Pharmacoeconomics of Orphan Disease Treatment with a Focus on Hereditary Angioedema

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KEYWORDS

• Pharmacoeconomics • Orphan disease • Hereditary angioedema • Burden
• Treatment

KEY POINTS

- Orphan diseases affect 1 in 10 individuals.
- Legislation has been successful in encouraging development of orphan disease therapies but barriers to their availability exist.
- Expenditures on orphan drugs are less than 10% of pharmaceutical expenditures and 1% of total health care costs.
- Patients with hereditary angioedema have benefited greatly from approval of novel disease-specific therapies.
- Availability of and access to these new therapies is a challenge for patients, families, and health care providers.

OVERVIEW

Hereditary angioedema (HAE) is a rare autosomal dominantly transmitted genetic disease.[1,2] It occurs in approximately 1 out of 30,000 to 80,000 individuals and affects fewer than 8000 individuals in the United States, 15,000 in North America, and 200,000 worldwide.[3,4] Although available in other countries since 1979,[5] disease-specific therapy for HAE only recently became available in the United States and North America. With the US Food and Drug Administration (FDA) approval of a human

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nanofiltered plasma-derived C1 inhibitor (C1INH) concentrate for routine prophylaxis of HAE attacks on October 10, 2008, a new era in therapy for HAE began.[6] Since 2008, 4 therapies to treat HAE attacks have received FDA approval, including a pasteurized human plasma–derived C1INH and ecallantide in 2009, icatibant in 2011, and a recombinant C1INH in 2014. These therapies are currently registered in many countries around the world (**Table 1**). (See Meng Chen and Marc Riedl's article, "Emerging Therapies in Hereditary Angioedema", in this issue.)

This burst of development and approvals has greatly benefited individuals with HAE, their families, caregivers, physicians, and health care providers.[12,13] The burden of HAE has been reduced; quality of life improved; and utilization of urgent care, emergency facilities, and hospitals decreased significantly.[14,15] Concerns have been raised, however, by health care payers in the United States and health care systems in other countries about the financial impact of these newly approved therapies on health care payment systems.[16–19] These concerns have led to barriers to and limitation of access to these potentially life-changing and lifesaving therapies.[16,17,20]

This article discusses the prevalence of orphan diseases, legislative incentives to encourage development of orphan disease therapies, and the impact of orphan disease treatment on health care payment systems. More specifically, the cost burden of HAE on patients, health care systems, and society is reviewed. The impact of availability of and access to novel and specific therapies on morbidity, mortality, and the overall burden of disease is explored. Changes in the treatment paradigms to improve effectiveness and reduce cost of treatment are presented.

ORPHAN DRUG DEVELOPMENT POLICIES AND REIMBURSEMENT ISSUES

Orphan drug policies have been established in the United States, the European Union (EU), and Japan to encourage the development of safe and effective therapies for rare diseases. The US Orphan Drug Act was enacted in 1983.[21] Under this act, a drug is given orphan designation if the disease it treats affects fewer than 200,000 individuals or if there is no reasonable expectation of profitability for the drug. Some of the incentives provided include tax credits for research costs, grants to aid in clinical research, and a 7-year marketing exclusivity for approved orphan drugs.

In 1999, the EU enacted its orphan drug policy that defines an orphan disease as a disease with 5 patients per 100,000 individuals. Research incentives are available within the EU and its member states and fees are waived for approval of the marketing application. Approved orphan drugs in the EU are given a 10-year marketing exclusivity.[22]

These policies have been successful in incentivizing companies to research and develop therapies for a wide variety of rare conditions. Before the passage of the orphan drug policies, orphan disease therapies were often neglected by pharmaceutical companies. In January, 1983, there were 38 drugs approved in the United States for orphan disorders.[23] In December 2016, 588 approved drugs are listed in the Orphan Disease Therapeutic Registry[24] and 86 designated orphan drugs approved for marketing in the EU.[25]

PREVALENCE OF ORPHAN DISEASES

There are 25 to 30 million individuals, 8% to 10% of the population of the United States, affected by 1 of the 7000 diseases designated as orphan diseases who may benefit from provisions of the Orphan Drug Act.[16,23] Treatments for these rare diseases have provided great benefits to affected individuals and their families. The high cost of many of these therapies has led to the perception by payers and society in general that treatment of orphan diseases places an inordinate burden on the health