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Medicine Guideline

Icatibant for the treatment of hereditary and non-hereditary forms of angioedema

Areas where Protocol/Guideline applicable	SESLHD Inpatients >16 years
Paediatrics:	Contact Paediatric Immunologist on-call for further advice
Authorised Prescribers:	Immunologists, or Medical Officers under the direct supervision of or in consultation with an Immunologist.
Indication for use	• Hereditary Angioedema (HAE) • Non- hereditary angioedema, including Angiotensin- converting enzyme (ACE) inhibitor induced angioedema or angioedema due to acquired C1-inhibitor deficiency Icatibant is listed on the PBS for hereditary angioedema
Clinical condition	Airway, life or organ-threatening angioedema. This is a clinical diagnosis, and no specific laboratory results or investigations are required. Angioedema can be bradykinin or histamine-mediated. Icatibant is likely to be effective only in the former group of patients, however there are no clinical or laboratory features which can definitely distinguish between the two forms.
Proposed Place in Therapy	Usually the patient will have received intramuscular adrenaline prior to proposed administration of icatibant (i.e. it will be second line therapy). This is not mandatory however, as there may be circumstances in which it is clear that the angioedema is likely to be bradykinin- rather than histamine-mediated (such as ACE-inhibitor induced angioedema). In such cases it may be appropriate to use icatibant first line. As outlined in the ASCIA Management Plan for Hereditary Angioedema, there are specific circumstances where C1- esterase inhibitor (Berinert®) is the preferred option for acute attack management, including:- - When icatibant is contraindicated or not tolerated. - Pregnancy and lactation - When icatibant is not effective in known HAE cases.
Adjunctive Therapy	There are no other medications with proven efficacy in management of non-hereditary angioedema. Histaminergic angioedema may respond to intra-muscular adrenaline, corticosteroids and anti-histamines. Otherwise, care usually consists of appropriate monitoring in a high-

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	acuity environment and airway management involving ENT, anaesthetics and ICU as appropriate.
Contra-indications	Hypersensitivity to the active substance or its excipients
Precautions	Acute ischaemic heart disease, unstable angina or stroke Elderly > 65 years Pregnancy, lactation
Important Drug Interactions[2]	ACE inhibitors (theoretical) Avoiding ARBs would be based on individual assessment
Dosage	**Adults:** **Icatibant 30 mg subcutaneous injection stat** (first dose) *If insufficient relief or recurrence of symptoms after 6 hours:-* Further advise should be sought from an Immunologist and a second and/or third dose of icatibant considered. • icatibant 30mg subcutaneous injection (second dose) *If insufficient relief or recurrence of symptoms after **further** 6 hours:-* • icatibant 30mg subcutaneous injection (third dose) **Maximum dose of icatibant = 90mg in 24 hours.** No dose adjustment is required in patients with renal or hepatic impairment.
Duration of therapy	Usually under 24 hours. Consideration may be given to additional doses in consultant with specialist immunologist in cases of prolonged angioedema (for example, in an intubated patient).
Prescribing Instructions	Icatibant must be prescribed on the eMR or eRIC. In the absence of eMM systems, the appropriate paper medication chart may be used.
Administration	Administer by **slow** subcutaneous injection preferentially into the abdominal area.

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Instructions	
Adverse effects	Injection site reactions: erythema, swelling, warm sensations, itching and/or cutaneous pain
Monitoring requirements	No specific monitoring is required from a safety perspective apart from routine observations and awareness of any injection site reactions. Patients with HAE self-administer icatibant outside the hospital setting and it has a favourable safety profile. Efficacy will be judged by objective assessment of the degree of angioedema. Methods of assessment will vary on the site of angioedema and may involve direct visual assessment or flexible naso-endoscopy. Time to extubation in an intubated patient is also a measure of efficacy.
Management of Complications	Local injection site reactions can be managed symptomatically. Other specific complications are not anticipated but can be managed by cessation of icatibant and discussion with the treating physician.
Basis of Protocol/Guideline:	Data on the efficacy of icatibant for non-hereditary angioedema are mixed, which possibly reflects the inclusion of histaminergic angioedema in trials of bradykinin antagonists. There is RCT level evidence to support its use in ACE-inhibitor angioedema.[1] Case studies support its use in idiopathic non-histaminergic angioedema.[2],[3] In situations of airway or life-threatening angioedema, the costs-benefits analysis is in favour of icatibant given it is a safe medication and can potentially avoid death, intubation and prolonged ICU admission. 1. Bas et al, A Randomised Trial of Icatibant in ACE-Inhibitor Induced Angioedema, N Engl J Med 2015;372:418-425 2. Lleonart et al, Treatment of Idiopathic Nonhistaminergic Angioedema with Icatibant, World Allergy Organ J, 2012 Feb 17;5 S46 3. Stahl et al, Idiopathic Nonhistaminergic Angioedema successfully treated with ecallantide, icatibant and C1 esterase inhibitor replacement, Journal of Allergy and Clinical Immunology in Practice, 2014, 2(6), 818-819 4. Icatibant (Fyzant®) Product Information. Last MIMs revision date 1 March 2025. Accessed via CIAP. 5. ASCIA Management Plan for Hereditary Angioedema. 2022. Hereditary Angioedema - Australasian Society of Clinical Immunology and Allergy (ASCIA)

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GOVERNANCE	
Enactment date *Reviewed* (Version 2) *Reviewed* (Version 3)	August 2025
Expiry date:	31 August 2027
Ratification date by SESLHD DTC	7 August 2025
Chairperson, SESLHD DTC	Dr John Shephard
Version Number	1.0