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# Improvement in Health-related Quality of Life with Sebetralstat for HAE Attacks in Adolescents and Adults


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## Key Takeaways

**Sebetralstat was associated with meaningful improvement in AE-QoL**

**45.2%**
**of participants achieved a clinically meaningful improvement in LOESS fitted AE-QoL total score**

**Locally estimated scatterplot smoothing (LOESS) fitted AE-QoL total score improved**
from baseline to Month 15

- **7.2** points — Overall population
- **18.2** points — Adolescents
- **5.3** points — Adults

## Background

- Hereditary angioedema (HAE) is characterized by unpredictable, painful, and debilitating attacks that have negative effects on health-related quality of life (HRQoL)[1]
  - Adolescent and adult patients have reported that injectable on-demand treatments, while effective, also have negative impacts on HRQoL, including anxiety and pain associated with administration. Daily activities or work/school are impacted to a greater extent in adolescent patients with HAE[1]
- Sebetralstat is the first and only oral on-demand therapy approved for patients with HAE aged ≥12 years[2,3] and is included as a first-line option in international HAE treatment guidelines[4]
  - KONFIDENT-S, a 2-year open-label extension trial (NCT05505916), investigated the long-term safety and effectiveness of on-demand sebetralstat[5]

## Objective

- To present Angioedema Quality of Life Questionnaire (AE-QoL) data from participants treating attacks with sebetralstat film-coated tablet in KONFIDENT-S, stratified by age group

## Methods

- Eligible participants were ≥12 years of age with HAE with C1-inhibitor deficiency and had ≥2 documented attacks within 3 months, or had completed the phase 3 KONFIDENT trial[4] (**Figure 1**)
  - Participants receiving long-term prophylaxis were required to be on a stable dose and regimen for ≥3 months immediately before the study
- Participants self-administered sebetralstat 600 mg as early as possible after attack onset
- Participants completed the AE-QoL questionnaire at enrollment (baseline) and in the eDiary every 28 (±7) days thereafter (**Figure 2**)

### Figure 1. KONFIDENT-S Study Design




**Real-world elements to align with HAE treatment guidelines**
- Portable multidose packs
- No need to contact a call center or investigator before, during, or after attacks
- Consider treatment of all attacks (any severity, any location)
- Self-administer 600 mg sebetralstat as early as possible[a,b]

[a]Participants were instructed to treat their attacks involving the larynx immediately with conventional on-demand therapy if the attack symptoms worsened after the initial sebetralstat administration. [b]Participants were transitioned from sebetralstat 600 mg film-coated tablet to sebetralstat 300 mg orally disintegrating tablet in August 2024 based on evaluation of data from the KONFIDENT trial; all KONFIDENT-S data presented are for patients who administered the 600 mg dose.
HAE, hereditary angioedema.

### Figure 2. AE-QoL Overview

- **17-items across 4 domains**
  - Functioning • Fatigue/Mood
  - Fears/Shame • Food
- **28-day recall period**
- **5-point Likert scale** (1 2 3 4 5)
  Converted to a 0–100 scale; Higher scores = greater QoL impairment
- **Clinically meaningful change**
  Minimal clinically important difference of ≥6-point reduction[6]

## Results

- As of September 30, 2025, 138 patients received ≥1 dose of 600 mg sebetralstat film-coated tablets in the KONFIDENT-S trial (**Table 1**)
  - 126 participants (21 adolescents, 105 adults) reported AE-QoL outcomes

### Table 1. Participant Demographics

| | Participants N=138 |
|---|---|
| **Age, mean (range), years** | 36.2 (12-77) |
| **Sex, female, n (%)** | 90 (65) |
| **Race, n (%)[a]** | |
| White | 103 (75) |
| Asian | 17 (12) |
| Other or multiple | 11 (8) |
| **BMI, mean (range), kg/m²** | 26.5 (16-43) |
| **HAE-C1INH-Type 1, n (%)** | 129 (94) |
| **Treatment regimen at screening, n (%)** | |
| On-demand only | 101 (73) |
| LTP + on-demand | 37 (27) |
| **Time since diagnosis, median (IQR), years** | 12.1 (7, 21) |

[a]Not reported, 7 participants (5.1%).
BMI, body mass index; HAE-C1INH, hereditary angioedema with C1-inhibitor deficiency; IQR, interquartile range; LTP, long-term prophylaxis.

- Most attacks treated with sebetralstat were subcutaneous and of mild or moderate severity (**Table 2**)

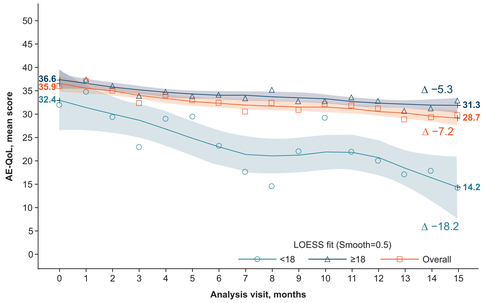
### Table 2. Sebetralstat-treated Attack Characteristics

| | Sebetralstat-treated Attacks n=2469 |
|---|---|
| **Baseline pooled primary attack locations, n (%)[a]** | |
| Mucosal | 1028 (44) |
| Laryngeal | 49 (2) |
| Subcutaneous | 1313 (56) |
| **Baseline PGI-S rating, n (%)[b]** | |
| Mild[c] | 913 (39) |
| Moderate | 985 (42) |
| Severe/Very Severe | 445 (19) |

[a]Missing: 128 (5.2%).
[b]Missing: 126 (5.1%).
[c]Includes PGI-S rating "None": 45 (2%).
PGI-S, Patient Global Impression of Severity.

- AE-QoL mean score improved over time in both age groups, with the greatest improvement observed among adolescents (**Figure 3**)

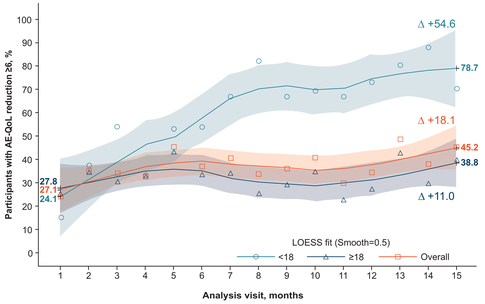
### Figure 3. AE-QoL Score Over Time by Age Group




Data cutoff: September 30, 2025.
AE-QoL, Angioedema Quality of Life Questionnaire; LOESS, locally estimated scatterplot smoothing.

- At Month 15, 45.2% of participants achieved a ≥6-point reduction (minimal clinically important difference) in LOESS fitted AE-QoL total score (**Figure 4**)

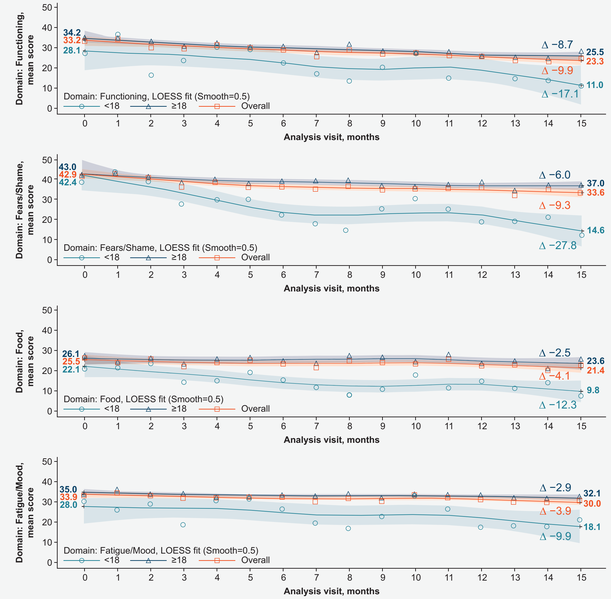
### Figure 4. Proportion of Participants with AE-QoL Reduction of ≥6 Points by Age Group




Data cutoff: September 30, 2025.
AE-QoL, Angioedema Quality of Life Questionnaire; LOESS, locally estimated scatterplot smoothing.

- For the domains of Functioning, Fears/Shame, Food, and Fatigue/Mood, the changes in LOESS estimate from baseline to Month 15 were −9.9, −9.3, −4.1, and −3.9, respectively (**Figure 5**)

### Figure 5. AE-QoL Domain Scores by Age Group




Data cutoff: September 30, 2025.
AE-QoL, Angioedema Quality of Life Questionnaire; LOESS, locally estimated scatterplot smoothing.


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