Healthcare Utilization and Costs Among Hereditary Angioedema Patients Receiving Long-Term Prophylaxis: Results of a Claims Database Analysis

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Introduction

- Hereditary angioedema (HAE) is a rare (1:50,000) genetic disease often associated with a defective level or function of the C1 esterase inhibitor (C1INH) protein[1]
- HAE is characterized by unpredictable, recurrent, and painful attacks of tissue swelling across multiple locations, including the face, limbs, and abdomen[2,3]
- HAE is managed by both the on-demand treatment of attacks in all patients, as well as the prevention of attacks via long-term prophylactic (LTP) therapies in appropriate patients[4]
- Most patients (~70%) with HAE in the United States (US) are treated with LTP therapies, primarily non-androgens[2,5]
- Multiple effective LTP therapies have become available in the past decade, however, patients with HAE still experience attacks and require extensive medical care, which can include visits to the hospital/emergency room (ER)[2]
- In previous research, healthcare practitioners reported frequent dosing schedule as one of the primary unmet needs/issues associated with LTPs[6]
- There are limited real-world data on LTP refill patterns and associated healthcare resource utilization and costs

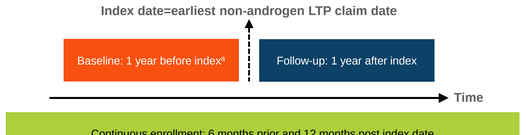
Objective

- To assess refill patterns in LTP and associated healthcare resource utilization and costs in patients with HAE in the US using a national administrative claims database

Methods

- Commercially insured patients from the IQVIA PharMetrics® Plus Database (January 2016–September 2023) with ≥1 claim for non-androgen LTP, with ≥6 months of continuous enrollment before and ≥12 months after index date (first non-androgen LTP claim) were included (**Figure 1**)
- Patients with multiple LTP therapies on index date or with an annualized claim amount more than mean ± 3 times the standard deviation (SD; ie, outliers) were excluded

Figure 1. Longitudinal retrospective study design



Outcomes (assessed at baseline and follow-up)

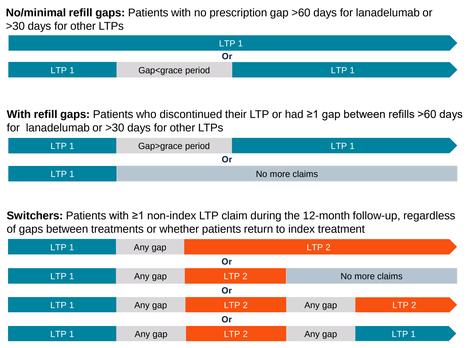
- Healthcare resource utilization
  - On-demand doses
  - Utilization of inpatient/outpatient/ER/home health visits
- Healthcare costs
  - Pharmacy
  - Inpatient/outpatient/ER/home health visits

[a]For patients with a baseline period shorter than 364 days, these data are annualized; for patients with baseline period 364 days or longer, the entire 12-month period is considered without annualization.

ER, emergency room; LTP, long-term prophylaxis.

- Annualized mean on-demand therapy claims, inpatient visits, outpatient visits, ER visits, home health visits, and HAE-related healthcare costs were evaluated 1 year before and after the index date
- Patients were classified into the following cohorts: no/minimal refill gaps, with refill gaps, or switchers (**Figure 2**)

Figure 2. LTP patient cohort definitions



LTP 1 is the LTP at index date; LTP 2 is any non-index LTP.

LTP, long-term prophylaxis.

- Proportion of days covered (PDC) was calculated as the percentage of days covered by index LTP prescription fills during follow-up for both the cohorts with refill gaps and without (ie, no/minimal refill gaps). A high PDC percentage signifies good adherence to chronic treatment regimens, commonly accepted with a threshold of 80%[7]

Results

- Data for 328 patients with HAE taking LTP were analyzed; mean age was 41.2 years and 70% were female
- Baseline demographics were similar across LTPs; year of LTP initiation reflects FDA approval dates (**Table 1**)

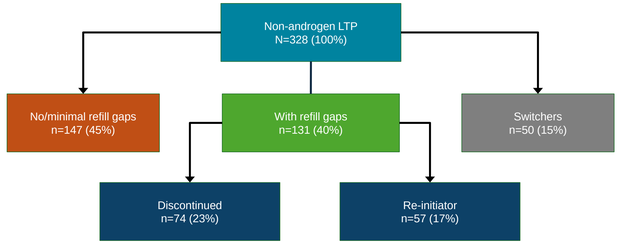
Table 1. Baseline demographics of the overall study population and by index LTP

	Overall LTP	IV C1INH	SC C1INH	Berotralstat	Lanadelumab
Patients, n (%)	328 (100)	54 (17)	97 (30)	39 (12)	138 (42)
Female, n (%)	230 (70)	42 (78)	72 (74)	25 (64)	91 (66)
Age (y) at index date, mean ± SD	41.2 ± 15.5	39.3 ± 18.3	38.8 ± 15.9	45.3 ± 14.5	42.3 ± 14.3
Region, n (%)					
South	152 (46)	23 (43)	47 (48)	14 (36)	68 (49)
Midwest	73 (22)	14 (26)	16 (16)	10 (26)	33 (24)
West	52 (16)	5 (9)	19 (20)	8 (21)	20 (14)
East	51 (16)	12 (22)	15 (15)	7 (18)	17 (12)
Year of initiation, n (%)					
2016	10 (3)	10 (19)	0	0	0
2017	35 (11)	26 (48)	9 (9)	0	0
2018	72 (22)	12 (22)	36 (37)	0	24 (17)
2019	68 (21)	2 (4)	19 (20)	0	47 (34)
2020	33 (10)	1 (2)	15 (15)	1 (3)	16 (12)
2021	69 (21)	2 (4)	13 (13)	23 (59)	31 (22)
2022	41 (13)	1 (2)	5 (5)	15 (38)	20 (14)

C1INH, C1 esterase inhibitor; IV, intravenous; LTP, long-term prophylaxis; SC, subcutaneous; SD, standard deviation; y, years.

- Of 328 LTP users, 147 (45%) had no or minimal refill gaps, 131 (40%) had refill gaps (including 74 who discontinued), and 50 (15%) switched LTPs (**Figure 3**)
- Mean PDC among those patients with no/minimal refill gaps was 93% compared with 42% among those with refill gaps

Figure 3. Patient cohort populations



LTP, long-term prophylaxis.

- Overall, most patients (67.1%; 220/328) had ≥1 post-index on-demand therapy claim (**Table 2**)
- During the 1-year follow-up period, 17% of LTP patients had at least 1 HAE-related claim for an ER visit; among whom the average number of visits was 3.4 (**Table 2**)
- The proportion of patients admitted for inpatient stay decreased from 12% pre-LTP to 8% post-LTP. Among those with ≥1 visit during follow-up, there was an average of 2.2 inpatient visits with a median of 3 days of stay (**Table 2**)

Table 2. Annualized HAE-related healthcare resource utilization by LTP patient cohort

Parameter, all patients	Overall LTP		No/minimal refill gaps		With refill gaps		Switchers	
	Baseline (n=300)	Follow-up (n=328)	Baseline (n=138)	Follow-up (n=147)	Baseline (n=116)	Follow-up (n=131)	Baseline (n=46)	Follow-up (n=50)
ER visits								
% of patients with ≥1 visit	21%	17%	18%	12%	22%	17%	26%	30%
No. visits[a]	3.1	3.4	2.1	1.8	4.4	4.4	2.6	3.9
Home health visits								
% of patients with ≥1 visit	3%	9%	1%	5%	4%	8%	7%	20%
No. visits[a]	9.9	15.8	20.3	31.6	4.9	6	11.5	15.6
Outpatient visits								
% of patients with ≥1 visit	88%	81%	88%	84%	86%	73%	89%	96%
No. visits[a]	3.2	3.9	2.9	3.3	3.7	3.7	3.3	5.8
Inpatient visits								
% of patients with ≥1 visit	12%	8%	9%	5%	13%	9%	20%	10%
No. visits[a]	1.8	2.2	1.3	2.3	1.9	1.8	2.2	3.0
Length of stay, days								
Mean ± SD	3.1 ± 2.6	4.3 ± 4.8	2.3 ± 1.7	5.3 ± 5.5	4.2 ± 3.3	4 ± 5.1	2.4 ± 1.6	3.5 ± 3.3
Median (IQR)	2 (1.0, 4.0)	3 (1.0, 5.0)	2 (1.0, 3.0)	3 (1.0, 7.0)	3 (1.0, 7.0)	2 (1.0, 5.0)	2 (1.0, 3.0)	3 (1.0, 3.5)

[a]Mean number of visits per patient per year among patients with ≥1 visit.

ER, emergency room; HAE, hereditary angioedema; IQR, interquartile range; LTP, long-term prophylaxis; SD, standard deviation.

- HAE-related healthcare costs per patient per year were $165,348 pre-LTP and $515,333 post-LTP, driven by LTP pharmacy costs ($395,845) (**Table 3**)
  - The no/minimal refill gaps cohort had the highest increases in LTP pharmacy costs ($524,191), partially offset by decreased on-demand pharmacy costs (–$107,919); changes in other costs were minimal
  - Costs increased 143% in the refill gaps cohort, with the smallest increase in LTP costs ($219,900), partially offset by reduced on-demand pharmacy costs (–$16,152)
  - LTP switchers had cost increases of 224%, driven by increases in LTP ($479,487) and on-demand pharmacy costs ($11,079)

Table 3. Annualized mean cost per patient by cost type and by LTP patient cohort

Parameter, all patients	Overall LTP		No/minimal refill gaps		With refill gaps		Switchers	
	Baseline (n=300)	Follow-up (n=328)	Baseline (n=138)	Follow-up (n=147)	Baseline (n=116)	Follow-up (n=131)	Baseline (n=46)	Follow-up (n=50)
Medical costs								
ER/IP[a]	$23,060	$14,716	$10,284	$12,230	$31,159	$15,646	$31,385	$16,235
OP/HH/other[a]	$2255	$1668	$808	$934	$4552	$1869	$970	$3214
Pharmacy costs								
On-demand	$217,857	$167,462	$217,740	$109,821	$202,768	$186,616	$247,543	$258,622
Other[a]	$14,214	$4193	$26,935	$653	$4075	$7928	$2340	$1327
LTP	$0	$395,845	$0	$524,191	$0	$219,900	$0	$479,487
Total healthcare costs	$165,348	$515,333	$165,937	$597,851	$143,843	$350,098	$217,812	$705,647

[a]Average costs calculated among those with ≥1 claim for healthcare resource utilization.

ER, emergency room; HH, home health; IP, inpatient; LTP, long-term prophylaxis; OP, outpatient.

Conclusions

- **In patients with LTP refill gaps, the utilization of ER and inpatient visits was proportionally higher, and reductions in on-demand pharmacy costs were lower, compared with those with no/minimal refill gaps**
- **Total HAE-related healthcare costs increased after LTP initiation, primarily driven by LTP pharmacy costs, without significant offset in overall medical cost reduction or non-LTP pharmacy costs**
- **Annualized on-demand pharmacy costs pre- and post-LTP initiation and total healthcare costs were highest in LTP switchers**

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