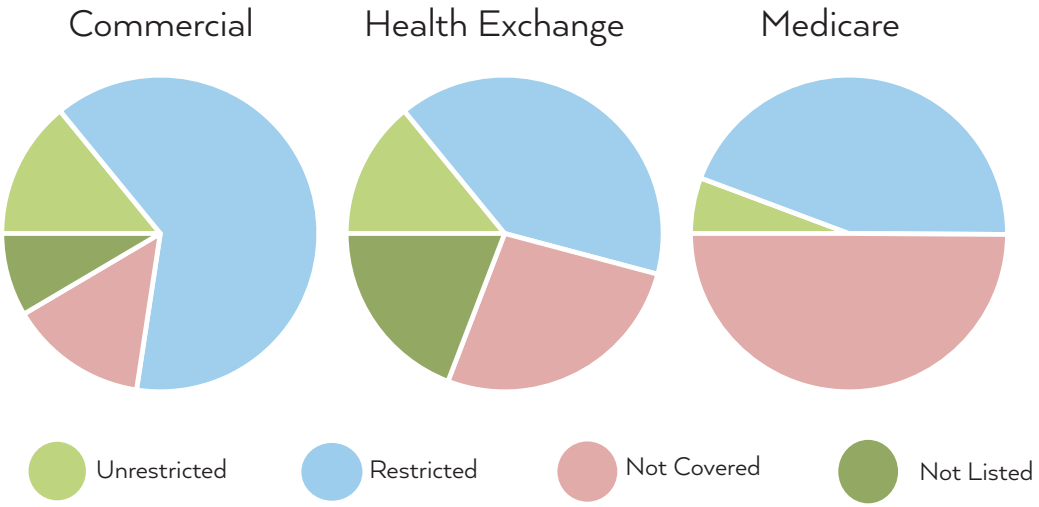


Reality Check: **Hereditary Angioedema**

Coverage

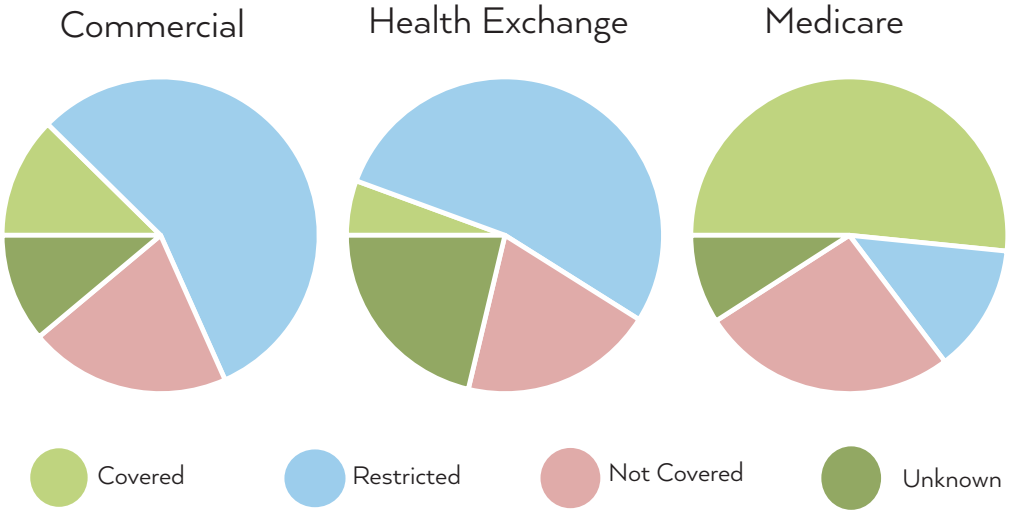
Pharmacy Benefit

Under the pharmacy benefit , more than 63% of the covered lives in commercial formularies have utilization management restrictions on hereditary angio-edema (HAE) medications. About half of the lives under Medicare pharmacy benefit formularies are not covered for at least one of the drugs.



Medical Benefit

Payer medical benefit cover-age for HAE treatments provides a different view of the situation. More than 50% of the lives under commercial and health exchange policies are covered with management restrictions, while only 13% of Medicare beneficiaries have such restrictions in place.



Key Players

CSL Behring
Biotherapies for Life™

Pharming

Shire



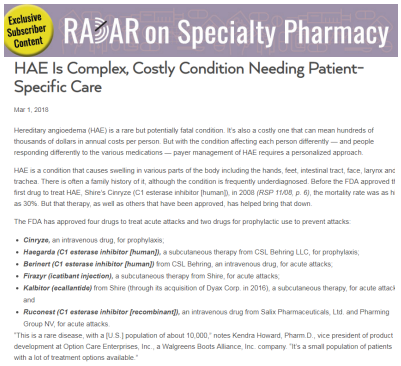
Reality Check: **Hereditary Angioedema**

Trends

HAE Needs Patient-Specific Care

HAE is a rare but potentially fatal condition, which can cost hundreds of thousands of dollars annually per person. In addition, management of this condition cannot simply be a one-size-fits-all approach. HAE is "variable and patient specific," says Kendra Howard, Pharm.D., vice president of product development at Option Care Enterprises, Inc., and "you want to manage at the patient level, patient by patient."

Subscribers to AIS's *RADAR on Specialty Pharmacy* may read the in-depth article online



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RADAR on Specialty Pharmacy

HAE Is Complex, Costly Condition Needing Patient-Specific Care

Mar 1, 2018

Hereditary angioedema (HAE) is a rare but potentially fatal condition. It's also a costly one that can mean hundreds of thousands of dollars in annual costs per person. But with the condition affecting each person differently — and people responding differently to the various medications — payer management of HAE requires a personalized approach.

HAE is a condition that causes swelling in various parts of the body including the hands, feet, intestinal tract, face, larynx and trachea. There is often a family history of it, although the condition is frequently underdiagnosed. Before the FDA approved the first drug to treat HAE, Shire's Cinryze (C1 esterase inhibitor [human]), in 2008 *(RSP 11/08, p. 6)*, the mortality rate was as high as 30%. But that therapy, as well as others that have been approved, has helped bring that down.

The FDA has approved four drugs to treat acute attacks and two drugs for prophylactic use to prevent attacks:

- ***Cinryze,*** an intravenous drug, for prophylaxis;
- ***Haegarda (C1 esterase inhibitor [human]),*** a subcutaneous therapy from CSL Behring LLC, for prophylaxis;
- ***Berinert (C1 esterase inhibitor [human])*** from CSL Behring, an intravenous drug, for acute attacks;
- ***Firazyr (icatibant injection),*** a subcutaneous therapy from Shire, for acute attacks;
- ***Kalbitor (ecallantide)*** from Shire (through its acquisition of Dyax Corp. in 2016), a subcutaneous therapy, for acute attacks; and
- ***Ruconest (C1 esterase inhibitor [recombinant]),*** an intravenous drug from Salix Pharmaceuticals, Ltd. and Pharming Group NV, for acute attacks.

"This is a rare disease, with a [U.S.] population of about 10,000," notes Kendra Howard, Pharm.D., vice president of product development at Option Care Enterprises, Inc., a Walgreens Boots Alliance, Inc. company. "It's a small population of patients with a lot of treatment options available."

FDA Approves New Medication

In August 2018, the FDA approved Shire plc's Takhzyro (lanadelumab-flyo) for prophylaxis to prevent hereditary angioedema attacks in people at least 12 years old. The plasma kallikrein inhibitor is the first monoclonal antibody the agency has approved for this indication.

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New FDA Specialty Approvals

Sep 1, 2018

Aug. 15: The FDA expanded the approval for Kalydeco (ivacaftor) to include the treatment of children with cystic fibrosis a least 12 months old who have at least one mutation in their cystic fibrosis transmembrane conductance regulator (CFTR) gen that is responsive to Kalydeco based on clinical and/or in vitro assay data. The agency first approved the Vertex Pharmaceuticals Inc. drug in January 2012 *(RSP 2/12, p. 8)*. Dosing is age- and weight-based. The product is available as a 150 mg tablet and oral granules. Website GoodRx lists the price of one carton containing 56 150 mg tablets as more than $23,700. Visit www.kalydeco.com.

Aug. 16: The FDA granted an additional approval to Lenvima (lenvatinib) for the first-line treatment of people with unresectable hepatocellular carcinoma (HCC). The agency initially approved the capsule from Eisai Inc. and Merck & Co., Inc for the treatment of differentiated thyroid cancer in 2015 *(RSP 3/15, p. 11)*; it's also approved for renal cell carcinoma *(RSP 6/16, p. 6)*. Dosing for the newest indication is 12 mg once daily for people weighing at least 60 kg and 8 mg once daily for people less than 60 kg. According to Reuters, Eisai will price the recommended starting dose for HCC at $15,970 for a 30-day supply. Visit www.lenvima.com.

Aug. 17: The FDA gave accelerated approval to Opdivo (nivolumab) for the treatment of people with metastatic small cell lung cancer whose cancer has progressed after platinum-based chemotherapy and at least one other line of therapy. The FDA first approved the Bristol-Myers Squibb Co. programmed death receptor-1 (PD-1) inhibitor in December 2014 for the treatment of unresectable or metastatic melanoma *(RSP 1/15, p. 6)*. Dosing for the newest indication is 240 mg as a 30-minute intravenous infusion every two weeks. GoodRx lists the price of one 100 mg/10 mL vial as more than $2,600. Visit www.opdivo.com.

Aug. 17: The FDA gave an additional indication to Eylea (aflibercept) for the treatment of wet age-related macular degeneration on a 12-week dosing schedule. The Regeneron Pharmaceuticals, Inc. intravitreal injection already was approved for use every four weeks and every eight weeks after three initial monthly doses. The FDA initially approved the drug in November 2011 *(RSP 12/11, p. 8)*. Website Drugs.com lists Eylea's price as more than $1,900. Visit www.eylea.com.

Managing HAE Is Complicated

HAE is a complex condition to manage, as patients can differ greatly in multiple aspects, such as severity and frequency of attacks, and response to therapy. Another complication in managing this patient population is that the therapies may be adjudicated under both the pharmacy and the medical benefit.

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Exclusive Subscriber Content

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Managing Hereditary Angioedema Is Complicated by Drug Coverage in Both Medical, Pharmacy Benefits

Mar 1, 2018

Hereditary angioedema (HAE) is a rare yet potentially fatal condition. It's also a complex one to manage, as patients can differ greatly in multiple aspects, such as severity and frequency of attacks, and response to therapy.

Another complication in managing this patient population is that the therapies may be adjudicated under both the pharmacy and the medical benefit. "Because of differences in route of administration, these products may vary in where these fall for coverage under the prescription vs. medical benefit," points out Lynn Nishida, area vice president of pharmacy at Solid Benefit Guidance.

There is also some overlap between the benefits. The 12th edition of the *EMD Serono Specialty Digest*, which was released in 2016, revealed that among respondents from 58 commercial health plans representing more than 146 million lives, 33% of the plans covered the HAE therapies under both the pharmacy and the medical benefits. Forty-nine percent of respondents covered the products under the medical benefit, with 18% covering them under the pharmacy benefit.

"I think the reason why we see this [overlap] is some products are labeled for self-administration," so they tend to fall on the pharmacy side, says Kendra Howard, Pharm.D., vice president of product development at Option Care Enterprises, Inc., a Walgreens Boots Alliance, Inc. company. "But they can also be given by a health care professional," she notes, so "if a nurse sent to administer Kalbitor, for example," in a patient's home, that would typically fall under the medical benefit.

Coverage ultimately depends upon "the payer, how the product is being used and how the pharmacy provider is contracted," she says.

In Prime Therapeutics LLC's 15 million commercially insured lives for which it has integrated medical and pharmacy claims data, 50% of its HAE drug costs are under the medical benefit, and 50% are under the pharmacy benefit, says April Kunze, Pharm.D., senior director of clinical formulary development and trend management strategy at Prime.



Reality Check: **Hereditary Angioedema**

Key Findings

Market Events Drive Changes

The FDA on Aug. 23, 2018, approved Shire plc's Takhzyro. CSL Behring in July 2017 launched Haegarda, the first subcutaneous C1 esterase inhibitor approved for prophylaxis against HAE attacks. In phase III is Shire's subcutaneous formulation of Cinryze.

Competition Is Expected

Health plans don't differentiate coverage among provider-administered products, and access to HAE products is not limited at the brand-level. However, increased competition is expected as more prophylactic therapies enter the market.

Medical and Pharmacy Benefit Implications

Coverage is under both the pharmacy and medical benefits. All products are specialty drugs. Self-administered products are usually covered under the pharmacy benefit. Drugs for this indication are generally covered with prior authorization (PA). When PA is defined, diagnosis of HAE is confirmed by C4 and C1-INH levels below normal as defined by the laboratory performing the test. A history of HAE attacks is required. There is minimal step restriction, with the exception of Cinryze, for which most policies will require a step through a generic alternative prophylaxis.

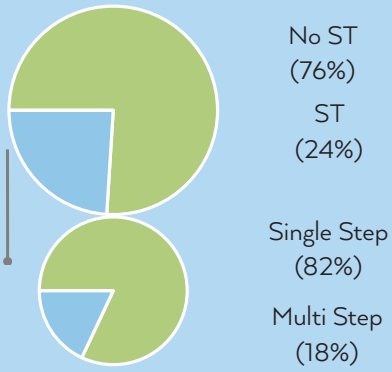
Characteristics

Indications

Hereditary Angioedema

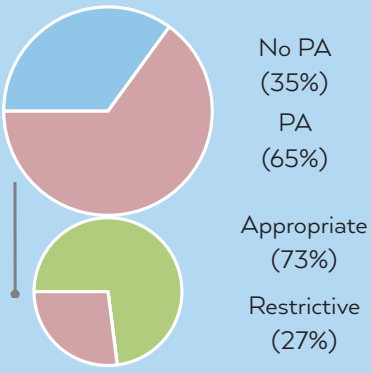
Step-Therapy (ST) Policies

A review of ST policies for payer-controlled formularies:



Prior-Authorization (PA) Policies

A review of PA policies for payer-controlled formularies:



DATA CURRENT AS OF Q1 2019