Ulcerative colitis (UC), an inflammatory bowel disease that often causes chronic inflammation of the digestive tract, can be debilitating and may lead to life-threatening complications. UC affects more than 620,000 people in the United States. More common than Crohn’s disease, the incidence of UC is 1.2 cases to 20.3 cases per 100,000 people annually, whereas Crohn’s disease has an incidence of 0.03 cases to 15.6 cases per 100,000 people annually.

Although UC can occur at any age, it is diagnosed most frequently in young adults between the ages of 15 years and 25 years. Men and women are affected equally by UC; however, men in their 50s and 60s are more likely to be diagnosed with UC than women of those age-groups. The onset of UC is thought to be triggered by a combination of factors, including environment, genetics, and immune-system overactivity.

UC is associated with potentially serious complications, including intestinal bleeding, severe abdominal distention, and, in rare cases, toxic megacolon. UC is also associated with substantial costs, which were underestimated in the past. Based on a 2010 analysis, the total economic burden of UC in the United States is estimated to be $8.1 billion to $14.9 billion annually and accounts for annual per-patient direct medical costs ranging from $6217 to $11,477 (in 2008 dollars). In that analysis, hospitals accounted for 41% to 55% of the direct medical costs, and indirect costs accounted for an estimated 33% of the total costs. Moreover, direct costs, hospitalizations, and surgeries increased as the severity of UC worsened.

Early diagnosis and management of UC are crucial to improving outcomes, given that effective treatment may control UC and help achieve remission of the disease. The therapeutic goals for UC are to reduce the inflammation that triggers the signs and symptoms, which in turn may lead to symptom relief and to long-term remission. Treatment helps to decrease the abnormal inflammation in the lining of the colon, permitting the colon to heal. Moreover, treatment often helps to alleviate diarrhea, rectal bleeding, abdominal pain, and other symptoms.

Medications used to treat UC include the aminosalicylates, corticosteroids, immunomodulators, and the biologic therapies known as anti–tumor necrosis factor (TNF) agents. Antibiotics may also be used to combat infections, such as abscesses, that may occur in association with UC.

In recent years, the availability and use of anti-TNF therapies have helped to change the landscape of UC management, because these agents have shown efficacy in achieving steroid-free remission and mucosal healing.

A New Subcutaneous Option for the Treatment of UC

On May 15, 2013, golimumab (Simponi; Janssen Biotech) injection was approved by the US Food and Drug Administration (FDA) for the treatment of UC that is resistant to previous treatment or requires continuous steroid therapy. Golimumab is the first and only subcutaneously administered anti–TNF-alpha therapy approved by the FDA to induce and maintain clinical response in patients with UC and to improve the endoscopic appearance of the mucosa during induction. It is also indicated to induce clinical remission in patients with UC and to achieve and sustain clinical remission in induction responders.

The FDA approval of golimumab, a self-injectable biologic therapy, for the treatment of UC was based on 2 major clinical studies in patients with moderate-to-severe UC. Golimumab was previously approved by the FDA for the treatment of psoriatic arthritis, alone or in combination with methotrexate, and for active ankylosing spondylitis. On July 19, 2013, golimumab (Simponi Aria) was approved by the FDA for patients with rheumatoid arthritis in combination with methotrexate.

According to Andrew E. Mulberg, MD, CPI, Deputy Director, Division of Gastroenterology and Inborn Errors Products, FDA’s Center for Drug Evaluation and Research, “Simponi is an important new treatment option for patients with moderate-to-severe ulcerative colitis. It is critical that patients suffering from the serious and painful symptoms of ulcerative colitis have additional treatment options since patients experience the effects of the disease and respond to treatments differently.”
Clinical Studies

Lead investigator, William J. Sandborn, MD, Professor of Medicine and Chief, Division of Gastroenterology, and Director, University of California, San Diego (UCSD) Inflammatory Bowel Disease Center, UCSD School of Medicine, commented, “The FDA approval of Simponi brings an important, new subcutaneous therapeutic option to adults living with moderate-to-severe ulcerative colitis, a disease where treatment options have been limited. Simponi has demonstrated significant benefits in the treatment of ulcerative colitis, a chronic inflammatory bowel disease, and represents a meaningful addition to the treatment armamentaria for gastroenterologists.”

Mechanism of Action

Golimumab is a human monoclonal antibody that binds to the soluble and transmembrane bioactive forms of human TNF-alpha to its receptors, thereby inhibiting the biologic activity of TNF-alpha (a cytokine protein). Elevated TNF-alpha levels in the blood, synovium, and joints have been implicated in the pathophysiology of several chronic inflammatory diseases, such as rheumatoid arthritis, psoriatic arthritis, and ankylosing spondylitis. TNF-alpha is an important mediator of the articular inflammation that is characteristic of these diseases. The exact mechanism by which golimumab is beneficial in patients with UC is unknown.

Dosing

The recommended initial dose of golimumab for UC is 200 mg by subcutaneous injection at week 0, followed by 100 mg at week 2 and then 100 mg every 4 weeks. Golimumab is available in 50-mg/0.5-mL and 100-mg/1-mL single-dose, prefilled SmartJect autoinjectors, and 50-mg/0.5-mL and 100-mg/1-mL single-dose, prefilled syringes.

Clinical Studies

The safety and efficacy of golimumab were evaluated in 2 randomized, double-blind, placebo-controlled studies of patients aged ≥18 years.

In Trial UC-1, an induction trial conducted in patients with moderate-to-severe active UC, a greater proportion of patients achieved clinical response and clinical remission, and showed improvement of the endoscopic appearance of the mucosa at week 6 in the golimumab 200/100-mg group compared with the placebo group (Table 1).

Trial UC-2, a randomized withdrawal maintenance trial, evaluated patients who achieved clinical response with golimumab induction and tolerated treatment with golimumab (Table 2). In this study, a greater proportion of patients maintained clinical response through week 54 in the group receiving golimumab 100 mg compared with the placebo group. Trial UC-2 also reassessed patients receiving golimumab in clinical response (which included the subset of patients in clinical remission) in Trial UC-1 for clinical remission at week 30 and week 54. A greater proportion of patients had clinical remission at week 30 and week 54 without demonstrating a

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Table 1: UC-1 Trial: Efficacy Results of 6-Week Induction of Golimumab versus Placebo in Patients with Ulcerative Colitis

<table>
<thead>
<tr>
<th>Efficacy parameter</th>
<th>Placebo, % (N = 256)</th>
<th>Golimumab 200/100 mg, % (N = 257)</th>
<th>Treatment difference, %</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical response&lt;sup&gt;a&lt;/sup&gt; at week 6</td>
<td>30</td>
<td>52</td>
<td>22 (95% CI, 14-30)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Clinical remission&lt;sup&gt;a&lt;/sup&gt; at week 6</td>
<td>6</td>
<td>19</td>
<td>12 (95% CI, 7-18)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Improvement of endoscopic appearance of the mucosa at week 6&lt;sup&gt;a&lt;/sup&gt;</td>
<td>29</td>
<td>43</td>
<td>15 (95% CI, 6-23)</td>
<td>.005</td>
</tr>
</tbody>
</table>

<sup>a</sup>Patients who had a prohibited change in concomitant UC medication, an ostomy, or a colectomy; discontinued trial agent because of a lack of therapeutic effect; or had a dose adjustment in Trial UC-2 were considered not to be in clinical response, clinical remission, or not to have an endoscopic improvement. CI indicates confidence interval; UC, ulcerative colitis.

Source: Simponi (golimumab) injection prescribing information; 2013.

Table 2: UC-2 Trial: Efficacy Results of 54-Week Maintenance with Golimumab versus Placebo<sup>b</sup>

<table>
<thead>
<tr>
<th>Efficacy parameter</th>
<th>Placebo, % (N = 156)</th>
<th>Golimumab 200/100 mg, % (N = 154)</th>
<th>Treatment difference, %</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical response&lt;sup&gt;b&lt;/sup&gt; through week 54</td>
<td>31</td>
<td>51</td>
<td>19 (95% CI, 8-30)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Clinical remission&lt;sup&gt;b&lt;/sup&gt; at week 30 and week 54&lt;sup&gt;c&lt;/sup&gt;</td>
<td>15</td>
<td>29</td>
<td>13 (95% CI, 4-22)</td>
<td>.003</td>
</tr>
</tbody>
</table>

<sup>b</sup>These results are based on patients who were in clinical response to golimumab at trial entry.

<sup>c</sup>Patients who had a prohibited change in concomitant UC medication, an ostomy, or a colectomy; discontinued golimumab because of a lack of therapeutic effect; or had a dose adjustment in Trial UC-2 were considered not to be in clinical response, clinical remission, or not to have an endoscopic improvement.

<sup>d</sup>A patient had to be in remission at weeks 30 and 54 (without a loss of response at any point) to achieve sustained remission. CI indicates confidence interval; UC, ulcerative colitis.

Source: Simponi (golimumab) injection prescribing information; 2013.
loss of response at any time point through week 54 in the group receiving golimumab 100 mg compared with the placebo group.11

**Adverse Events**

The most common adverse reactions (incidence >5%) are upper respiratory tract infection, nasopharyngitis, and injection-site reactions. Additional adverse events include vascular disorders, central nervous system disorders, and gastrointestinal disorders (Table 3).11

Serious infections leading to hospitalization or death, including tuberculosis (TB), bacterial sepsis, invasive fungal (ie, histoplasmosis), and other opportunistic infections, have occurred in patients receiving golimumab.

Lymphoma and other malignancies, some fatal, have been reported in children and in adolescent patients treated with TNF blockers, of which golimumab is a member.11

**Other Warnings and Precautions**

**Boxed warning.** Golimumab was approved with a boxed warning about serious infections and malignancy. Therapy with golimumab should not be started during an active infection. If an infection develops, the patient should be monitored carefully and golimumab treatment should be stopped if the infection becomes serious. Patients should be tested for latent TB before the initiation of golimumab therapy. If the TB test is positive, treatment should be started for TB before initiating therapy with golimumab. Patients should be monitored for active TB during treatment, even if the initial latent TB test is negative.11

**Invasive fungal infections.** For patients who develop a systemic illness while taking golimumab, empiric antifungal therapy should be considered for those who live in or travel to regions where mycoses are endemic.

**Hepatitis B reactivation.** Hepatitis B virus carriers should be monitored during and several months after therapy with golimumab. If reactivation occurs, treatment with golimumab should be discontinued and antiviral therapy should be initiated.

**Malignancies.** The incidence of lymphoma was greater than in the general US population. Cases of

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### Table 3: Adverse Drug Reactions Reported by ≥1% of Patients Receiving Golimumab and with a Higher Incidence than with Placebo in Phase 3 Trials of Rheumatoid Arthritis, Psoriatic Arthritis, and Ankylosing Spondylitis through Week 16

<table>
<thead>
<tr>
<th>Adverse reaction</th>
<th>Golimumab ± DMARDs, % (N = 1659)</th>
<th>Placebo ± DMARDs, % (N = 639)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Infections/infestations</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Upper respiratory tract infection (ie, nasopharyngitis, pharyngitis, laryngitis, hiniitis)</td>
<td>16</td>
<td>13</td>
</tr>
<tr>
<td>Viral infections (eg, influenza, herpes)</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td>Bronchitis</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Superficial fungal infections</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Sinusitis</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td><strong>General disorders and administration-site conditions</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Injection-site reaction (eg, injection-site erythema, urticaria, induration, pain, bruising, pruritus, irritation, paresthesia)</td>
<td>6</td>
<td>2</td>
</tr>
<tr>
<td><strong>Investigations</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alanine aminotransferase increased</td>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td>Aspartate aminotransferase increased</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td><strong>Vascular disorders</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td><strong>Central nervous system disorders</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dizziness</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Paresthesia</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td><strong>Gastrointestinal disorders</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Constipation</td>
<td>1</td>
<td>&lt;1</td>
</tr>
</tbody>
</table>

*Patients may have taken concomitant methotrexate, sulfasalazine, hydroxychloroquine, low-dose corticosteroids (≤10 mg of prednisone daily or equivalent), and/or nonsteroidal anti-inflammatory drugs during the trials.

DMARDs indicates disease-modifying antirheumatic drugs.

Source: Simponi (golimumab) injection prescribing information; 2013.
other malignancies have been observed among patients receiving TNF blockers.

**Heart failure.** The worsening or new onset of heart failure may occur with golimumab. If worsening symptoms occur, the use of golimumab should be stopped.

**Demyelinating diseases.** The exacerbation or new onset of demyelinating diseases may occur with golimumab.

**Hypersensitivity reactions.** Serious systemic hypersensitivity reactions, including anaphylaxis, may occur with golimumab.

**Live vaccines.** Live vaccines should not be given concurrently with golimumab.11

### Use in Specific Populations

**Pregnancy.** There are no adequate and well-controlled trials of golimumab in pregnant women. Golimumab should be used during pregnancy only if clearly needed.

**Nursing mothers.** It is not known whether golimumab is excreted in human milk or absorbed systemically after ingestion. Because many drugs are excreted in human milk, and there is a potential for adverse reactions from golimumab in nursing infants, consideration should be given as to whether to discontinue nursing or to discontinue golimumab, taking into account the importance of the drug to the mother.

**Pediatric use.** The safety and effectiveness of golimumab in pediatric patients aged <18 years have not been established.

**Geriatric use.** With respect to UC, there were insufficient numbers of patients aged ≥65 years to determine whether they respond different from patients aged 18 years to 65 years. Because there is generally a higher incidence of infections in the geriatric population, caution should be used in treating geriatric patients with golimumab.11

### Conclusion

The FDA approved Simponi (golimumab) injection in May 2013 for a new indication—the treatment of UC that is resistant to previous treatment or that requires continuous steroid therapy. Golimumab was previously approved by the FDA for the treatment of rheumatoid arthritis in combination with methotrexate, for the treatment of psoriatic arthritis either alone or in combination with methotrexate, and for the treatment of ankylosing spondylitis.

Golimumab, a biologic agent, is the first and only subcutaneous anti–TNF-alpha therapy approved by the FDA to induce and maintain clinical response and to improve the endoscopic appearance of the mucosa during induction. Golimumab is also indicated to induce clinical remission and to achieve and sustain clinical remission in induction responders.

**Golimumab, a biologic agent, is the first and only subcutaneous anti–TNF-alpha therapy approved by the FDA to induce and maintain clinical response and to improve the endoscopic appearance of the mucosa during induction.**

The FDA approval of golimumab for the treatment of patients with UC was based on 2 clinical studies in patients with moderate-to-severe UC. In the first study, a greater proportion of golimumab-treated patients achieved clinical response, clinical remission, and improved the endoscopic appearance of the mucosa at 6 weeks compared with the placebo group. In the second study, patients who responded to golimumab were randomly assigned to receive golimumab or placebo. Based on this study, a greater proportion of golimumab-treated patients maintained a clinical response through week 54 and demonstrated clinical remission at week 30 and week 54 compared with the placebo group.

The most common adverse reactions (incidence >5%) seen with golimumab are upper respiratory tract infection, nasopharyngitis, and injection-site reactions.

### References