Clinical Priorities Advisory Group Summary Report

Agenda item	2.1
Date of Meeting	07/05/2025
Title of the Proposition	Icatibant for treatment of moderate to severe acute swellings due to bradykinin-mediated angioedema with normal C1 inhibitor in adults
Unique Reference Number	2315
Programme of Care	Blood and Infection
Clinical Reference Group	Immunology and Allergy
Service/treatment status	delegated

Action requested

Support the adoption of the policy proposition

Recommended its approval as an in year service development.

Summary of the proposition:

This clinical commissioning policy proposition is for the use of icatibant for the treatment of moderate to severe acute swellings due to bradykinin-mediated angioedema with normal C1 inhibitor in adults. Two subgroups of people are included, those with:

- Hereditary angioedema with normal C1 esterase inhibitor (HAE-nC1-INH)
- Idiopathic non-histaminergic angioedema (INHA) with normal C1 inhibitor

The recommendations are outside of the marketing authorisation for icatibant, so use is off-label and Trust policy regarding unlicensed medicines should apply. Icatibant is on the NHS Payment Scheme Annex A, that is, it is a high-cost drug.

The policy proposition covers use in adults, in line with the findings from the evidence review. Icatibant may be used in children aged 2 – 17 years by application of the NHS England's Policy 170001/P Commissioning Medicines for Children in Specialised Services (NHS England » Commissioning medicines for children in specialised services), as icatibant is listed in the British National Formulary for Children (BNFC) with a recommended dosage schedule relative to the age of the child.

Clinical Panel recommendation:

The Clinical Panel recommended that the policy proposition progress as a routine commissioning policy.

Assurances

The committee is asked to receive the following assurance:		
1.	The Deputy Director of Clinical Effectiveness confirms the proposition has completed the appropriate sequence of developmental and governance steps.	
2.	The Deputy Director of Acute Programmes confirms the proposition is supported by the following documentation (please tick the box where applicable)	
	Draft Clinical Commissioning policy proposition	☒
	Evidence Review	☒
	Public Health Evidence Report	☐
	Evidence to Decision Making (EtD) Summary	☒
	Equalities and Heath Inequalities Assessment (EHIA)	☒
	Prior Approval Form	☒
	Engagement Report	☒
	13Q Assessment and Patient & Public Voice Assurance	☒
	Clinical Panel Report	☒
	Policy Working Group membership	☒

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	Other (please state if required)	☐
3.	The Deputy Director of Finance (Specialised Commissioning) confirms that the Impact Assessment has reasonably estimated a) the incremental cost and b) the budget impact of the proposal.	
4.	The Director of Clinical Commissioning (Specialised Commissioning) confirms that the Service and Operational Impact Assessments have been completed.	
5.	The Deputy Director of Quality and Nursing (Specialised Commissioning) confirms that the proposed quality indicators have been adequately defined (where applicable).	

Evidence Review Summary

In the Population what is the clinical effectiveness and safety of the Intervention compared with Comparator?

Clinical effectiveness	
Critical outcomes	
Outcome 1 Total attack/swelling duration **Certainty of evidence:** Very low	This outcome is important to patients as attacks/swellings in this condition are frequent, unpredictable and potentially fatal, and if untreated may last for 3-4 days; therefore, a rapid response to treatment is likely to mitigate the morbidity and mortality associated with this condition. In total, four retrospective cohort studies provided evidence relating to total attack/swelling duration in patients with idiopathic/hereditary angioedema with normal C1 inhibitor. The studies included patients that met the PICO criteria (i.e. patients with HAE PLG or HAE-nC1 INH) but also patients who did not meet the PICO criteria (i.e. patients with C1-INH abnormalities) and/or interventions that did not meet the PICO criteria. However, results were reported separately for patients and interventions that were in scope for this review. Two studies provided comparative evidence on the duration of attacks in patients with HAE PLG. One study compared icatibant treated attacks to previously untreated attacks in the same patients and the other study compared icatibant treated attacks to attacks not treated with icatibant, but the comparator group population was not clearly defined.[1] The two remaining studies provided non-comparative evidence on the duration of icatibant treated attacks in patients with HAE-nC1 INH. **Total attack/swelling duration** • One retrospective cohort study (Bork et al 2020) (n=13 in scope patients) reported an 88% reduction in duration of attacks[2] in icatibant treated attacks (201 attacks; mean 4.3, SD 2.6 hours) compared to previously untreated attacks in the same patients with HAE PLG (149 attacks; mean 44.7, SD 28.6 hours). The difference was statistically significant, favouring treatment with icatibant ($p<0.0001$). **(VERY LOW)**

[1] It was unclear how the reduction in duration of attacks was calculated for Manto et al (2021) in terms of whether the comparison was between icatibant-treated vs untreated attacks in the same five patients with HAE PLG, or the comparison was between 5/14 patients with HAE PLG who were treated with icatibant vs 9/14 patients with HAE PLG who were not treated with icatibant.
[2] Defined as swellings attacks, with duration of attacks recorded by patients.

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	• One retrospective cohort study (Manto et al 2021) (n=5 in scope patients; 29 attacks) reported a 71.4%[1] reduction in total attack/swelling duration[3] after treatment with icatibant in patients with HAE PLG (mean attack/swelling duration of 12 hours). Statistical measures were not reported. **(VERY LOW)** **Time from symptom onset to complete symptom resolution** • Two non-comparative retrospective cohort studies (Bouillet et al 2017 [n=10 in scope patients; 90 attacks] and Grumach et al 2022 [n=8 in scope patients; 45 attacks]) reported median total attack/swelling durations of 32.5 (IQR 12.0 to 47.3) hours and 7.0 (range 0.3 to 99.0) hours, respectively, after treatment with icatibant in patients with HAE-nC1 INH. **(VERY LOW)** **Number of attacks shortened with icatibant treatment by >50%, 20% to 50%, <20%** • One retrospective cohort study (Bork et al 2020) (n=13 in scope patients) reported that 197 of 201 attacks were reduced in duration by more than 50% after treatment with icatibant, two out of 201 attacks were reduced by 20% to 50% and two out of 201 attacks were reduced by <20% after treatment with icatibant. **(VERY LOW)** **Four retrospective cohort studies provide very low certainty evidence on the effect of icatibant on total attack/swelling duration in patients with idiopathic/hereditary angioedema with normal C1 inhibitor. One study reported a *statistically significant* reduction in total attack/swelling duration after treatment with icatibant compared to previously untreated attacks in the same patients with HAE PLG. One study reported a reduction in total attack/swelling duration in patients with HAE PLG treated with icatibant but it was unclear how the reduction was calculated in terms of the comparison population and statistical significance was not reported. The remaining two studies were non-comparative and reported very different total attack/swelling durations in patients with HAE-nC1 INH.**
Outcome 2 Time to resolution **Certainty of evidence:** Very low	This outcome is important to patients as attacks/swellings in this condition are frequent and unpredictable and potentially fatal, and if left untreated may last for an average of 3-4 days; therefore, a rapid response to treatment is likely to mitigate the morbidity and mortality associated with this condition. One SRMA (Jeon et al 2019) of three RCTs (n=179[4]) provided evidence relating to time to complete resolution of symptoms after initiation of treatment and resolution of symptoms within four hours after treatment in patients with ACEI-induced angioedema. The SRMA of three RCTs compared results between patients with ACEI-induced angioedema who were treated with icatibant plus current standard care versus those treated with current standard care or placebo with current standard care. Two of the RCTs included in the SRMA defined time to resolution as 'time to complete resolution of symptoms or oedema' and one RCT defined this outcome as 'time to meeting discharge criteria'[5]. **Time to complete resolution of symptoms or time to meeting discharge criteria[5]:** • The SRMA of three RCTs (Jeon et al 2019) (n=179 patients[4]) reported that there were *no statistically significant* differences between patients with ACEI-induced angioedema treated with icatibant plus current standard care compared to current standard care or placebo with current standard care in time to complete resolution: MD -7.77 (95% CI -25.18 to 9.63); p=0.38. There was evidence of considerable heterogeneity (I^2=83%). **(VERY LOW)**

[3] Not clearly defined; Manto et al (2021) stated that data on disease manifestation (defined as the incidence of clinical symptoms [peripheral oedema, abdominal attacks, oedema of the face and neck, oedema of the tongue, oedema of the larynx, marginal erythema]) and outcomes were obtained from medical records of patients and the database of NRC Institute of Immunology FMBA of Russia.
[4] Although Straka et al (2017) stated that their final analysis was based on ITT, they excluded one patient in the icatibant group from the final analysis due to the patient being unable to complete the visual analogue scale. Jeon et al (2019), however, included this patient in their ITT analysis.
[5] Defined as absence of breathing and swallowing difficulty and mildness or absence of voice change and tongue swelling.

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	Proportion of patients exhibiting complete resolution of symptoms (or meeting discharge criteria[5]) within four hours after initiation of treatment: • The SRMA of three RCTs (Jeon et al 2019) (n=176 patients[4]) reported that in patients with ACEI-induced angioedema complete resolution of symptoms within four hours after initiation of treatment was achieved in 41 patients treated with icatibant plus current standard care compared to 39 patients treated with current standard care or placebo with current standard care. The difference in favour of icatibant plus current standard care was *not statistically significant*: RR 1.20 (95% CI 0.48 to 3.04); p=0.70. There was evidence of moderate heterogeneity (I^2=46%). **(VERY LOW)** **One SRMA of three RCTs provides very low certainty evidence that there is *no statistically significant* difference in time to complete resolution of symptoms after initiation of treatment or resolution of symptoms within four hours of treatment with icatibant plus current standard care versus current standard care or placebo with current standard care in patients with ACEI-induced angioedema.**
Outcome 3: Treatment response **Certainty of evidence:** Very low to High	This outcome is important to patients as these attacks/swellings are debilitating and potentially fatal; therefore, a response to treatment is likely to mitigate the morbidity and mortality associated with this condition. Untreated attacks may otherwise last for 3-4 days. In total, three RCTs comparing icatibant plus current standard care to current standard care or placebo with current standard care reported outcomes related to treatment response in patients with ACEI-induced angioedema. **Number of patients who did not have a response to treatment (use of rescue medication)[6] up to six hours after initiation of study treatment** • One RCT (Bas et al 2015) (n=27) reported that 0 of 13 patients with ACEI-induced angioedema did not have a response to treatment with icatibant plus current standard care after six hours compared to three of 14 patients with ACEI-induced angioedema who received current standard care. No statistical measures were reported. **(VERY LOW)** **Number of patients who required additional medication** *Up to 48 hours after initiation of study treatment:* • One RCT (Straka et al 2017) (n=30) reported the frequency of administering additional treatments in patients with ACEI-induced angioedema. Epinephrine was used by 17% of patients in the placebo with current standard care group compared to 0% in the icatibant plus current standard care group. 92% of icatibant plus current standard care treated patients required H1 blockers, H2 blockers or corticosteroids compared to 88.9%, 78% and 88.9% of patients in the placebo with current standard care group, respectively. The differences between treatment groups were *not statistically significant* (p-values ranged from 0.14 for epinephrine to 0.80 for H1 blockers and corticosteroids). **(MODERATE)** *Day three after study treatment, or approximately two days after discharge, if patient discharged on or after day three:* One RCT (Sinert et al 2017) (n=118) reported that 58.3% of 60 patients with ACEI-induced angioedema used corticosteroids, antihistamines, or epinephrine after initiation of icatibant plus current standard care compared to 60.3% of 58 ACEI-induced angioedema patients in the placebo with current standard care group. The difference was *not statistically significant* (p≥0.58). **(HIGH)** **Three RCTs provide very low to high certainty evidence on outcomes related to treatment response in patients with ACEI-induced angioedema. Two RCTs provide moderate to high evidence that there was *no statistically significant* difference in the number of patients with ACEI-induced angioedema who**

[6] 30 mg of icatibant with 500 mg of prednisolone.

	required additional treatment up to 48 hours or three days after administration of icatibant plus current standard care compared to current standard care or placebo with current standard care. One RCT provides very low certainty evidence that no patients with ACEI-induced angioedema required rescue treatment up to six hours after initiation of icatibant plus current standard care compared to three out of 14 patients who received current standard care. No statistical measures were reported.
Important outcomes	
Outcome 4 Time to the onset of symptom regression **Certainty of evidence:** Very low	This outcome is important to patients as attacks/swellings in this condition are frequent and unpredictable and potentially fatal, and untreated may last for several days; therefore, a rapid response to treatment is likely to mitigate the morbidity and mortality associated with this condition. One SRMA (Jeon et al 2019) included two RCTs (n=148) comparing time to onset of symptom regression between icatibant plus current standard care and current standard care or placebo with current standard care in patients with ACEI-induced angioedema; follow-up durations were not reported. **Time to decrease of at least one point in symptom score or scale** • The SRMA (Jeon et al 2019) reported that there was *no statistically significant difference* in time to the onset of symptom relief between ACEI-induced angioedema patients treated with icatibant plus current standard care compared to current standard care or placebo with current standard care: MD -0.50 (95% CI -1.30 to 0.30), p=0.22. There was evidence of considerable statistical heterogeneity (I^2=96%). **(VERY LOW)** **One SRMA including two RCTs provides very low certainty evidence that there is *no statistically significant* difference in time to the onset of symptom relief between patients with ACEI-induced angioedema treated with icatibant plus current standard care compared to current standard care or placebo with current standard care.**
Outcome 5: Symptom progression **Certainty of evidence:** Very low to Moderate	This outcome is important to patients because it provides a holistic evaluation and indication of the patient's general health and their perceived well-being and their ability to participate in activities of daily living. This outcome is both a key indicator of the effectiveness of treatment and provides an insight into the patient's perception of the effectiveness of treatment. In total, three RCTs provided evidence on symptom progression in patients with ACEI-induced angioedema, measured up to six or 48 hours after treatment. One RCT compared icatibant plus current standard care versus current standard care and two RCTs compared icatibant plus current standard care to placebo with current standard care. **Progression of symptoms leading to airway intervention** One RCT (Bas et al 2015) (n=27) reported that one of 14 ACEI-induced angioedema patients in the current standard care group were classified as having treatment failure and required tracheotomy for dyspnoea by six hours after treatment compared to 0 of 13 patients with ACEI-induced angioedema in the icatibant plus current standard care treatment group. No statistical measures were reported. **(VERY LOW)** • One RCT (Sinert et al 2017) (n=118) reported that one of 60 patients with ACEI-induced angioedema who received icatibant plus current standard care required endotracheal intubation 1.5 hours after receiving treatment and 4.75 hours after attack onset compared to 0 of 58 patients with ACEI-induced angioedema who received placebo with current standard care. No statistical measures were reported. **(MODERATE)** • One RCT (Straka et al 2017) (n=30) reported that two of 12 patients with ACEI-induced angioedema in the icatibant plus current standard care treatment group and one of 18 patients with ACEI-induced angioedema in the placebo with current standard care group required intubation up to 48 hours after treatment.

	The difference between the two treatment groups was *not statistically significant* (p=0.32). **(MODERATE)** **Three RCTs provide very low to moderate certainty evidence that a similar number of patients with ACEI-induced angioedema required airway intervention after administration of icatibant plus current standard care compared to current standard care or placebo with current standard care; one of the RCTs reported statistical measures indicating that the difference was *not statistically significant*.**
Outcome 6: HRQoL **Certainty of evidence:** N/A	This outcome is important to patients as attacks/swellings can progress to the extent that fatal airway obstruction can occur; therefore, a reduction in progression is likely to mitigate the morbidity and mortality associated with this condition. **No evidence was identified for this outcome.**
Outcome 7: Hospital attendances **Certainty of evidence:** Moderate to High	This outcome is important to patients because severe acute episodes most often require hospital admission, including intensive care monitoring. However, not all acute episodes require hospital admission and if they do not, this signifies reduced severity. Two RCTs provided evidence on the number of hospital/ICU admissions required by patients with ACEI-induced angioedema up to 48 hours after treatment with icatibant plus current standard care or placebo with current standard care on day three after treatment with icatibant plus current standard care or placebo with current standard care, or approximately two days after discharge, if patient discharged on or after day three. Hospital attendances after initiation of treatment (excluding patients hospitalised before initiation of treatment) • One RCT (Sinert et al 2017) (n=96) reported the same proportions of patients with ACEI-induced angioedema who were admitted to hospital in the icatibant plus current standard care compared to placebo with current standard care groups on day three after treatment and after hospital discharge, or two days after discharge, if patient discharged on or after day three (45.8% in each group). No statistical measures were reported. **(HIGH)** **Hospital attendances after initiation of treatment (ICU admission)** • One RCT (Straka et al 2017) (n=30) reported that a higher proportion of patients with ACEI-induced angioedema treated with icatibant plus current standard care required admission to ICU compared to patients with ACEI-induced angioedema in the placebo with current standard care group up to 48 hours after initiation of treatment (50% versus 33%, respectively). The difference between treatment groups was *not statistically significant* (p=0.36). **(MODERATE)** **Two RCTs provide moderate or high certainty evidence relating to the number of patients with ACEI-induced angioedema who required admission to hospital/ICU after administration of icatibant plus current standard care or placebo with current standard care; one of the RCTs reported statistical measures indicating that the difference was *not statistically significant* and the second RCT showed that the same number of patients in both treatment arms required hospital admissions, but no statistical measures were reported.**
Safety	
Outcome 8: Complications of icatibant treatment **Certainty of evidence:**	Safety is important to patients as it reflects the risks involved in a treatment that may be required multiple times. This allows a risk benefit assessment to be undertaken. One SRMA of three RCTs (Jeon et al 2019) provided evidence on safety in patients with ACEI-induced angioedema. One of the included RCTs compared icatibant plus current standard care to current standard care and two RCTs compared icatibant plus current standard care to placebo with current standard care in patients with ACEI-induced angioedema. **Any adverse events:**

Very low to Moderate	• One SRMA of three RCTs (Jeon et al 2019) (n=179) reported that, of 88 patients with ACEI-induced angioedema in the icatibant plus current standard care group, 29 experienced an adverse event. Of 91 patients with ACEI-induced angioedema in the current standard care or placebo with current standard care group, 27 experienced an adverse event. The difference between the treatment groups was *not statistically significant*: RR 0.95 (95% CI 0.43 to 2.10); p=0.90. There was evidence of low statistical heterogeneity (I^2=20%). **(LOW)** **Drug-related adverse events:** • One SRMA of three RCTs (Jeon et al 2019) (n=179) reported that, of 88 patients with ACEI-induced angioedema in the icatibant plus current standard care group, 12 experienced a drug-related adverse event. Of 91 patients with ACEI-induced angioedema in the current standard care or placebo with current standard care group, nine experienced a drug-related adverse event. The difference between the treatment groups was *not statistically significant*: RR 1.29 (95% CI 0.58 to 2.87); p=0.53. There was no evidence of statistical heterogeneity (I^2=0%). **(VERY LOW)** **Injection site reactions (erythema):** • One SRMA of two RCTs (Jeon et al 2019) (n=178) reported that, of 75 patients with ACEI-induced angioedema in the icatibant plus current standard care group, 43 experienced erythema. Of 73 patients with ACEI-induced angioedema in the current standard care or placebo with current standard care group, 17 experienced erythema. The difference between the treatment groups was *statistically significant*, favouring the current standard care or placebo with current standard care group: RR 2.47 (95% CI 1.56 to 3.90); p=0.0001. There was no evidence of statistical heterogeneity (I^2=0%). **(MODERATE)** **Injection site reactions (swelling):** • One SRMA of two RCTs (Jeon et al 2019) (n=178) reported that, of 75 patients with ACEI-induced angioedema in the icatibant plus current standard care group, 25 experienced swelling. Of 73 patients with ACEI-induced angioedema in the current standard care or placebo with current standard care group, 16 experienced swelling. Although fewer swellings were reported in the current standard care or placebo with current standard care group compared to icatibant plus current standard care group, the difference was *not statistically significant*: RR 1.52 (95% CI 0.89 to 2.61); p=0.13. There was evidence of low statistical heterogeneity (I^2=23%). **(LOW)** **The SRMA of three RCTs provides very low to low certainty evidence that there is *no statistically significant* difference in the number of patients with ACEI-induced angioedema experiencing any adverse event or drug-related adverse event after treatment with icatibant plus current standard care compared to current standard care or placebo with current standard care. The SRMA, including two of the RCTs, provides moderate certainty evidence that there is *no statistically significant* difference in the number of patients with ACEI-induced angioedema experiencing injection site reactions (defined as swelling) after treatment with icatibant plus current standard care compared to current standard care or placebo with current standard care. However, the SRMA, including two of the RCTs, reported a *statistically significant* difference in the number of injection site reactions (defined as erythema), favouring the current standard care or placebo with current standard care group compared to icatibant plus current standard care group.**
Abbreviations	ACEI: angiotensin-converting enzyme inhibitor, CI: confidence interval, HAE-nC1 INH: hereditary angioedema with normal C1-esterase inhibitor, HAE PLG: hereditary angioedema with variant plasminogen gene, HRQoL: health-related quality of life, ICU: intensive care unit, IQR: interquartile range, MD: mean difference, PROM: patient-reported outcome measures, RCT: randomised controlled trial, RR: risk ratio, SD: standard deviation, SRMA: systematic review and meta-analysis

In the Population what is the cost effectiveness of the Intervention compared with Comparator?

Outcome	Evidence statement
Cost effectiveness	No evidence was identified for cost effectiveness.

From the evidence selected, are there any subgroups of patients that may benefit from the intervention more than the wider population of interest?

Outcome	Evidence statement
Subgroups – adults and children or patients with differing number of attacks per patient **Certainty of evidence:** N/A	No evidence was identified for subgroups of patients.

Patient Impact assessment

Patient Impact Summary
The condition has the following impacts on the patient's everyday life: • **mobility:** patients with angioedema, including bradykinin-mediated angioedema with normal C1, experience acute swellings. When these involve the feet this will interfere with mobility as not only would shoes be impossible to wear, but walking is virtually impossible. • **ability to provide self-care:** Current treatment during acute swellings involves observation and if the airway is involved this is life threatening and intensive care admission may be required for intubation to prevent asphyxiation. Even when the airway is not involved, acute episodes often still require hospital admission for observation. These recurrent admissions significantly interfere with patient ability to self-care, due to inability to walk/ get to the toilet associated with feet swellings;

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inability to hold a knife and fork and therefore self-feed or use the toilet if swellings affect upper limb; temporary eyelid closure and therefore 'blindness' when swellings affect eyes. Abdominal swellings can also cause pain so severe that the patient cannot stand, sit or get comfortable therefore also limiting self-care.

- **undertaking usual activities:** As above, recurrent admissions to hospital/ITU, especially for patients with more frequent swellings, will severely impact ability to carry out their usual activities, activities of daily living, attending school, and employment. The disease can begin at the onset of puberty (due to changes in hormones) with some patients having attacks from the age of 2 years, with varied frequency. The aftermath of an attack is severe exhaustion for 24-48 hours. The impact of attacks varies depending on location but can severely hinder school and employment attendance. In some children (under 18 years old) this can be misunderstood and documented as 'school avoidance'.
- **experience of pain/discomfort:** Multiple admissions to hospital or intensive care will cause significant discomfort to patients. The more specific complications experienced by these patients depend on the location of swellings. Symptoms associated with swelling in the digestive system (gastrointestinal tract) include nausea, vomiting, acute abdominal pain, and/or other signs of obstruction. Swellings involving the larynx or pharynx can result in pain, difficulty swallowing (dysphagia), difficulty speaking (dysphonia), noisy respiration (stridor), and potentially life-threatening asphyxiation. Whist the pain experienced can be debilitating, the aftermath from an attack can take 24 to 28 hours and is associated with fatigue.
- **experience of anxiety/depression:** The anxiety around having further life-threatening swellings and the lack of prophylactic treatment currently available is extremely difficult for patients. Frequent intensive care and A&E admissions are associated with increased anxiety and post-traumatic stress. A&E attendances can be stressful as not all departments understand or are familiar with the condition and therefore patients/families may have to explain the condition. Multiple admissions can also directly cause stress, anxiety, frustration, isolation and low mood for the patient and their families, and can impact personal relationships within families

Further details of impact upon patients:
The condition severely impacts all areas of everyday life given the recurrent hospitalisations with life threatening swellings. Anxiety can be a cause of attacks – including "good" anxiety like looking forward to a birthday/wedding/festival, and so the condition may also affect these experiences.

Further details of impact upon carers:
Those living with and caring for people with angioedema are very affected, especially when the patient is a child. They may be required to help with activities of daily living, as well as hospital appointments and emergency attendances for acute episodes. The stress of not knowing when the patient may experience a sudden life-threatening swelling is likely to impact carers, especially if the patient is a child.

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Considerations

Equality and Health Inequalities Impact Assessment (EHIA)	
Summary of any potential impacts of the proposal	This policy proposition aims to make icatibant available for all adult patients with severe acute swellings due to bradykinin-mediated angioedema with normal C1 inhibitor who otherwise have no licensed treatment options. Routine approval as an intervention with appropriate oversight would allow equity of access for patients with a rare condition to potentially lifesaving treatment that is currently not routinely available to them. This policy proposition is restricted to adults in line with the findings from the evidence review. However, as icatibant has a licensed indication in children aged two years and older for other conditions, NHS England's Policy 170001/P Commissioning Medicines for Children in Specialised Services (commissioning medicines children) can be applied to this policy for children with bradykinin-mediated angioedema with normal C1 inhibitor aged two years and older if clinically eligible. The use of icatibant would prevent acute hospital admissions and associated risk of death and intensive support needs and costs. Furthermore, it would prevent interruption to patients' daily activities of life, inability to work or attend school, or inability to look after their children or dependents. Patients can self-administer the subcutaneous treatment, which is usually a one-off dose, and treat acute swellings. No adverse impacts of this proposition have been identified.
13Q Assessment	
PPVAG outcome	No consultation required
Were PPVAG assured of the level of stakeholder testing?	Yes
Rare Disease Advisory Group	
Yes RDAG fully supported the proposal.	

Pharmaceutical

Yes

This clinical commissioning policy proposition is for the use of icatibant for the treatment of moderate to severe acute swellings due to bradykinin-mediated angioedema with normal C1 inhibitor in adults. The policy proposition applies to patients with recurrent, or long-term, symptoms in two subgroups of bradykinin-mediated angioedema with normal C1 inhibitor:

- Hereditary angioedema with normal C1 esterase inhibitor (HAE-nC1-INH)
- Idiopathic non-histaminergic angioedema with normal C1-inhibitor (INHA)

The recommendations are outside of the marketing authorisations for icatibant, so use if off-label and Trust policy regarding unlicensed medicines should apply. Icatibant is on the NHS Payment Scheme Annex A, that is, it is a high-cost drug.

The policy proposition covers use in adults in line with the findings from the evidence review. Icatibant may be used in children aged 2 – 17 years by application of the NHS England's Policy 170001/P Commissioning Medicines for Children in Specialised Services (commissioning medicines children), as icatibant is listed in the BNF Children with a recommended dosage schedule relative to the age of the child.

National Programme of Care

Blood and Infection Programme of Care

The proposition received the full support of the Blood and Infection Programme of Care on the 25th February 2025.

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