New Specialty Drug for Atopic Dermatitis

1.6M Americans Could Be Candidates for Costly Treatment

Payors already dealing with the exploding cost of prescription medication – and specialty drugs in particular – are expected to face the budget impact sometime next year from at least one and perhaps more new pivotal treatments for a chronic skin condition called atopic dermatitis.

The new therapies are likely to generate high demand from patients with moderate to severe atopic dermatitis, as an estimated 19 percent of patients don’t respond to currently available treatment regimens. Patient groups are eagerly trumpeting the promise of the new treatments, partnering with the manufacturers in an awareness campaign even before all clinical trials are concluded and the U.S. Food and Drug Administration (FDA) approval is finalized.

In the fall of 2014, the FDA granted a Breakthrough Therapy designation for a biologic drug called dupilumab, jointly developed by Regeneron and Sanofi that is expected to come to market in the first quarter of 2017.

We expect the new treatment to be costly and demand will likely be high. It is critical for payors to have the right utilization management (UM) strategies, such as step therapy and prior authorization (PA), in place to help ensure the spend impact is predictable and patients are guided to the most cost-effective treatments possible.
What is Atopic Dermatitis?

About 17.8 million people in the United States – including 3 percent of adults – have some form of atopic dermatitis, an itchy, red rash that is often called eczema. It can appear all over the body, though infants often have it on the face, especially on the cheeks and chin, while children and adults tend to get it on the on the neck, wrists, and ankles, and in areas that bend, like the inner elbow and knee.

Causes of atopic dermatitis are not known but are often linked to other allergic conditions such as hay fever or asthma. There is most likely a genetic component as well.

People with atopic dermatitis are usually diagnosed when they are infants or young children, and for some, it continues into adulthood. A small number of atopic dermatitis patients are first diagnosed as adults.

Generally, people with atopic dermatitis suffer from dry, sensitive skin, and the condition is known for its intense itch. For some, especially those with moderate-to-severe atopic dermatitis, the itch may be so strong that the patient scratches until the skin bleeds. That makes the rash worse, leading to even more inflammation and itching. It also increases the potential for infection. The condition is also affected by a wide range of irritants including soaps and disinfectants, and can be affected by other factors such as food and stress.

According to the American Academy of Dermatology (AAD), the atopic dermatitis that emerges in adults is often different and more severe than what infants and children face. It can be especially noticeable around the neck and face, and cause very dry skin with a non-stop itch. For 30 percent to 50 percent of children with atopic dermatitis, the condition persists into adulthood and is a waxing and waning chronic condition.

Topical corticosteroids have been the standard treatment for most patients with atopic dermatitis for more than 60 years. Topical steroids can range from mild agents such as hydrocortisone cream (Synacort and Nutracort) to highly potent ones such as clobetasol propionate (Cormax cream/solution) and betamethasone dipropionate (Diprolene ointment). Combined with moisturizers, these topical steroid treatments can be effective. However, they can have a range of side effects from mild to severe including striae (stretch marks) and telangiectasia (purple clusters), as well as skin atrophy.

As a second-line therapy, many physicians recommend topical calcineurin inhibitors, which are nonsteroidal anti-inflammatory applications such as tacrolimus ointment (Protopic) and pimecrolimus cream (Elidel). These have been available since 2000.

These treatments, which modulate the body’s immune reaction in order to reduce inflammation, generally are reserved for short-term or intermittent long-term therapy in persons with moderate to severe atopic dermatitis, given the risks of lasting adverse effects such as atrophy. Common side effects include mild burning or stinging sensation when the medication is first applied to the skin. For patients that don’t respond to topical treatments, the AAD recommends light therapy and the use of oral immunosuppressants, such as cyclosporine, azathioprine and methotrexate, which can also have a wide range of adverse effects if used long term.

Many patients with moderate to severe atopic dermatitis continually struggle with the condition because of the lack of a long-term, effective treatment.

An estimated 1.6 million patients in the U.S. are expected to be candidates for the new treatment.
Novel Therapy

Dupilumab has a novel mechanism of action that inhibits the cytokines Interleukin 4 and Interleukin 13, thus reducing the inflammation. In studies, dupilumab has shown efficacy as both monotherapy and in combination with topical corticosteroids.

Because of this novel mode of action, dermatologists are expected to prescribe dupilumab to address a large number of patients who are not adequately controlled on topical corticosteroids, Protopic or Elidel. Based on clinical trial results, the recommended dose is likely to be 300 mg injected subcutaneously every week or every two weeks.

Expected recommendation is that the new drug should be injected every week or two.

High Trend Impact Expected

A price has not yet been announced but based on other biologic monoclonal antibodies such as Xolair and Nucala, some analysts estimate that dupilumab may cost up to $30,000 a year.

Even at a somewhat lower price estimate of $20,000 a year – about one third that of Humira – and a market penetration of 10 percent, our analysis projects an annual sales run rate of $3.2 billion. This is obviously significantly higher than the current cost of treatment which can range from as little as a dollar a day for treatments like methotrexate to nearly $500 a month for topical immunosuppressants. Corticosteroids, which are the most commonly used treatment, cost less than $150 per month per utilizer.

The trend impact of atopic dermatitis will also most likely rise in the future. Initially, dupilumab is expected to be approved for the treatment of moderate to severe atopic dermatitis in pediatric patients by 2020, which would dramatically increase the patient pool – one study estimates that in the U.S., 10.7 percent of children have atopic dermatitis.

Dupilumab is also being studied for asthma and for patients with chronic sinusitis and nasal polyposis. In addition, other companies have atopic dermatitis drugs in their pipelines. Leo Pharma and AstraZeneca are developing tralokinumab and Galderma has bought the rights to nemolizumab from Chugai Pharmaceutical. Both these injectable drugs were in Phase II clinical trials as of July 2016. In addition, Anacor Pharmaceuticals is developing crisaborole, a non-steroidal topical anti-inflammatory, for mild to moderate atopic dermatitis which may also have significant utilization.

The robust drug pipeline shows that manufacturers see a large potential market for atopic dermatitis treatments, but competing treatments also give payors the opportunity to implement additional UM tools to keep spend in line.

Cost of Treating Atopic Dermatitis

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methotrexate</td>
<td>$30</td>
</tr>
<tr>
<td>Per month</td>
<td></td>
</tr>
<tr>
<td>Topical Corticosteroids</td>
<td>$150</td>
</tr>
<tr>
<td>Per month</td>
<td></td>
</tr>
<tr>
<td>Topical Immunosuppressants</td>
<td>$500</td>
</tr>
<tr>
<td>Per month</td>
<td></td>
</tr>
<tr>
<td>Dupilumab</td>
<td>$1,500-$2,500</td>
</tr>
<tr>
<td>(estimated)</td>
<td></td>
</tr>
</tbody>
</table>
**Patient Considerations**

Atopic dermatitis, especially in its most severe form, impacts sleep and reduces the quality of life for patients and their partners. Positive clinical trials for dupilumab generated positive reaction from patient groups and also garnered significant media attention.

Given the large population of patients that could benefit from this drug, significant direct-to-consumer advertising is likely to begin after final FDA approval. It is also likely that patients who receive dupilumab prescriptions will be new to specialty pharmacy. They will be unfamiliar with the UM guidelines that come with many expensive specialty therapies. Effective communication and education will be critical to help ensure that patients who meet treatment criteria have access to treatment while managing trend impact for payors.

CVS Specialty™ offers patients with autoimmune conditions like atopic dermatitis comprehensive care with therapy-specific care teams. These experienced clinicians not only help address patient concerns about medication, but also help manage comorbidities that contribute to adverse events.

---

**Monitoring, Managing Spend**

The drug currently has no final FDA-approved label because it is still undergoing review. However in order that we – and our clients – are fully prepared for when the drug comes to market, we are monitoring literature and conducting research to help ensure the right UM guidelines are in place. It is important to note that with a patient population estimated at 1.6 million the potential for dupilumab’s impact on specialty drug spend is significant.

At CVS Health, we continually monitor the drug pipeline to proactively identify potential trend drivers and provide solutions such as Dynamic Trend Manager that rapidly identify changes in utilization and pricing that impact client trend. Our Interactive RxInsights® tool also offers clients enhanced visibility to trend drivers both at the market and plan member level, and the ability to explore specific management opportunities. Combined with our expertise in clinical information surveillance, this helps us develop effective UM programs to support clients and their members.

**In addition to PA, we expect UM criteria for dupilumab to include:**

- **Step Therapy**
  
  To promote use of first- and/or second-line effective, but less costly, treatments before providing coverage for the more expensive treatment

- **Age Authorization Check**

  Limit coverage to the age range where the drug has been shown to be safe and effective

- **Disease Severity**

  Coverage will likely be reserved for treatment situations that are on the severe end of the atopic dermatitis disease spectrum – and will align with FDA-approved labeling and clinical compendia

---

2. 2016 CVS Health Analysis.

**Subject to state law restrictions**

This document contains references to brand-name prescription drugs that are trademarks or registered trademarks of pharmaceutical manufacturers not affiliated with CVS Health.

©2016 CVS Caremark. All rights reserved. 106-39257A1 101816

---

Troy Brennan, MD
Executive Vice President, Chief Medical Officer