia/agranulocytosis
- Concomitant use of ACE inhibitors with racecadotril, mTOR inhibitors (e.g. sirolimus, everolimus, temsirolimus) and vildagliptin may lead to an increased risk for angioedema
- See BNFC for a full list

4.8 Adverse effects

- Hypotension including significant first dose hypertension
- Arrhythmias
- Renal impairment
- Discontinue if marked elevation of hepatic enzymes or jaundice occur due to reports of cholestatic jaundice, hepatitis, fulminant hepatic necrosis and hepatic failure.
- Non-productive, persistent cough – uncommon in children Persistent dry cough, although rare, is sometimes alleviated by reducing dose however it is rapidly reversible upon withdrawal of drug. Another ACEI may be tried.
- Hyperkalaemia
- Neutropenia/agranulocytosis, thrombocytopenia and anaemia, Encourage parents to report any signs of infection
- Insomnia
- Dizziness
- Gastrointestinal disturbance
- Rash - Rashes may occur but usually disappear if dose is reduced. Rash caused by captopril does not necessarily indicate cross-reactivity with other ACE inhibitors.
- Alopecia
- Angioedema (Can be delayed and more common in black patients)
- Pancreatitis
- Hypoglycaemia
- Stroke
- MI/Chest pain/Palpitations

- Dyspnoea.
- See BNFC for a full list

Evidence Review and Evaluation

References

- Captopril 5mg/5ml SPC accessed 25/3/25
<https://www.medicines.org.uk/emc/product/9477/smpc#>
- Enalapril 10mg tablet SPC accessed 26/03/25
<https://www.medicines.org.uk/emc/product/561/smpc>
- BNFC Accessed 25/3/25
- GSTT formulary
- Leeds guideline 'Guideline on the use of ACE inhibitors (angiotensin converting enzyme inhibitors) in children with cardiac failure or hypertension
[Use of ACE inhibitors \(angiotensin converting enzyme inhibitors\) in children with cardiac failure or hypertension](#)
- Leicester Aqumeldi guidance [Starting Aqumeldi© \(Enalapril\) UHL Childrens Hospital Guideline.pdf](#)

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Appendix 1: Conversion of Captopril to Aqumeldi

Weight	Captopril	Aqumeldi
<i>kg</i>	<i>total dose mg/day¹</i>	<i>total dose mg/day²</i>
3	9	0.9
4	12	1.2
5	15	1.5
6	18	1.8
7	21	2.1
8	24	2.4
9	27	2.7
10	30	3
11	33	3.3
12	36	3.6
13	39	3.9
14	42	4.2
15	45	4.5
16	48	4.8
17	51	5.1
18	54	5.4
19	57	5.7
20	60	6
1	1mg/kg/dose 3 times per day	
2	0.3mg/kg total in 1-2 divided doses	

Appendix 2: Administration rounding guide for Aqumeldi under 20kg

Weight banding (kg)	Aqumeldi dose (mg/day)	Number of 1mg tablets/day	Number of 0.25mg tablets/day
3-5	0.9-1.5	1	4
6-8	1.8-2.4	2	8
9-12	2.7-3.6	3	12
13-15	3.9-4.5	4	N/a
16-18	4.8-5.4	5	N/a
19-20	5.7-6	6	N/a

Appendix 3: Blood pressure monitoring values

Age	Systolic Pressure (mmHg)	Diastolic Pressure (mmHg)	Mean Arterial Pressure (mmHg)
Birth (12h, <1000g)	40-60	20-40	25-45
Birth (12h, 3kg)	50-70	30-50	45-55
Neonate (96hr)	60-90	35-55	45-60
Infant (1-12mth)	70-105	40-60	50-65
Toddler (1-2yr)	85-105	40-65	50-65
Preschool (3-5yr)	90-115	45-70	55-70
School age (6-7yr)	95-115	55-75	65-75
Preadolescent (10-12yr)	100-120	60-80	70-80
Adolescent (12-15yr)	110-130	65-85	75-85

Above table reproduced using below references:

1. Dionne, Janis & Abitbol, Carolyn & Flynn, Joseph. (2011). Hypertension in infancy: Diagnosis, management and outcome. *Pediatric nephrology* (Berlin, Germany). 27. 17-32. 10.1007/s00467-010-1755-z.
2. Flynn JT, et al. Clinical Practice Guideline for Screening and Management of High Blood Pressure in Children and Adolescents. *Pediatrics*. 2017;140(3):e20171904
3. Carissa M Baker-Smith, Joseph T Flynn, 2023 European Pediatric Hypertension Guidelines: has anything changed?, *Nephrology Dialysis Transplantation*, Volume 39, Issue 3, March 2024, Pages 382–384, <https://doi.org/10.1093/ndt/gfad207>