Hereditary Angioedema (HAE) Real-World Prophylactic and On-demand Treatment Cost in a 15 Million Commercially Insured Population: Comparison of C-1 Inhibitor (Haegarda®) versus Lanadelumab (Takhzyro®) Treated Members

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BACKGROUND

- HAE is a rare autosomal dominant disease characterized by recurrent episodes of subcutaneous or submucosal edema, typically involving the arms, legs, hands, feet, bowels, genitalia, trunk, face, tongue, or larynx.[1] Most cases of HAE are caused by mutations that result in quantitative deficiency of, or dysfunctional, C-1 esterase inhibitor (C1-INH), a protease inhibitor involved in the kallikrein-bradykinin pathway.
- Four different products are approved for on-demand treatment of acute episodes: subcutaneous (SC) ecallantide (Kalbitor®), a plasma kallikrein inhibitor; SC icatibant (Firazyr®), a bradykinin receptor antagonist; and two intravenous (IV) C1-INH drugs, Berinert® and Ruconest®.
- Patients with frequent episodes may be treated with long-term prophylaxis. Three products have FDA approval for prophylaxis: IV C1-INH (Cinryze®), approved 10/10/2008; SC C1-INH (Haegarda®), 6/22/2017; and SC lanadelumab (Takhzyro®), 8/23/2018, a monoclonal antibody that inhibits plasma kallikrein.
- The Institute for Clinical and Economic Review (ICER) conducted a review of the prophylactic agents from their clinical trials.[2] Models showed that all three drugs had incremental cost-effectiveness ratios above the commonly accepted willingness-to-pay threshold of $150,000 per quality-adjusted life year, but "results of the models were very sensitive to baseline attack rates, prophylactic and on-demand drug costs, and treatment effect estimates."[3]
- Real-world total HAE treatment cost associated with the newest prophylactic therapies is needed to help inform formulary placement decisions, cost-effectiveness comparisons, and value-based contract negotiations.

TABLE 1

Haegarda and Takhzyro Analytic Sample Identification

	Member Attrition	
Analytic sample identification criteria	**Takhzyro**	**Haegarda**
Any claim for the drug between June 2017 and Sept 2019	106	105
Index claim prior to Feb 1, 2019	50	84
Continuously eligible for 6 months prior to index claim (or since FDA approval)	50	70
Continuously eligible for 6 months after index claim	40	58
Claim(s) for only 1 HAE prophylaxis agent during 6 months after index claim	36	40
Claim for drug between 150 and 180 days after index claim	29	29

HAE = Hereditary Angioedema

OBJECTIVE

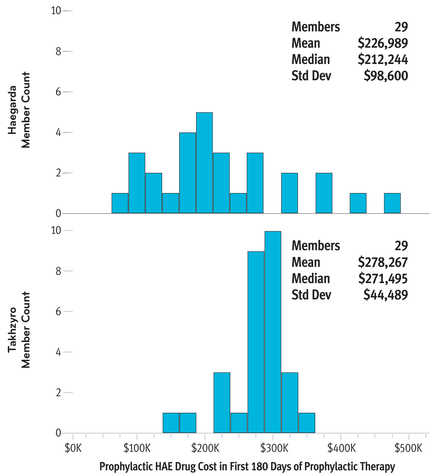
- Among commercially insured members newly starting prophylactic therapy with Haegarda (Haeg) or Takhzyro (Tak), compare six-month:
  1) HAE prophylactic drug cost,
  2) percentage using any on-demand agents, and
  3) cost of HAE on-demand agents.

METHODS

- From 15 million commercially insured members with integrated medical and pharmacy claims, we identified members newly starting Haeg or Tak prior to 2/1/2019 who had continuous eligibility for at least 180 days following their first Haeg or Tak claim.
- New starts were defined as members continuously eligible for six months prior to their first Haeg or Tak claim (index claim) or, for Tak, continuously eligible since the FDA approval date.
- The comparison sample was further limited to those who used only one prophylactic agent during follow-up and continued therapy for at least 150 days.
- Cost was defined as the plan-plus-member cost after network discounts, but with no other adjustments. Cost comparisons were made using Student's T-test.

FIGURE 1

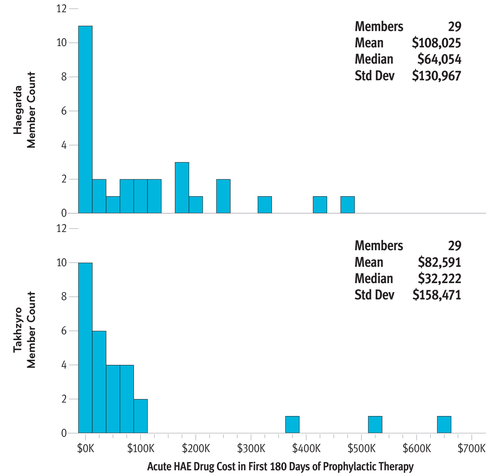
Per patient cost of Haegarda or Takhzyro during the first 180 days of therapy



HAE = Hereditary Angioedema
Std Dev = Standard Deviation

FIGURE 2

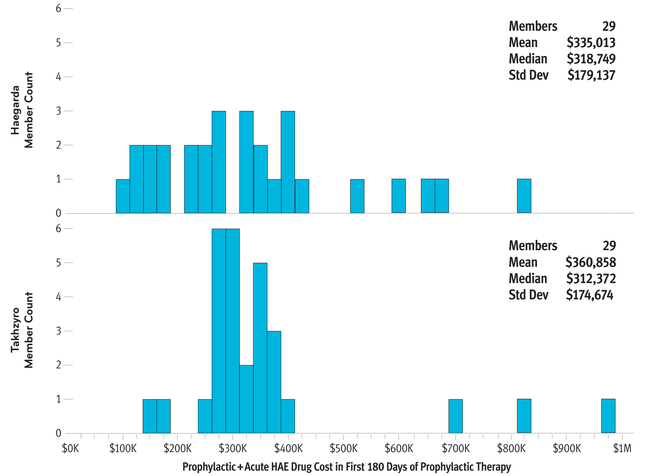
Per patient cost of acute HAE drugs during the first 180 days of therapy of Haegarda and Takhzyro



HAE = Hereditary Angioedema
Std Dev = Standard Deviation

FIGURE 3

Per patient prophylactic plus acute HAE drugs cost during the first 180 days of Haegarda or Takhzyro therapy



HAE = Hereditary Angioedema
Std Dev = Standard Deviation

RESULTS

- There were 84 Haeg and 50 Tak members with first claim before 2/1/2019, 29 of each who met the additional analytic criteria. Table 1 shows the number of members excluded by sequential criteria.
- 23 of 29 (79.3%) Haeg and 21 of 29 (72.4%) Tak were female. Mean age (years) was 40.1 for Haeg and 43.5 for Tak.
- Figures 1–3 show observed HAE drug cost distributions.
  - Cost of prophylactic therapy for 180 days was: mean $226,989 Haeg vs. $278,267 Tak, p = 0.013.
  - 18 of 29 (62.1%) Haeg vs. 19 of 29 (65.5%) Tak had a claim for an on-demand agent. Cost of on-demand therapy for 180 days was: mean $108,025 for Haeg vs. $82,591 for Tak, p = 0.508.
  - Total cost of prophylactic plus any on-demand therapy for 180 days was: mean $335,013 for Haeg vs. $360,858 for Tak, p = 0.580.

LIMITATIONS

- The researchers did not have access to patient body weight. If the Haeg users had lower weight than the Tak users, this may have contributed to lower cost of prophylactic therapy since Haeg is dosed by body weight while Tak has a fixed dosing.
- This study compares utilization and cost of HAE drugs during the first 180 days after newly starting prophylactic therapy with either Haeg or Tak. If a patient is well-controlled after more than six months of therapy, Tak dosing recommendations allow for doubling the time interval between doses from every two weeks to every four weeks, which would significantly reduce the cost for Tak users, so additional follow-up is needed to assess the average cost of long-term prophylaxis.
- The results from this study population may not be representative of other populations due to the small size of the sample.

CONCLUSIONS

- In this small sample of members newly starting prophylactic therapy for HAE with either SC C1-inhibitor (Haegarda) or lanadelumab (Takhzyro), mean prophylactic treatment cost for 180 days was over $51,000 (22%) higher for lanadelumab.
- There was no difference in the percentage of members with any use of on-demand HAE agents and no significant difference in the mean cost of on-demand therapy, although Takhzyro averaged $25,500 less.
- These real-world data suggest Haegarda may be lower cost than Takhzyro during the first 180 days of HAE prophylaxis treatment; however, the analysis consisted of a small sample size. It will be important to have longer follow-up of members treated with Takhzyro to determine what fraction of members reduce their dosing frequency.
- These findings may be used to inform cost-effectiveness modeling and value-based contract negotiations.

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