Reductions in Healthcare Resource Utilization in Adolescents with Hereditary Angioedema on Berotralstat

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BACKGROUND

- Hereditary angioedema (HAE) is a rare inherited condition marked by recurrent attacks of painful and unpredictable swelling of the skin and mucous membranes, which can be life-threatening when affecting the upper airway.[1]
- Berotralstat is the only targeted, once-daily, oral prophylactic therapy for the prevention of HAE attacks in adults and pediatric patients 2 years and older.[2]
- A prior real-world study using Optime Care Specialty Pharmacy data observed significant reductions in HAE attacks following berotralstat initiation among adolescents.[3]
- Additionally, significant reductions in healthcare resource utilization (HRU) following berotralstat initiation among patients aged 12 years or older with HAE have been published using Komodo Healthcare Map claims data.[4]
- This study evaluated reductions in angioedema-related HRU following berotralstat initiation among adolescents aged 12–17 years using linked Optime Care and Komodo Healthcare Map data.

METHODS

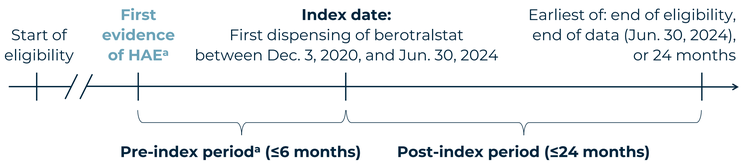
Data Source

- Optime Care Specialty Pharmacy data (Dec. 3, 2020 – Jun. 30, 2024) was linked with Komodo Healthcare Map administrative claims data (Oct. 1, 2015 – Jun. 30, 2024) at the patient level using de-identified Datavant tokens.
- Optime Care is the sole dispenser of berotralstat in the United States, and the database includes berotralstat shipment information, self-assessments of HAE attacks, and laboratory results (C1INH levels, C1INH function, and C4 levels) for HAE type identification.
- Komodo Healthcare Map contains pharmacy and medical claims data for more than 320 million patient-lives in the United States, including information on diagnoses, treatments, and HRU.

Study Design and Analysis

- This retrospective pre–post study selected patients with ≥2 berotralstat dispensings based on Optime data (first dispensing = index), ≥6 months of continuous insurance eligibility prior to the index date based on Komodo data, evidence of HAE during continuous eligibility any time pre-index in Komodo data, and were adolescents aged 12–17 years at index.
- The pre-index period spanned from first evidence of HAE to the index date, with a maximum of 6 months. The post-index period spanned the index date to the earliest of the end of continuous eligibility, end of data, or 24 months.
- HAE type was identified using laboratory measurements of C1INH levels, C1INH function, and C4 levels.[5] Patients with undetermined HAE type may have had missing laboratory values in the database or a combination of values that could not reliably be classified.
- Angioedema-related medical visits were identified using claims with a primary diagnosis code for HAE or angioedema, on-demand or LTP medications, and diagnostic tests for complement components associated with HAE. Medical visits, outpatient (OP)/emergency department (ED) visits, and hospitalizations were reported.
- Rates of visits post-index were compared with pre-index using rate ratios, 95% confidence intervals (CIs), and p-values from generalized estimating equation (GEE) Poisson regression models with robust standard errors.

Figure 1. Pre-Post Study Design



HAE, hereditary angioedema; LTP, long-term prophylaxis.
[a]First evidence of HAE was assessed any time pre-index (during continuous eligibility). Evidence of HAE was defined as a pharmacy or medical claim for an HAE on-demand or LTP medication, an angioedema or HAE diagnosis (in any position), or measurement of complement function. If the first evidence of HAE was ≥6 months pre-index, then the pre-index period was 6 months; if the first evidence of HAE was <6 months pre-index, then the pre-index period spanned from the first evidence of HAE to the index date.

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FUNDING

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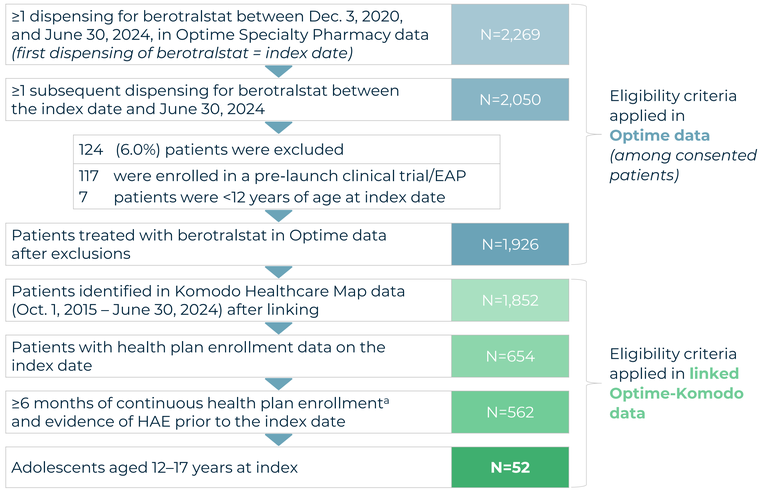
1. Betschel S, et al. *Allergy Asthma Clin Immunol.* 2019;15(1):1-29 . **2.** Berotralstat [package insert]. Durham, NC: November 2023. **3.** Lumry WR, et al. Real-World Hereditary Angioedema Attack Rates Before and After Berotralstat Initiation Among Adolescents. Presented at the International Society for Pharmacoeconomics and Outcomes Research (ISPOR); May 13–16, 2025; Montreal, QC, Canada. **4.** Christiansen S, et al. *J Manag Care Spec Pharm.* 2025;31(6):578-589. **5.** Davis-Lorton M, et al. *Allergy Asthma Clin Immunol.* 2026;22(1):10

RESULTS

- The study population comprised 52 adolescents with HAE initiating berotralstat (**Figure 2**).
- Mean age was 15.1 years, 65.4% were female, and 51.9% had Medicaid insurance at index (**Table 1**).
- Most individuals had HAE type 1 or 2 (61.5%); 9.6% had HAE with normal C1 esterase inhibitor and 28.9% had undetermined HAE type (**Figure 3**).
- Prior to berotralstat initiation, the mean rates of angioedema-related outpatient/emergency department (OP/ED) visits and hospitalizations were 4.7 and 0.5 per patient-year, respectively (**Figure 4**).
- Rates of angioedema-related OP/ED visits decreased significantly by 58% after berotralstat initiation ($p<0.05$) (**Figure 5**).
- Rates of angioedema-related hospitalizations were lower post-index but reductions were non-significant (**Figure 5**).

Figure 2. Berotralstat Patient Disposition



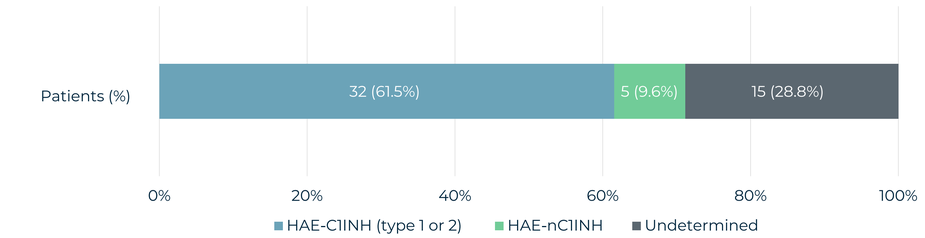
EAP, expanded access program; HAE-C1INH, hereditary angioedema with C1 esterase inhibitor deficiency.
[a]Continuous health plan enrollment was defined as continuous periods with both medical and pharmacy insurance eligibility.

Table 1. Demographics and Clinical Characteristics

Characteristics	Patients (N=52)
Demographics[*,a]	
Age, years, mean ± SD [median]	15.1 ± 1.7 [15]
Female, n (%)	34 (65.4)
Region of residence, n (%)	
South	20 (38.5)
Midwest	13 (25.0)
West	13 (25.0)
Northeast	6 (11.5)
Insurance plan type, n (%)[†,a]	
Commercial	25 (48.1)
Medicaid	27 (51.9)
Medicare	0 (0.0)
Healthcare practitioner specialty, n (%)*,a	
Allergist/Immunologist	46 (88.5)
Nurse practitioner	2 (3.8)
Other	4 (7.7)
Quan-CCI score, mean ± SD [median][†,b]	0.23 ± 0.47 [0]
Patients with ≥1 claim for an ODT pre-index, n (%)[†,c]	22 (42.3)
Patients with ≥1 claim for an LTP pre-index, n (%)[†,c]	12 (23.1)

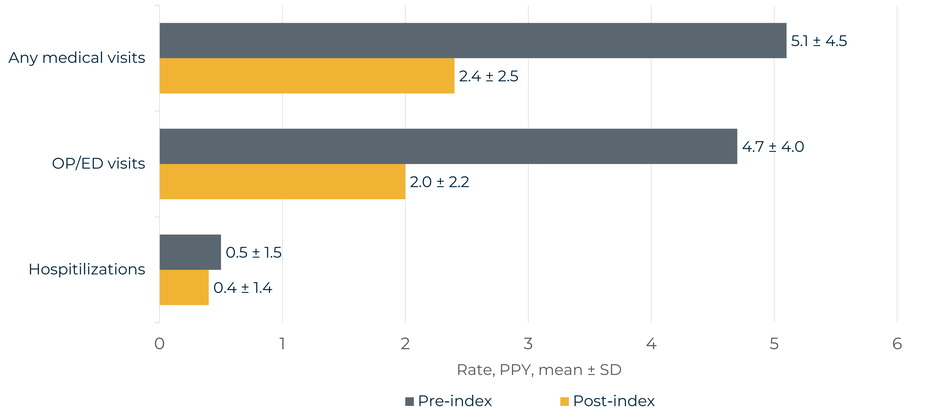
CCI, Charlson comorbidity index; LTP, long-term prophylaxis; ODT, on-demand therapy; SD, standard deviation.
*Identified from Optime Care Specialty Pharmacy data. †Identified from Komodo Healthcare Map data.
[a]Assessed on the index date. [b]Assessed during the 6 months pre-index. [c]Assessed any time pre-index (from the start of continuous eligibility to the index date).

Figure 3. HAE Type



HAE-C1INH, HAE with C1 esterase inhibitor deficiency; HAE-nC1INH, HAE with normal C1 esterase inhibitor.

Figure 4. Rates of Angioedema-Related Healthcare Resource Utilization



ED, emergency department; OP, outpatient; PPY, per person-year; SD, standard deviation.

Figure 5. Comparison of Angioedema-Related Healthcare Resource Utilization

CI, confidence interval; ED, emergency department; OP, outpatient. *$p<0.05$.

Limitations

- Dispensed medications do not indicate that the medication was ingested.
- While matching data sources via tokenization achieves high precision, it does not ensure perfect accuracy in matching patients between different sources within the Komodo database or between Optime and Komodo data.

CONCLUSION

Adolescents with HAE experienced significant reductions in angioedema-related medical visits after the initiation of berotralstat.