New Treatments, Added Costs

Hemophilia, HAE Drugs Offer Options, Carry High Price Tags
The specialty pharmaceutical market continues to grow as a percentage of the overall prescription drug market, and its impact on payor trend also is rising. Many of the new treatments in the specialty drug pipeline, especially novel or breakthrough therapies, can bring new hope and treatment options for patients.

They also come with high price tags and can be a significant cost management issue for payors. Through careful, ongoing monitoring, CVS Health can provide payors the tools and clinical insights to help them stay ahead of pipeline trends.

Hemophilia A and hereditary angioedema (HAE) are among the therapy classes with notable drugs in the near-term specialty pipeline that could have a significant potential impact for both patients and payors.

**First Subcutaneous Prophylactic for Hemophilia A Patients with Inhibitors**

A genetic bleeding disorder that prevents blood from clotting, hemophilia is estimated to affect about 20,000 people in the U.S. It has two main forms:

- Hemophilia A is about four times as common as hemophilia B and occurs in 1 in 5,000 births. It is caused by a deficiency of factor VIII.
- Hemophilia B is caused by a deficiency of factor IX.

There is no cure for hemophilia and patients need lifelong treatment and care. Some treatments can be administered prophylactically to prevent bleeds. **Treatment with clotting factor replacement** is administered as on-demand therapy — when a bleeding episode occurs.

With current therapies, prophylactic treatment for hemophilia A patients varies from every other day to twice a week.

The overall hemophilia pharmaceutical market is estimated to be more than $10 billion, and is expected to grow to more than $25 billion by 2024. It is a highly competitive therapy class. All current hemophilia treatments are intravenous (IV) infusions, which have to be administered directly into the blood stream, therefore risking infection.

One of the most serious side effects of factor replacement treatment in hemophilia A and B patients is the development of inhibitors — or antibodies — which are targeted against the infused factor and neutralize its ability to stop or prevent bleeding. Approximately 25 to 30 percent of hemophilia A and 1 to 4 percent of hemophilia B patients develop inhibitors. Current treatment for patients who develop inhibitors includes the use of bypassing agents, which go around an inhibitor that is blocking the replacement factor, to help form a clot. They are typically more costly than the factor replacement products.

In the near-term hemophilia pipeline is emicizumab by Roche, which has been granted a Breakthrough Therapy Designation by the U.S. Food and Drug Administration (FDA). In clinical trials, prophylactic therapy with emicizumab has been shown to reduce bleeding in people, age 12 and older, with hemophilia A with factor VIII inhibitors. If approved, it would be the first subcutaneously administered medication for prophylactic hemophilia treatment for uses other than surgical bleeding.
In February, Roche reported the death of a patient in Phase 3 clinical trials. This followed another incident, in November 2016, of four patients demonstrating adverse reactions in emicizumab trials. However, the death was judged not to be related to the drug and the adverse events were resolved. A decision by the FDA is expected in the first quarter of 2018.

Emicizumab is also being studied in hemophilia A patients without inhibitors.

The drug could have a significant impact on the hemophilia market because subcutaneous injections may be easier for patients to administer than intravenous infusions. Patients may be able to self-administer the drug by injecting it under the skin rather than into a vein. The opportunity for improved compliance is significant. Some payors might choose to cover this medication under the medical benefit even though it is self-administered.

Another hemophilia drug that has shown promise as a prophylactic treatment in early-stage trials is fitusiran by Alnylam Pharmaceuticals. If it progresses, it could add further competition to the market. Fitusiran has shown effectiveness as a prophylactic treatment for both forms of hemophilia and would also be a subcutaneously administered treatment for patients with and without inhibitors.

HAE treatments come with high price tags

$3,117-$6,800 cost per dose

$350,000 estimated annual cost of Cinryze

Hope for Patients With a Deadly Disease

HAE is a rare hereditary condition that causes episodic attacks of swelling, which can affect different parts of the body. A protein imbalance in the body causes fluid buildup in body tissue. Both the severity of the attacks and the location of swelling can vary. Most commonly affected areas include the mouth, throat, hands, feet, face, abdomen and genitals. Bouts of swelling can last two to five days and depending on the location of the swelling, cause extreme pain, nausea and vomiting. Swelling of the larynx can be fatal.

Until recently, there were no effective treatments for HAE. The first such treatment, Cinryze, was approved as a prophylactic by the FDA in 2008. Berinert was approved in 2009 to treat acute facial and abdominal attacks, and later received expanded indications to treat laryngeal attacks and for patients younger than age 12. Both medications are administered as IV infusions.

The same year, the FDA also approved the first subcutaneous treatment for acute HAE attacks, Kalbitor.

Currently, IV-infused Cinryze is the only approved prophylactic HAE treatment. The manufacturer is also testing a subcutaneous prophylactic form of the drug. However, a new formulation of Berinert, Haegarda, is likely to be the first subcutaneous prophylaxis to be approved. A decision is expected toward the end of the second quarter.

While the HAE population is relatively small, treatment can add significant costs for payors. HAE treatments typically come with high price tags with a per-dose cost ranging from $3,117 to $6,800. At an estimated annual cost of $350,000 a year, Cinryze was one of the most expensive drugs on the market in 2016. Since there is no cure, patients require lifelong treatment.

Cinryze, the first prophylactic therapy for HAE, was approved by the FDA in 2008
Developments in the hemophilia and HAE pipelines bring new hope for many patients and have demonstrated clinical efficacy. However, existing treatments are expensive and new ones are likely to come to market with even bigger price tags. Careful monitoring of the pipeline and specialty guideline management tools will be needed to help ensure appropriate use in order to manage the impact on payor trend.

Management tools for new, high-cost specialty drugs to help mitigate payor trend impact include:

- New-to-Market Review
- Prior Authorization
- Clinical Diagnosis Review
- Utilization Management

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