Pharmacy Focus: Hereditary Angioedema Treatment

Overview

Hereditary angioedema (HAE) is a rare hereditary disease characterized by recurrent episodes or attacks of severe swelling. Swelling most commonly occurs in the limbs, face, intestinal tract and airway. Most attacks last from two to five days. Because severe swelling can occur in the airway, urgent treatment is necessary. For billing purposes, the HAE ICD-10 definition is "Defects in the Complement System." It should not be confused with angioneurotic edema, which is an adverse event after allergen exposure that can be prevented without high-cost medications. However, be aware that specialty medications for HAE are sometimes erroneously billed under the ICD-10 code for angioneurotic edema.

In a recent advancement, the first once-daily, oral medication to prevent HAE attacks, Orladeyo™ (berotralstat), was approved by the Food and Drug Administration (FDA) December 3, 2020, at a cost of $485,000 per year.

Who Is Affected?

The prevalence of HAE in the United States is one in 50,000 individuals, without major sex or ethnic differences. There are three types of HAE. Type 1 is estimated to occur in 80 percent to 85 percent of HAE patients, while type 2 occurs in the remaining 15 percent to 20 percent. Type 3 is more common in women than men and is extremely rare, accounting for <1 percent of all cases. All three types are often managed by high-cost specialty medications.

Treatment Options

Management of HAE involves treatment of acute attacks to alleviate symptoms and chronic prophylaxis to prevent or reduce the severity of attacks.

Most recently, Orladeyo™ (berotralstat) was approved to prevent attacks of HAE in patients 12 years and older. Orladeyo™ is a once-daily, oral medication. The approval of an oral treatment under prescription benefits points to more predictable costs for HAE patients. The wholesale acquisition price is set at $485,004 annually. Orladeyo™ should be expected to be used in combination with acute medications.

All recently approved HAE medications are specialty injectables. Original low-cost, first-line therapies include danazol and stanozolol. Unapproved medications also used in the management of HAE include oxandrolone, methyltestosterone, aminocaproic acid and tranexamic acid.

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Other FDA-Approved Specialty Treatment Options

Acute Treatments

Specialty Medication	Approval	Administration	Cost Per Dose; Cost Per Month; Cost Per Year*	HCPCS Codes	ICD-10 Codes
Ruconest® (C1 esterase inhibitor [recombinant])	Approved for acute attacks in adult and adolescent patients	IV; approved for self-administration	$13,000; $13,000–$52,000; $169,000–$676,000	J0596	**D84.1** Defects in the complement system (C1 esterase inhibitor [C1-INH] deficiency) **T78.3** Angioneurotic edema
Firazyr® (Icatibant)	Approved for acute attacks in adults 18 years and older	Self-administered subcutaneous injection	$36,000; $36,000–$144,000; $468,000–$1,872,000	J1744	
Kalbitor® (Ecallantide)	Approved for acute attacks in patients 12 years and older	Subcutaneous; must be administered by a health care professional	$31,000; $31,000–$124,000; $403,000–$1,612,000	J1290	
Berinert® (complement C1 esterase inhibitor)	Approved for treatment of acute abdominal or facial attacks of hereditary angioedema (HAE) in adult and adolescent patients	IV; approved for self-administration	$26,000; $26,000–$104,000; $338,000–$1,352,000	J0597	

**Acute medications are typically reserved for as-needed use in the most serious episodes, but reserving often leads to stockpiling and attaining the maximum number of refills.*

Prophylactic Treatments

Drug	Approval	Administration	Annual Cost	HCPCS Codes	ICD-10 Codes
Cinryze® (C1 Esterase Inhibitor [Human])	Approved for routine prophylaxis against attacks in adolescent and adult patients	IV; approved for self-administration	$1,000,000 – $1,500,000	J0598	**D84.1** Defects in the complement system (C1 esterase inhibitor [C1-INH] deficiency) **T78.3** Angioneurotic edema
Haegarda® (C1 Esterase Inhibitor [Human])	Approved for routine prophylaxis to prevent attacks in adolescent and adult patients	Subcutaneous; approved for self-administration	$600,000	J0599	
Takhzyro® (lanadelumab-flyo)	Approved for routine prophylaxis to prevent attacks in people 12 years and older	Subcutaneous; approved for self-administration	$572,000	J0593	
Orladeyo™ (berotralstat)	Approved for routine prophylaxis to prevent attacks in people 12 years and older	Oral	$485,000	None	

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Plan Considerations

Hereditary Angioedema (Defects in the Complement System) is a very intimidating diagnosis for members and health plans. Some thoughts for driving quality and cost containment include:

- Providing the member with access to a disease state management program
  - — Either via the TPA, Pharmacy Benefit Manager (PBM) or pharmacy manufacturer
- Implementing utilization management tactics
  - — Create monthly and annual quantity limits
    - To deter stockpiling, which could lead to waste as the product approaches expiration
    - To control Specialty Pharmacy automatic refill programs, which could allow for claims paid for 500 days in a 365 day plan year
- Ensuring the medications are fulfilled via in-network Specialty Pharmacies
- Considering a deductible and co-insurance and the ability to receive treatment options through a Patient Assistance Program

Pharmacy Focus provides valuable information about pharmaceutical industry developments and their associated costs that can impact the growing claims trend in the self-funded insurance market. Be aware of influences and gain insight into approaches that may help to contain costs. Please share topic suggestions or feedback with **HMPharmacyServices@hmig.com**.

Resources: "Hereditary Angioedema: Epidemiology, Management, and Role of Icatibant," Ghazi A, Grant JA. Biologics. 2013, 7:103-113. doi:10.2147/BTT.S27566; Aygören-Pürsün E, Bork K. Hereditäres Angioödem [Hereditary angioedema]. Internist (Berl). 2019 Sep, 60(9):987-995. German. doi: 10.1007/s00108-019-0644-1. PMID: 31363809; "Biocryst's Orladeyo Cleared for HAE, Priced High; Is Oral Appeal Enough," Bioworld, https://www.bioworld.com/articles/500936-biocrysts-orladeyo-cleared-for-hae-priced-high-is-oral-appeal-enough, accessed December 4, 2020; Ruconest® Prescribing Information, https://www.ruconest.com/PDF/RUCONEST-Updated-Patient-PI-4.10.18.pdf, accessed December 4, 2020; Firazyr® Prescribing Information, http://www.shirecontent.com/?product=FIR&language=ENG&country=USA&contenttype=PI, accessed December 4, 2020; Kalbitor® Prescribing Information, http://www.shirecontent.com/PI/PDFs/Kalbitor_USA_ENG.pdf, accessed December 4, 2020; Berinert® Prescribing Information, http://cslbehring.vo.llnwd.net/o33/u/central/PI/US/Berinert/EN/Berinert-Prescribing-Information.pdf, accessed December 4, 2020; Cinryze® Prescribing Information, https://www.fda.gov/media/75907/download, accessed December 4, 2020; Haegarda® Prescribing Information, https://labeling.cslbehring.com/PI/US/HAEGARDA/EN/HAEGARDA-Prescribing-Information.pdf; accessed December 4, 2020; Takhzyro® Prescribing Information, https://www.shirecontent.com/PI/PDFs/TAKHZYRO_USA_ENG.pdf, accessed December 4, 2020; "US HAEA Medical Advisory Board 2020 Guidelines for the Management of Hereditary Angioedema," The Journal of Allergy and Clinical Immunology: In Practice, https://www.jaci-inpractice.org/article/S2213-2198(20)30878-3/abstract, accessed December 4, 2020.

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