More than 8 million people in the United States have psoriasis, which is a chronic disease associated with overactive immune and inflammatory responses. Plaque psoriasis is the most common type of psoriasis, affecting 80% to 90% of patients. Plaque psoriasis is characterized by raised, red or purple patches of inflamed, itchy, and painful skin, which is sometimes covered with silvery-white scales. Although psoriatic plaques can form anywhere on the skin, they occur most often on the knees, elbows, scalp, nails, torso, and lower back.

An estimated 10% to 30% of patients with psoriasis will also have psoriatic arthritis. Furthermore, individuals with psoriasis have an increased risk for other conditions, including type 2 diabetes, hypertension, cardiovascular disease, eye disorders, Parkinson’s disease, and certain autoimmune disorders. Overall, nearly 60% of patients with psoriasis report that the disease affects their everyday life; those with moderate-to-severe psoriasis report the greatest negative impact on their quality of life.

Treatments for plaque psoriasis include phototherapy, topical therapies, conventional systemic therapies (ie, acitretin, cyclosporine, and methotrexate), other systemic therapies (an oral phosphodiesterase-4 inhibitor), and biologic therapies, including tumor necrosis factor blockers, interleukin (IL)-17A antagonists, IL-23 antagonists, and an IL-12/IL-23 antagonist. Biosimilar agents are also used to treat psoriasis.

Ilumya Approved for Plaque Psoriasis

On March 20, 2018, tildrakizumab-asmn (Ilumya; Sun Pharmaceutical Industries), an IL-23 antagonist, was approved by the US Food and Drug Administration (FDA) for the treatment of adults with moderate-to-severe plaque psoriasis who are candidates for systemic therapy or phototherapy. The approval of tildrakizumab-asmn was based on findings from 2 phase 3 clinical trials—reSURFACE 1 and reSURFACE 2. Ilumya (Tildrakizumab-asmn), Interleukin-23 Antagonist, Approved for the Treatment of Patients with Moderate-to-Severe Plaque Psoriasis

By Loretta Fala, Medical Writer

Overall, nearly 60% of patients with psoriasis report that the disease affects their everyday life; those with moderate-to-severe psoriasis report the greatest negative impact on their quality of life.

Mechanism of Action

Tildrakizumab-asmn is an IL-23 antagonist—a humanized immunoglobulin (Ig) G1 monoclonal antibody that selectively binds to the p19 subunit of IL-23, inhibiting its interaction with the IL-23 receptor, thereby blocking the release of proinflammatory cytokines and chemokines. IL-23, a naturally occurring cytokine, is a mediator of inflammatory and immune responses involved in the pathogenesis of psoriasis.

Dosing and Administration

Tildrakizumab-asmn is available as a 100-mg/mL solution in a single-dose prefilled syringe. The recommended dosage of tildrakizumab-asmn is 100 mg at weeks 0, 4, and every 12 weeks thereafter, and is administered by subcutaneous injection.

Pivotal Phase 3 Clinical Trials

The efficacy and safety of tildrakizumab-asmn were evaluated in 2 randomized, double-blind, placebo-controlled clinical trials—reSURFACE 1 and reSURFACE 2.
These 2 studies included 926 patients (mean age, 46 years) who were randomized to placebo or to tildrakizumab-asmn 100 mg at week 0, week 4, and every 12 weeks thereafter for up to 64 weeks. Approximately 34% of the patients previously had received phototherapy, 39% had received conventional systemic therapy, and 18% had received biologic therapy for the treatment of psoriasis. In addition, approximately 16% of patients had a history of psoriatic arthritis.

In the reSURFACE 1 and reSURFACE 2 studies, tildrakizumab-asmn 100 mg met the primary efficacy end points, showing significant clinical improvement in the proportion of patients whose Psoriasis Area and Severity Index (PASI) score was reduced by at least 75% (≥75% skin clearance) and in the Physician Global Assessment (PGA) score of 0 (clear) or 1 (minimal) at week 12 compared with placebo (Table). In reSURFACE 1, patients who were initially randomized to tildrakizumab-asmn and whose disease responded to tildrakizumab-asmn at week 28 were rerandomized to an additional 36 weeks of placebo or the same dose of tildrakizumab-asmn (every 12 weeks). At week 28, 74% of the patients who received 100 mg of tildrakizumab-asmn achieved a PASI-75 response; at week 64, 84% of the patients who received 100 mg of tildrakizumab-asmn sustained a PASI-75 response compared with 22% of the patients who received placebo. Furthermore, among patients who were rerandomized and who had a PGA score of 0 or 1 at week 28, 69% of the patients who continued to receive tildrakizumab-asmn 100 mg every 12 weeks sustained a PGA score of 0 or 1 at week 64 compared with 14% of patients who received placebo.

Table Tildrakizumab-asmn versus Placebo at Week 12 in Patients with Plaque Psoriasis*

<table>
<thead>
<tr>
<th>Efficacy parameter</th>
<th>reSURFACE 1 study</th>
<th>reSURFACE 2 study</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Tildrakizumab-asmn 100 mg, N (%) (N = 309)</td>
<td>Placebo, N (%) (N = 154)</td>
</tr>
<tr>
<td>Co-primary end points</td>
<td>179 (58)</td>
<td>11 (7)</td>
</tr>
<tr>
<td>PASI-75</td>
<td>197 (64)</td>
<td>9 (6)</td>
</tr>
<tr>
<td>Select secondary end points</td>
<td>107 (35)</td>
<td>4 (3)</td>
</tr>
<tr>
<td>PASI-90</td>
<td>43 (14)</td>
<td>2 (1)</td>
</tr>
</tbody>
</table>

*Nonresponder imputation.

Adverse Reactions

The most common (incidence ≥1%) adverse reactions associated with tildrakizumab-asmn therapy were upper respiratory infections (14%), injection-site reactions (3%), and diarrhea (2%). During the placebo-controlled periods of the 2 reSURFACE studies in the tildrakizumab-asmn 100-mg group, adverse reactions were reported in 48.2% of patients who received tildrakizumab-asmn compared with 53.8% of patients who received placebo. The rates of serious adverse events were 1.4% versus 1.7%, respectively.

Infections occurred slightly more often in patients who received tildrakizumab-asmn than in the placebo group. The rate of severe infections for each group was ≤0.3%.

Contraindications

Tildrakizumab-asmn is contraindicated in patients who have a serious hypersensitivity reaction to treatment with tildrakizumab-asmn or to any of its excipients.

Drug Interactions

Live vaccines should not be administered to patients who receive tildrakizumab-asmn.

Use in Specific Populations

Data on the use of tildrakizumab-asmn in pregnant women are limited and therefore insufficient to establish a potential risk of adverse developmental outcomes on the fetus. Tildrakizumab-asmn can potentially transfer from the mother to the fetus via the transport of IgG across the placental barrier.

Data are insufficient to determine the effect of tildrakizumab-asmn on the breastfed infant or on milk production. The health benefits of breastfeeding and the mother’s clinical need for tildrakizumab-asmn should be weighed against the potential adverse effects of tildrakizumab-asmn on the breastfed child.

In clinical trials, no differences in the efficacy or safety of tildrakizumab-asmn were observed between patients aged ≥65 years and younger patients; however, the number of older patients was insufficient to establish response to tildrakizumab-asmn by age.

Warnings and Precautions

Tildrakizumab-asmn is associated with hypersensitivity reactions, including angioedema and urticaria. The drug should be discontinued promptly if a serious allergic reaction occurs, and appropriate treatment should be initiated.

The use of tildrakizumab-asmn is linked to an increased risk for infection. If a patient has a serious infection, discontinuation of tildrakizumab-asmn should be considered until the infection resolves.
Patients should be evaluated for tuberculosis before treatment with tildrakizumab-asrn is initiated. Patients should be monitored for active tuberculosis during and after treatment with tildrakizumab-asrn. Tildrakizumab-asrn should not be used in patients with active tuberculosis.\textsuperscript{8}

Completion of age-appropriate immunizations according to current immunization guidelines should be considered before treatment with tildrakizumab-asrn is initiated. The use of live vaccines should be avoided in patients who receive tildrakizumab-asrn treatment.\textsuperscript{8}

**Conclusion**

The FDA approval of tildrakizumab-asrn, a novel IL-23 antagonist, provides a new treatment option that may improve outcomes for patients with moderate-to-severe plaque psoriasis who are candidates for systemic therapy or phototherapy.

In 2 pivotal clinical studies, a significantly greater proportion of patients who received treatment with tildrakizumab-asrn achieved a PASI-75 response and a PGA score of 0 or 1, with at least a 2-point reduction from baseline, compared with the placebo group, at week 12. In addition, the response to tildrakizumab-asrn therapy was sustained through week 64.\textsuperscript{9}

**References**

8. Ilumya (tildrakizumab-asrn) injection, for subcutaneous use [prescribing information]. Cranbury, NJ: Sun Pharma Global; August 2018.

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