

Hereditary Angioedema: A Comprehensive Integrated Medical and Pharmacy Claims Analysis of Utilization and Costs Among 15 Million Commercially Insured Members

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Background

- Hereditary angioedema (HAE) is a rare genetic disease affecting about 1 in 50,000 people in the U.S. and treatment ranges from thousands of dollars to over a million per year.^{1,2}
- On-demand therapy for HAE attacks and HAE attack prophylaxis are both available. 2017 International guidelines recommend that all patients have enough medication available for on-demand of two attacks and always carry on-demand medication, however not every HAE patient will need or use prophylactic treatments.³
- 2017 International guidelines developed by the World Allergy Organization (WAO) in collaboration with the European Academy of Allergy and Clinical Immunology (EAACI) recommend that long-term prophylaxis be considered in all patients with severely symptomatic (Type 1 or Type 2) HAE, taking into consideration numerous factors such as disease activity, frequency of attacks, and failure to adequately control attacks with appropriate on-demand treatment.³
- Acute and prophylactic HAE specialty drugs are administered through both the medical and the pharmacy benefit.
- In 2016, the cost of HAE specialty drugs across Prime's commercial book of business was \$0.48 per member per month (PMPM).²
- A new HAE prophylaxis treatment, Haegarda[®], was approved in June 2017 and launched in July 2017. Haegarda and other HAE treatments in the pipeline increase the importance of insurers and health plans understanding their own HAE utilization and expenditures.
- Little real-world data is available examining HAE treatment patterns or cost of care.

Objective

- To identify individuals utilizing HAE drugs and describe their characteristics, health care services use, and expenditures.
- Identify managed care pharmacy management opportunities.

Methods

- Integrated medical and pharmacy claims data from an average of 15 million commercially insured members per month were queried from July 1, 2015 to June 30, 2017 (analysis period).
- Members were identified by the presence of a medical or pharmacy claim for at least one HAE specialty medication in the first half of 2016.
- HAE specialty drugs, defined as Berinert[®], Firazyr[®], Kalbitor[®], or Ruconest[®], were identified using Healthcare Common Procedure Coding System (HCPCS) or Generic Product Identifier (GPI) codes.
- A member's earliest HAE claim date of service in the first half of 2016 on the medical or pharmacy benefit was considered their index date.
- Members were required to be continuously enrolled six months prior to and 12 months following their index date, for a total of 18 months continuous enrollment.
- Member characteristics, health care utilization and expenditures were evaluated over the 12 months following their index date (post-period) and described based on total HAE expenditures, >\$1,000,000 and less than \$1,000,000 (\$1M).
- New starts were defined as members with no HAE claims in the pre-period (six months prior to index date).
- Members were classified as using two or more different HAE specialty drugs in the post-period.
- Members with HAE specialty pharmacy claims only, HAE medical claims only and members with both HAE pharmacy and medical claims were identified.
- Emergency room (ER) visits, hospitalizations and office visits were identified by revenue codes in the post-period.
- All medical and pharmacy claims allowed amounts (plan paid plus member paid) were summed to calculate total cost of care in the post-period.
- The proportion of days covered (PDC) for Cinryze users was calculated in the post-period. If a member's PDC was ≥ 80% they were assumed to be using Cinryze for prophylaxis (Food and Drug Administration [FDA] labeled indication).
 - For Cinryze medical claims, all claims were assigned a 30-day supply for PDC calculations.
- Figure 1 is a visual representation of the 10 members with over \$1 million (>\$1M) in HAE specialty drug expenditures over 12 months. There is one box for each HAE drug claim on the medical or pharmacy benefit in the post-period; the width of the box is the days supply from the pharmacy claim record. All medical claims were assigned a 30-day supply.

Results

- Between Jan. 1, 2016 and June 30, 2016, there were 226 commercially insured members with at least one HAE drug claim and 111 (49.1%) met continuous enrollment criteria.
- The 111 continuously enrolled members had an average age of 43 years old, with a range of 10 years to 71 years, and 75% (83 of 111) were female. (Table 1)
 - 48 (43%) had claims for two or more different HAE drugs.
 - 27 (24%) had HAE drug claims on both the medical and pharmacy benefits; 25 (23%) members had HAE drug claims on the medical benefit only.
 - 41 (37%) were new starts.
 - 10 (9%) had over \$1 million (>\$1M) in HAE drug spend during the post-period; none of these members were new starts.
 - 28 (61%) of 46 Cinryze users in the total HAE population were classified as Cinryze prophylaxis users.
- HAE specialty drug expenditures (Table 2)
 - The 10 members with over \$1 million (>\$1M) in HAE drug spend during the 12-month post-period accounted for \$13.3 million (30%) of the \$43.9 million overall HAE drug spend.
 - Of the HAE specialty drugs studied, Cinryze had the highest total spend at \$25.1M (57% of overall HAE drug spend) with 71% of these expenditures coming through the medical benefit.
 - Firazyr had the second highest total spend at \$13.2M (30% of overall HAE drug spend), with only 3% on the medical benefit.
- Total cost of care (Table 3)
 - The average total cost of care across all HAE members was \$409,925 over 12 months.
 - HAE drugs made up 97% of the total cost of care for HAE members, or \$395,507 over 12 months.
 - Among members with less than \$1M in HAE drug spend over 12 months, the average total cost of care was \$315,680 and the median total cost of care was \$197,210.

Limitations

- Pharmacy and medical claims have the potential to be miscoded and include assumptions of members' actual drug use and diagnoses.
- The data used in this study was limited to a commercial population and results are not generalizable to Medicare or Medicaid populations.
- Medical claims do not include days supply information. For this analysis, all medical claims were assigned a 30-day supply, which may not accurately represent the days supply for each individual medical claim. However, this would only affect the Cinryze PDC calculations and the visual representation of claims in Figure 1.

Table 1. Hereditary Angioedema Member (N = 111) Characteristics

Characteristics	All members N=111	>\$1M in HAE spend N=10	<\$1M in HAE spend N=101
Mean age, years (standard deviation)	43 (16)	43 (13)	42 (16)
Female	83 (75%)	9 (90%)	74 (73%)
2 or more different HAE specialty drugs	48 (43%)	7 (70%)	41 (41%)
New start—no HAE claim in pre-period	41 (37%)	0 (0%)	41 (41%)
At least 1 office visit	100 (90%)	10 (100%)	90 (89%)
At least 1 emergency room visit	50 (45%)	8 (80%)	42 (42%)
At least 1 hospitalization	11 (10%)	2 (20%)	9 (9%)
Cinryze prophylaxis users (PDC ≥80%)*	28 of 46 Cinryze users (61%)	7 of 8 Cinryze users (88%)	21 of 38 Cinryze users (55%)
HAE claims from both medical and pharmacy benefits	27 (24%)	4 (40%)	23 (23%)
HAE medical claims only	25 (23%)	4 (40%)	21 (21%)
HAE pharmacy claims only	59 (53%)	2 (20%)	57 (56%)

HAE = hereditary angioedema, M = million, PDC = proportion of days covered

*All Cinryze medical claims were assigned a 30-day supply for PDC calculations

Integrated medical and pharmacy claims data from an average of 15 million commercially insured members per month were queried from July 1, 2015 to June 30, 2017. Members with an HAE specialty medical or pharmacy claim in 1H2016 were included in the analysis. A member's index date was defined as the earliest HAE claim date of service in 1H2016. Members were required to be continuously enrolled six months prior to (pre-period) and 12 months following their index date (post-period). Emergency room (ER) visits, hospitalizations and office visits were identified by revenue codes in the post-period. All medical and pharmacy claims allowed amounts (plan paid plus member paid) were summed to calculate total cost of care in the post-period.

Table 2. Hereditary Angioedema Drug Expenditures Medical and Pharmacy Benefits: One Year Follow-up Among 111 Hereditary Angioedema (HAE) Utilizers

HAE drug/route of administration	HAE population N=111		>\$1M in HAE spend N=10		<\$1M in HAE spend N=101	
	Total HAE drug spend	% on medical benefit	Total HAE drug spend	% on medical benefit	Total HAE drug spend	% on medical benefit
Cinryze (C1 esterase inhibitor, human)/IV	\$25,143,795	71%	\$7,428,501	78%	\$17,715,295	67%
Firazyr (icatibant)/SC	\$13,254,966	3%	\$3,650,390	0%	\$9,604,577	4%
Kalbitor (ecallantide)/SC	\$2,634,429	69%	\$2,225,937	70%	\$408,493	66%
Berinert (C1 esterase inhibitor, human)/IV	\$2,228,365	7%	\$8,049	100%	\$2,220,315	7%
Ruconest (C1 esterase inhibitor, recombinant)/IV	\$139,671	26%	\$36,305	100%	\$103,366	0%
Total	\$43,901,227	46%	\$13,349,181	55%	\$30,552,046	42%

HAE = hereditary angioedema, IV = intravenous, SC = subcutaneous, M = million

Integrated medical and pharmacy claims data from an average of 15 million commercially insured members per month were queried from July 1, 2015 to June 30, 2017. Members with an HAE specialty medical or pharmacy claim in 1H2016 were included in the analysis. A member's index date was defined as the earliest HAE claim date of service in 1H2016. Members were required to be continuously enrolled six months prior to (pre-period) and 12 months following their index date (post-period). Emergency room (ER) visits, hospitalizations and office visits were identified by revenue codes in the post-period. All medical and pharmacy claims allowed amounts (plan paid plus member paid) were summed to calculate total cost of care in the post-period. Some totals may not sum due to rounding.

Conclusions

- Individuals utilizing HAE drugs were extremely rare at 15 per million in this commercial population, for a prevalence of 1 per 66,667.
- HAE specialty drugs accounted for the majority (97%) of the total cost of care for these members. There is no opportunity for medical cost offset, so savings must come from ensuring appropriate HAE pharmacotherapy.
- HAE analyses require integrated medical and pharmacy claims, as one in four HAE drug utilizers had an HAE drug claim in both the medical and pharmacy benefits and 46% of the HAE drug expenditures were through the medical benefit.

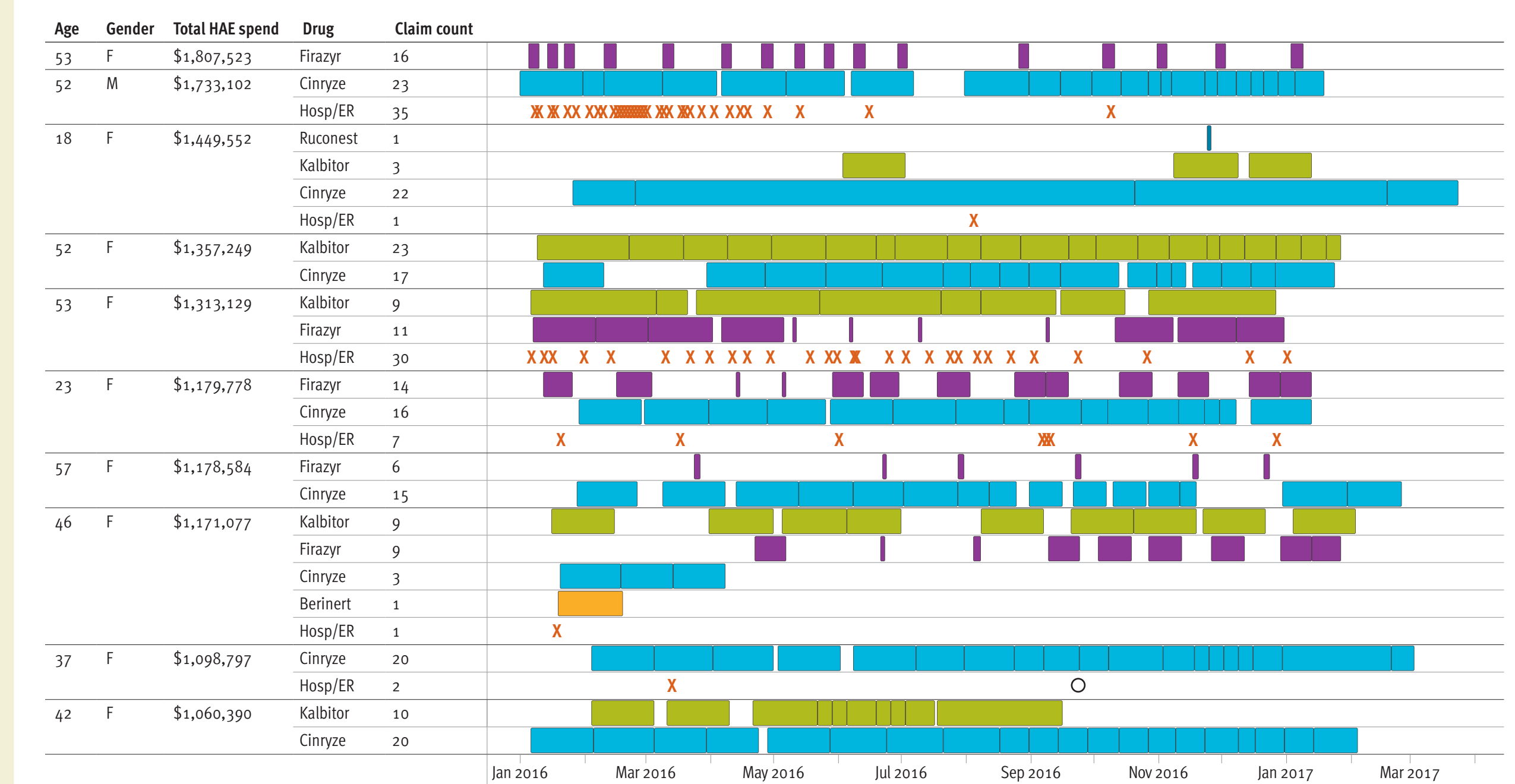
Table 3. Hereditary Angioedema Members (N = 111) Total Cost of Care Over One Year Follow-up

Cost of care	HAE population N=111	>\$1M in HAE spend N=10	<\$1M in HAE spend N=101
HAE drug expenditures (% of total cost of care)	\$43,901,227 (97%)	\$13,349,181 (98%)	\$30,552,046 (96%)
All other medical and pharmacy costs	\$1,600,485	\$268,867	\$1,331,618
Total cost of care	\$45,501,712	\$13,618,048	\$31,883,664
Mean cost per patient	\$409,925	\$1,361,805	\$315,680
Median cost per patient	\$339,302	\$1,296,882	\$197,210

HAE = hereditary angioedema, M = million

Integrated medical and pharmacy claims data from an average of 15 million commercially insured members per month were queried from July 1, 2015 to June 30, 2017. Members with an HAE specialty medical or pharmacy claim in 1H2016 were included in the analysis. A member's index date was defined as the earliest HAE claim date of service in 1H2016. Members were required to be continuously enrolled six months prior to (pre-period) and 12 months following their index date (post-period). Emergency room (ER) visits, hospitalizations and office visits were identified by revenue codes in the post-period. All medical and pharmacy claims allowed amounts (plan paid plus member paid) were summed to calculate total cost of care in the post-period.

Figure 1. Hereditary Angioedema: 10 Members with >\$1 Million in Hereditary Angioedema Drug Expenditures Over One Year Among 15 Million Commercially Insured Members



HAE = hereditary angioedema, Hosp = hospitalization, ER = emergency room (visit)

Members were derived from a population of 15 million commercially insured members with any claim for an HAE specialty drug (Berinert, Cinryze, Firazyr, Kalbitor, Ruconest) on the medical or pharmacy benefit in the first half of 2016 (1H2016) and had over \$1 million HAE expenditures over the 12-month follow up period. Each box represents an HAE medical or pharmacy claim and the corresponding days supply is represented by the box width. All medical claims were assigned a 30-day supply.

References

- Zuraw BL. *N Engl J Med*. 2008;359:1027-1036. <https://www.ncbi.nlm.nih.gov/pubmed/18768946>.
- Prime Therapeutics LLC Internal Data 2016.
- Maurer M, et al. *Allergy*. 2018 Jan 10 [Epub ahead of print]. <https://www.ncbi.nlm.nih.gov/pubmed/29318628>.