LRI Emergency Department and Children's Hospital

Hereditary Angioedema (HAE) UHL Childrens Guideline

Staff relevant to:	Medical & Nursing staff working within UHL Children's Hospital & Children's Emergency Department
Team approval date:	September 2022
Version:	2
Revision due:	September 2025
Written by: Reviewed by:	Dr Arthur Price Dr Arthur Price
Trust Ref:	D7/2019

1. Introduction and Who Guideline applies to

Background

Hereditary angioedema (HAE) is characterized by recurrent episodes of angioedema without urticaria, usually affecting the skin or mucosa of the upper respiratory and gastrointestinal tracts (causing pain and diarrhoea). Laryngeal attacks are rare but a medical emergency and may cause fatal airway obstruction.

A small group of patients (around 50) with known HAE live within the catchment area of our Trust. Most are adults and many now have two pre-filled syringes of Icatibant (a bradykinin B2 receptor antagonist) at home to treat their acute attacks. C1 esterase inhibitor and Icatibant are the only approved on-demand treatments for children with HAE. Icatibant(Firazyr) is approved for symptomatic treatment of acute attacks of HAE in adolescents and children aged 2 years and older, with C1-esterase-inhibitor deficiency.

Some paediatric patients will carry a letter from the Immunology department regarding their treatment however as attacks often do not present until puberty, some patients may present to ED with their first attack. If this is a first presentation, the patient should be referred to immunology on discharge. Secretaries can be contacted on 16702 Mon-Fri 0900-1700 or referrals emailed to PaedsImmunology@uhl-tr.nhs.uk.

2. Guideline Standards and Procedures

Emergency management in the ED

Clinical presentation of HAE shares features with that of anaphylaxis but features usually develop much more slowly. Standard anaphylaxis treatment (i.e. adrenaline, steroids, antihistamines) is thought to be ineffective but should still be tried if the patient is becoming rapidly compromised.

In the rare patients with signs of airway compromise (such as stridor, dyspnoea, hoarseness or reduced SpO2), early fibreoptic airway examination should be considered. Once the decision to intubate has been made, the procedure should be undertaken jointly by an experienced anaesthetist and ENT surgeon. Failed intubation attempts or other instrumentation may worsen airway compromise and staff need to be ready to proceed to a surgical airway ('front of neck access').

Usually, however, emergency treatment with C1 esterase inhibitor is effective.

Six 500unit vials of this medication in the form of Berinert® are stocked in the Adult ER (resuscitation room) medi365 robot, to be used as first line of treatment. If there are supply issues with Berinert® alternatives include Cinryze® and Ruconest® and dosing for them is contained below. Ruconest® is contraindicated in those with a known rabbit allergy. Cinrzye® and and Ruconest® are only licenced for age 2 years and above, however if Berinert® is unavailable they may have to be used off licence in acute situations.

The currently recommended dose of Berinert® is 20units/kg, rounded to the nearest 500 units. Therefore, unless the patient's letter from the UHL immunology department states otherwise, the following doses should be given by IV injection, slowly over several minutes:

Dosing regimen for Berinert®

Weight	Dose
< 38kg	500 units
38kg - 62kg	1000 units
63kg - 87kg	1500 units

> 87kg 2000 units

Dosing regimen for Cinryze®

Age 2-11 years (body weight 10-25kg)	500units for 1 dose, dose may be repeated if necessary, after 60 minutes
Age 2-11 years (body weight 26kg and above)	1000units for 1 dose, dose may be repeated if necessary, after 60 minutes
Child 12-17 years	1000units for 1 dose, dose may be repeated if necessary, after 60 minutes or sooner if experiencing laryngeal attacks or delay in commencement

Ruconest dosing

Body weight up to 84kg	50U/kg
Body weight of 84kg or greater	one IV injection of 4200U (two vials)

No more than two doses should be administered in 24 hours

Volume to infuse (in ml) can be calculated using Body Weight in Kg/3

See UHL adult IV monograph C1 esterase inhibitor (C1-INH; trade name Berinert®, on 'Medusa') for more details on how to give it. Clinical improvement after administration usually occurs within 60min. Similar Monographs for Cinryze® and Rocunest® are also available via Medusa.

NB: As an alternative agent, Icatibant is not stocked in the ED but patients arriving in the ED with their own supply can also be managed with that drug. It is administered by slow subcutaneous injection over several minutes. A second injection can be given after six hours if clinical response to the first dose is inadequate, followed if required by a third after a further six hours. The maximum of three doses within 24 hours should not be exceeded. The dose of Icatibant is recommended to be weight based and this should be clearly directed by the immunologist overseeing the patient's care. No dosage regimen for children aged less than 2 years or weighing less than 12 kg can be recommended, as the safety and efficacy in this paediatric group has not been established.

A small number of patients may not respond fully to icatibant. Therefore if there are significant symptoms despite icatibant, or airway symptoms not rapidly responding to

Icatibant, consideration should be given to administered C1 Inhibitor concentrate dosed as above.

In children and adolescents (aged 2 to 17 years), the recommended dose of Icatibant based on body weight is as below:

Dosage regimen for Icatibant for paediatric patients

Body Weight	Dose (Injection Volume)
12 kg to 25 kg	10 mg (1.0 ml)
26 kg to 40 kg	15 mg (1.5 ml)
41 kg to 50 kg	20 mg (2.0 ml)
51 kg to 65 kg	25 mg (2.5 ml)
>65 kg	30 mg (3.0 ml)

Please note that peripheral and gastrointestinal attacks can be very painful: Give effective analgesia.
Following successful emergency treatment, paediatric patients should be admitted to CSSU for observation and can usually be discharged after 6-12h if no evidence of wheeze, stridor or other signs of airway compromise. Peripheral and abdominal attacks may be able to be discharged sooner. Note peripheral swellings do not have to completely resolve before discharge provided there is evidence of improvement.

3. Education and Training

None required

4. Monitoring Compliance

What will be measured to monitor compliance	How will compliance be monitored	Monitoring Lead	Frequency	Reporting arrangements
Paediatric ED C1 inhibitor use	to be audited through pharmacy records (along with use from adult ED) to ensure given in a timely manner to diagnosed HAE patients	Consultant Immunologist	Every 2 years	Discuss at Immunology MDT

5. Supporting References

1. Longhurst HJ, Tarzi MD, Ashworth F, Bethune C, Cale C, Dempster J, et al. C1 inhibitor deficiency: 2014 United Kingdom consensus document. Clin Exp Immunol [Internet]. 2015 Jun;180(3):475–83. Available from: http://www.ncbi.nlm.nih.gov/pubmed/25605519
2. Marcus Maurer, Markus Magerl, Stephen Betschel, Werner Aberer, Ignacio J Ansotegui et al. World Allergy Organ 2022 Apr 7;15(3):100627. doi: 10.1016/j.waojou.2022.100627. The international WAO/EAACI guideline for the management of hereditary angioedema – 2021 revision and update.

6. Key Words

C1 Esterase Inhibitor, Hereditary angioedema (HAE), Icatibant, Immunology

---

The Trust recognises the diversity of the local community it serves. Our aim therefore is to provide a safe environment free from discrimination and treat all individuals fairly with dignity and appropriately according to their needs.
As part of its development, this policy and its impact on equality have been reviewed and no detriment was identified.

CONTACT AND REVIEW DETAILS			
Guideline Lead (Name and Title) A Price - Consultant			**Executive Lead** Chief Medical Officer
Date	**Issue Number**	**Reviewed By**	**Description Of Changes (If Any)**
Septemeber 2019	**1**	A Price	**New document**
26/03/2020	**1.1**	A Sivadasan	**Ruconest licensed for use in children over 2 years of age**
September 2022	**2**	A Price	**Updated as Icatibant now accessible to paediatric population**