Tackling Unmet Need in Hereditary Angioedema

Optimising care and treatment

This White Paper captures the perspectives and insights from leading clinicians, academics and HAE patient organisation representatives in the HAE Expert Group that was convened by KalVista Pharmaceuticals and HAE UK in April and May 2025. The views expressed in the paper represent a consensus reached through deliberation and exchange. All participants contributed to this paper independently and retained their autonomy throughout the drafting process. KalVista reviewed the White Paper for accuracy and compliance purposes only. APCO, an independent advocacy and advisory firm, was engaged to assist throughout the process, including providing writing support.

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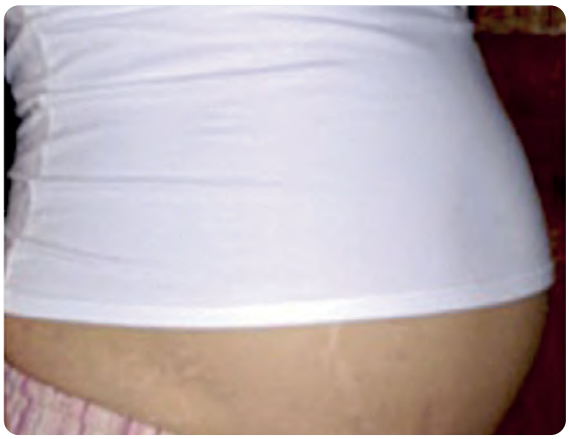
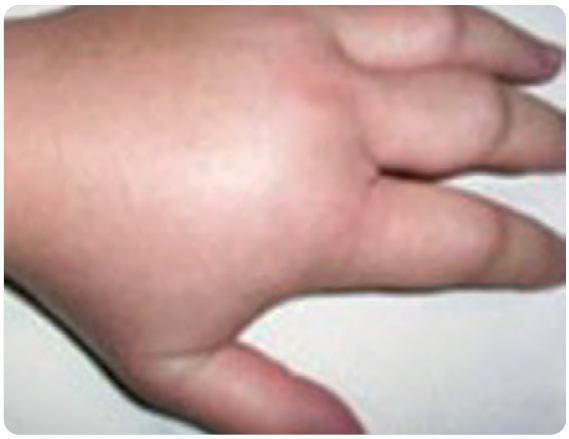
Content

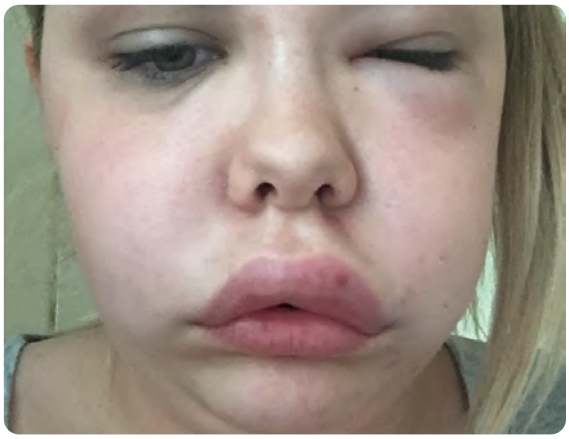
It’s not about simply existing with HAE, the goal is to live a full life.

Angela Metcalfe, CEO, HAE UK

Foreword







Photos were provided by HAE UK

Hereditary Angioedema (HAE) is a rare and potentially life-threatening inherited condition which impacts approximately 1 in 50,000 people.[1] While treatments for HAE are available, the disease's impact varies significantly from patient to patient. This variability highlights the critical need for personalized treatment plans and comprehensive care strategies. Despite the advancements in treatment options, there remains a substantial unmet need to guarantee that every patient receives the appropriate therapies and support tailored to their unique circumstances. Addressing this gap is essential to improve patient outcomes and ensure equitable access to care for all individuals affected by HAE.

This White Paper, developed by an Expert Group of clinicians and representatives from the patient community, aims to highlight remaining unmet needs in HAE and make the case for continued innovation in care and treatment options. It includes recommendations for optimising care and treatment so that individuals with HAE can achieve total disease control and live a "normal life".

As the first White Paper to address the critical unmet needs of HAE patients, this document provides a new perspective on policies relating to rare disease and the management of chronic illness in the UK. It is designed as a resource for all in the HAE community, including patients and their carers, healthcare professionals, commissioners, decision-making bodies such as NICE and those who influence and define the management of rare diseases in the UK.

About the HAE Expert Group

This White Paper captures the perspectives and insights from leading clinicians, academics and HAE patient organisation representatives in the HAE Expert Group that was convened by KalVista Pharmaceuticals and HAE UK in April and May 2025.

The HAE Expert Group was co-chaired by:

- **Angela Metcalfe**, CEO of HAE UK
- **Professor Sinisa Savic**, Consultant Immunologist, Leeds Teaching Hospitals NHS Trust and Chair of the British Society for Immunology Clinical Professional Network.

The following experts contributed and, together with the co-chairs, have authored the report:

- **Dr Tomaz Garcez,** Consultant Immunologist, Manchester University NHS Foundation Trust
- **Dr Patrick Yong,** Consultant Immunologist, Frimley Health NHS Foundation Trust
- **Emily Carne,** Nurse Consultant, Immunodeficiency Centre for Wales
- **Dr Anthony Dorr,** Consultant Immunologist, Barts Health NHS Trust
- **Nick Meade -** CEO, Genetic Alliance UK

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1 What is HAE and what is it like to live with?

What is HAE?

Hereditary Angioedema (HAE) is a rare disease that causes unpredictable attacks of tissue swelling. NHS England estimates it affects 1,000 to 1,500 patients in the UK.[2] Mostly inherited, with a 50% chance of passing it to children, it can also result from the development of spontaneous genetic variants in patients without a family history.[3]

An episodic condition, HAE is characterised by sudden, recurrent episodes of swelling which can last up to five days and occur without warning in body parts including hands, feet, genitals, face, tongue, neck, abdomen and airway with or without associated early signs.[4] Attacks can be functionally impairing, debilitating or in the case of airway involvement, potentially life-threatening.

In the past, up to 30% of HAE patients died from complications arising from lack of treatment, including asphyxiation.[5] Today, improved management and care has greatly reduced fatalities, with most deaths now occurring in undiagnosed individuals.[6] However, diagnosis can take over eight and a half years from symptom onset[7] and significant challenges remain that negatively impact Quality of Life for patients and carers alike.

I missed a lot of school because of HAE, and I think I was and still am a bit of a loner because of it. You end up spending a lot of time in your bedroom suffering, so as you get older and you reflect on HAE, it was tough.

Female patient aged 30

Living with HAE

The frequency and severity of HAE attacks varies significantly between patients and even within the same patient over time. Patients may face difficulties in work, school,[8] and daily activities, along with significant psychological burdens such as anxiety and depression.[9] The impacts of HAE on quality of life also vary amongst different patient cohorts. For children, symptoms can appear as early as the age of two, and about half of all children with the most common types of HAE show symptoms by the age of ten.[10]

For many children, this can lead to alienation from peers, frequent hospital visits, missing out on activities with their peers and challenges in school attendance and educational attainment. Adolescents with HAE report higher anxiety, attack treatment delays, and a greater impact on quality of life compared to adults with HAE.[11] For adults, the ability to work and employment issues come to the forefront, with frequent time off due to sickness and a lack of understanding from employers. Navigating life events such as pregnancy, breastfeeding, and menopause can limit treatment options and worsen disease control.

I'm not doing overtime at the moment because I'm trying to reduce the number of attacks I have. I'm not working out as much because I know what it will do. So HAE is controlling what I'm doing in my life at the minute.

Male patient aged 29

2 Achieving a global standard in HAE care and treatment

Treatment objectives for HAE are defined by the World Allergy Organisation (WAO) and European Academy of Allergy and Clinical Immunology (EAACI) as total disease control (zero attacks) and normalisation of patients' lives.[12]

> **I had to change my job because they kept telling me that they didn't want a sick person that could suddenly get ill.**
>
> Female patient aged 35

Managing HAE with prophylactic treatments

Achieving total disease control requires preventing attacks with long-term prophylaxis or in some cases, short–term prophylaxis in advance of angioedema-provoking events such as dental or surgical procedures. In the UK, two injectable and one oral prophylactic treatments are prescribed in accordance with international guidelines. However, NHS commissioning policy restricts access to two of the injectable treatments, limiting their use to patients who experience both frequent and severe attacks.[13, 14] In contrast, access to the oral treatment is determined solely by attack frequency, without consideration of severity.[15] The wider impact of HAE on quality of life and their individual circumstances are not taken into account in the access requirements for these treatments. Consequently, fewer patients are eligible for treatment that could keep their condition under control.

England's rigid commissioning guidelines run counter to the WAO/EAACI guidelines, which state that disease activity, burden, control, and patient preference should all be taken into consideration when evaluating them for long-term prophylaxis. The US guidelines specifically state that "the decision on when to use long-term prophylactic treatment cannot be made on rigid criteria but should reflect the needs of the individual patient. Decisions regarding which patients should be considered for long-term prophylactic treatment should take into account the patient's quality of life and treatment preferences in the context of attack frequency, attack severity, comorbid conditions, and access to emergent treatment." [16]

In the UK, the greatest barrier to optimum HAE treatment is therefore the restriction of long-term prophylactic treatments to a cohort of patients who have experienced attacks of a certain number and frequency. The bar for eligibility for preventative therapies should be lowered by taking into account the quality of life of the individual patient, as in the US.[17]

> **I had a very severe abdominal swelling. I didn't have any of my medication at home at the time, so I ended up going to the A&E department of my local hospital. The pain was off the scale.**
>
> Female patient aged 56

Treating HAE attacks in A&E

As long-term prophylactic treatments do not guarantee a zero-attack life, all patients need to be equipped with on-demand therapy, which are currently only available as injectable treatments. About half of patients manage their HAE with both prophylactic and on-demand treatments, and the other half rely solely on administering on-demand treatment when they experience an attack. While many patients are trained in injecting themselves and can manage their condition at home, others require A&E attendance in the event of an attack.

As is typical for those living with a rare condition, patients with HAE often face delays in getting access to treatment in A&E due to a lack of awareness and education among the staff. This happens despite information about patients' condition and treatment needs being routinely shared with A&E departments. Ideally an effective treatment plan should negate the need for patients to use A&E, other than in the most extreme cases. For example, introduction of treatment modalities that can be self-administered and effective at-home treatment programmes have been shown to improve patient experience and significantly reduce A&E attendance and hospital admissions.[18]

Holistic care including mental health support

The episodic nature of the condition means that quality of life can be worsened not just by the attacks themselves, but also the prospect of an attack occurring at any moment. With 63% of adults having some degree of fear of needles,[19] some studies have shown that treatment options that involve needles can curtail patients from seeking them.[20] The cycle of stress and anxiety often exacerbates the physical symptoms of HAE.[21] Therefore, a holistic approach to care, which incorporates mental health or psychological support, is crucial to the overall wellbeing of patients with HAE.

> **Every time I had a severe attack, I was extremely anxious about going to hospital because they often dismissed my attack as an insect sting or an allergy, despite my years of experience. I've only encountered one doctor outside of an allergist/immunologist who knew what HAE was.**
>
> Male patient aged 55

> **You need to treat the person as a whole and that may involve talking to them about other problems they may have, for instance their mental health and how they're actually coping with living with this.**
>
> Female patient aged 56

Shared decision making to enhance patient choice

As each person's experience of HAE is unique, shared decision-making is a fundamental part of effective management. HAE can worsen due to triggers such as stress, hormones, healthcare procedures, or medications, and naturally vary throughout life, meaning patients' needs often change as they progress through different life stages and circumstances. Therefore, clinicians should work with patients to adapt their treatment approach according to the individual's needs and life stage.[22]

The WAO and EAACI guidelines specify that all HAE patients carry on-demand treatment for two attacks at all times yet recent studies found that only a third of patients do so.[23] This is a major issue when early administration is key to effective attack treatment. Delays in treatment increase the severity and duration of the attacks, leading to more serious symptoms that prolong time to recovery, impact on quality of life and often require emergency medical intervention.[24]

We also know that patients delay or avoid treatment for reasons such as underestimating the severity of their attacks. Some prolong an attack by rationing or spacing out their medication because they are worried about wasting it on a mild attack or the cost of medications to the NHS. Sometimes, patients only have access to treatments that are not well suited to their specific needs, lifestyles, career or education. This is where personalised medical care is so important. The NHS sees patient choice as crucial for improving care,[25] yet up to a third of those with HAE in the UK feel their treatment options have not been influenced by their discussions with clinicians.[26]

> **When I was younger, I used to choose which attacks to treat because the injection was so painful, but I had a face attack, and I decided to wait, and it escalated badly. My physician was very mad at me for not treating it. She was right… I will never do it again.**
>
> Female patient aged 35

When agreeing a treatment plan, as more treatment options become available for patients, it is important for clinicians to recognise the treatment barriers patients face and that patients understand the pros and cons of each option and know they have a choice in their treatment. With numerous new treatment options on the horizon, decision-makers responsible for reimbursement decisions must remain open-minded and proactive in making these treatments accessible to patients to ensure they address the current unmet need.

The UK Government has committed to improving the lives of those living with rare diseases in the UK Rare Disease Framework[27] and is driving towards increasingly preventative healthcare[28]. More must be done for the Government to achieve these objectives and bring HAE management in the UK up to the global standard. A comprehensive approach is essential, encompassing improved access to treatments, shared decision-making, and mental health support. Addressing these unmet needs is crucial for enhancing the overall care and quality of life for HAE patients.

> **To feel in total control of the disease it's very important to have access to medication that you feel comfortable with, have a good relationship with your consultant, and have knowledge about the disease and YOUR disease.**
>
> Female patient aged 30

3 Policy solutions to optimize care and treatment

To address the unmet need for people living with HAE, the HAE Expert Group recommends the following actions are taken.

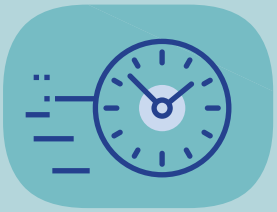
Expanded treatment options and personalised care plans

Enhance Access to Treatment:
Ensure patients have access to a range of treatments that align with their needs, providing them with optimal choices. This should be facilitated through shared decision-making between patients and healthcare professionals, allowing time to assess the patient's unique needs.

Improve access to prophylactic treatments:
Change commissioning guidelines so that patients who would benefit from prophylactic treatments are not denied treatment purely on the basis of insufficient frequency and/or severity of attacks.

Promote Innovation:
Decision-makers should remain open-minded about the need for new treatments in HAE and actively engage with the patient community to understand the unmet need and how treatments could be improved

Set a new standard for holistic care:
Ensure holistic care, including mental health support, is adequately resourced and integrated throughout the HAE treatment pathway.



Encourage usage of on-demand treatments:
Patients should not self-limit usage of on-demand treatments for their severe attacks and should be encouraged to carry two on-demand treatments at all times and administer them promptly when they recognise the onset of an attack.

Improving patient and professional understanding of HAE

Professional Training:
Educate HCPs to recognise the signs and symptoms of HAE early and understand the right pathway, reducing the diagnostic odyssey that many patients face.

Patient Education:
While valuable patient support resources already exist, the NHS should collaborate with patient groups to raise awareness of these tools and ensure equitable access. Additionally, the NHS could help identify and address any remaining gaps in patient education or support to further empower individuals in managing their condition and treatment choices.

Tailoring the health system for rare diseases

As the Government abolishes NHS England, there is a unique opportunity to re-evaluate how we manage rare conditions.

Data collection and analysis:
Invest in robust data collection systems to gather comprehensive information on rare conditions like HAE and ensure the NHS is able to share data across locations.

Specialist treatment centres:
Ensure all patients across the UK have equitable access to specialist treatment centres with home delivery services, by addressing regional disparities that currently require some patients to travel significantly further for care.

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