Pharmaceutical Approval Update

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Golimumab (Simponi Injection),
Solution for Subcutaneous Use


Indication: Golimumab is a tumor necrosis factor (TNF) blocker designed to treat (1) moderately to severely active rheumatoid arthritis (RA) in adults, in combination with methotrexate; (2) active psoriatic arthritis (PsA) in adults, alone or in combination with methotrexate; and (3) active ankylosing spondylitis (AS) in adults.

Drug Class: Golimumab is a human IgG-1 monoclonal antibody that targets human TNF-alpha (TNF-α). It exhibits multiple glycoforms with molecular masses of approximately 150 to 151 kilodaltons. Golimumab was created by using genetically engineered mice immunized with human TNF, resulting in an antibody with human-derived antibody variable and constant regions. Golimumab is produced by a recombinant cell line that is cultured by continuous perfusion and purified by measures to inactivate and remove viruses.

Uniqueness of Product: This human monoclonal antibody binds to both soluble and transmembrane bioactive forms of human TNF-α (a cytokine protein). This interaction prevents the binding of TNF-α to its receptors, thereby inhibiting the biological activity of TNF-α. There is no evidence that the golimumab antibody binds to other TNF superfamily ligands or that it binds to or neutralizes human lymphotoxin. Golimumab does not lyse human monocytes expressing transmembrane TNF in the presence of complement or effector cells.

Elevated TNF-α levels in the blood, synovium, and joints have been implicated in the pathophysiology of several chronic inflammatory diseases such as RA, PsA, and AS. TNF-α is an important mediator of the articular inflammation that is characteristic of these diseases. Golimumab modulates in vitro biological effects mediated by TNF in several bioassays, including:

- the expression of adhesion proteins responsible for leukocyte infiltration such as E-selectin; intercellular adhesion molecule-1 (ICAM-1), or cluster of differentiation 54 (CD54); and vascular cell adhesion molecule-1 (VCAM-1, or CD106)
- the secretion of proinflammatory cytokines, including interleukin-6 (IL-6), IL-8, granulocyte–colony stimulating factor (G–CSF), and granulocyte–monocyte CSF (GM–CSF).

Boxed Warning: Patients receiving golimumab are at increased risk for serious infections that may lead to hospitalization or death. Most patients who developed these infections were taking concomitant immunosuppressants such as methotrexate or corticosteroids. Golimumab should be discontinued if a serious infection develops, such as:

- active tuberculosis (TB), including reactivation of latent TB. Patients with TB have frequently presented with disseminated or extrapulmonary disease. Patients should be tested for latent TB before golimumab use and during therapy. Therapy for latent infection should be initiated prior to golimumab use.
- invasive fungal infections, including histoplasmosis, coccidioidomycosis, and pneumocystosis. Patients with histoplasmosis or other invasive fungal infections may present with disseminated rather than localized disease. Antigen and antibody testing for histoplasmosis may be negative in some patients with active infection. Empirical antifungal therapy should be considered in patients at risk for invasive fungal infections who develop severe systemic illness.
- bacterial, viral, and other infections caused by opportunistic pathogens.

The risks and benefits of treatment with golimumab should be carefully considered before patients with chronic or recurrent infection begin therapy. Patients should be closely monitored for signs and symptoms of infection during and after treatment, including the possible development of TB in patients who tested negative for latent TB infection before they began therapy.

Warnings and Precautions:

Serious infections. Serious and sometimes fatal infections resulting from bacterial, mycobacterial, invasive fungal, viral, protozoal, or other opportunistic pathogens have been reported in patients receiving TNF blockers (including golimumab) such as TB, histoplasmosis, aspergillosis, candidiasis, coccidioidomycosis, listeriosis, and pneumocystosis. Patients have frequently presented with disseminated rather than localized disease; these patients were often taking concomitant immunosuppressants such as methotrexate or corticosteroids. The concomitant use of a TNF blocker and abatacept (Ocrevus, Bristol-Myers Squibb) or anakinra (Kineret, Biovitrum), an IL-1 antagonist, was associated with a higher risk of serious infections; therefore, the concomitant use of golimumab and these biologic products is not recommended.

Treatment with golimumab should not be initiated in patients with an active or localized infection. The risks and benefits of treatment should be considered before therapy is to begin in patients:

- with chronic or recurrent infection.
- who have been exposed to TB.
- with a history of an opportunistic infection.
- who have resided or traveled in areas of endemic TB or...
Patients should be closely monitored for the development of signs and symptoms of infection during and after treatment with golimumab. Therapy should be discontinued if a serious infection, an opportunistic infection, or sepsis occurs. If a new infection develops during treatment with golimumab, the physician should perform a prompt and complete diagnostic evaluation that would be appropriate for an immunocompromised patient; antimicrobial therapy should be initiated; and patients should be closely monitored.

In controlled phase 3 trials through week 16 in patients with RA, PsA, and AS, serious infections were observed in 1.4% of golimumab-treated patients and in 1.3% of controls. In controlled phase 3 trials through week 16 in patients with RA, PsA, and AS, the incidence of serious infections per 100 patient-years of follow-up was 5.4 (95% confidence interval [CI], 4.0, 7.2) for the golimumab group and 5.3 (95% CI, 3.1, 8.7) for the placebo group. Serious infections observed in golimumab patients included sepsis, pneumonia, cellulitis, abscess, TB, invasive fungal infections, and hepatitis B infection.

### Tuberculosis

Cases of reactivation of TB or new TB infections have been observed in patients receiving TNF blockers, including patients who previously received treatment for latent or active TB. Patients should be evaluated for TB risk factors and should be tested for a latent infection before beginning golimumab therapy and periodically during therapy.

Treatment of latent TB infection prior to therapy with TNF blockers has been shown to reduce the risk of TB reactivation during therapy. Induration of 5 mm or greater with tuberculin skin testing should be considered a positive test result when the physician is determining whether treatment for latent TB is needed before initiating golimumab. This holds true even if patients have already received bacille Calmette-Guérin (BCG) vaccine.

Anti-TB therapy should also be considered before golimumab is initiated in patients with a history of latent or active TB when an adequate course of treatment cannot be confirmed and for patients with a negative test result for latent TB but who have risk factors for TB. Consultation with a physician with expertise in the treatment of TB is recommended to help determine whether initiating anti-TB therapy is appropriate.

Patients should be closely monitored for the development of signs and symptoms of TB, including patients with negative test results for latent TB infection prior to beginning golimumab therapy. TB should be strongly considered if a new infection develops during golimumab treatment, especially if the patient has traveled to countries with a high prevalence of TB or has been in close contact with a person with active TB.

In the controlled and uncontrolled portions of the phase 2 RA and phase 3 RA, PsA, and AS trials, the incidence of active TB was 0.23 and 0 (zero) per 100 patient-years in 2,347 golimumab patients and in 674 placebo patients, respectively. Cases included pulmonary and extrapulmonary TB. Most of the cases occurred in countries with a high incidence rate of TB.

### Invasive fungal infections

For golimumab-treated patients who reside or travel in regions where mycoses are endemic, invasive fungal infection should be suspected if a serious systemic illness occurs. Appropriate empirical antifungal therapy should be considered while a diagnostic evaluation is being performed. Antigen and antibody test results for histoplasmosis may be negative in some patients with active infection. When feasible, the decision whether to administer empirical antifungal therapy in these patients should be made in consultation with a physician with expertise in the diagnosis and treatment of invasive fungal infections. The decision should also take into account the risks of severe fungal infection and the risks of antifungal therapy.

### Hepatitis B virus reactivation

The use of TNF blockers, including golimumab, has been associated with reactivation of hepatitis B virus (HBV) in patients who are chronic hepatitis B carriers (i.e., surface antigen–positive). In some instances, HBV reactivation occurring in conjunction with TNF blockers has been fatal. Most of these reports have involved patients who received concomitant immunosuppressants.

Patients at risk for HBV infection should be evaluated for prior evidence of HBV infection before they begin TNF-blocker therapy. The risks and benefits of treatment should be considered before TNF-blockers, including golimumab, are prescribed to patients who are carriers of HBV. Adequate data are not available on whether antiviral therapy can reduce the risk of HBV reactivation in HBV carriers who use TNF blockers. Carriers of HBV who require treatment with TNF blockers should be closely monitored for clinical and laboratory signs of active HBV infection throughout therapy and for several months after therapy is terminated.

If HBV reactivation occurs, TNF blockers should be stopped and antiviral therapy with appropriate supportive treatment should be initiated. Whether it is safe to resume TNF blockers after HBV reactivation has been controlled is not known. Therefore, prescribers should exercise caution when they are considering resuming treatment with TNF blockers and should monitor patients closely.

### Malignancies

The risks and benefits of TNF blockers, including golimumab, should be considered before health care professionals prescribe golimumab for a patient with a known malignancy (other than successfully treated nonmelanoma skin cancer) or when they are considering whether to continue prescribing a TNF blocker in patients who develop a malignancy.

In the controlled portions of clinical trials of TNF blockers, including golimumab, more cases of lymphoma were observed among patients receiving anti-TNF treatment than among controls. During the controlled portions of phase 2 trials of RA and in the phase 3 trials of RA, PsA and AS, the incidence of lymphoma per 100 patient-years of follow-up was 0.21 (95% CI, 0.03, 0.77) in the combined golimumab group compared with an incidence of 0 (zero) (95% CI, 0, 0.96) in the placebo group.

In the controlled and uncontrolled portions of these clinical trials in 2,347 golimumab patients (median follow-up, 1.4 years), the incidence of lymphoma was 3.8-fold higher than expected in the general population in the U.S., according to the National Cancer Institute’s Surveillance Epidemiology and End Results (SEER) database, as adjusted for age, sex, and race. Patients with RA and other chronic inflammatory dis-
Pharmaceutical Approval Update

Golimumab is the first once-monthly single injection (SQ) biologic for the treatment of patients with moderately to severely active rheumatoid arthritis (RA), psoriatic arthritis (PsA), and ankylosing spondylitis (AS). It is available in a prefilled glass syringe or autoinjector and requires an injection every 4 weeks (three to four times per month) compared to TNF blockers, which require an injection every 2 to 4 weeks.

**Hematological cytopenias.** There have been post-marketing reports of pancytopenia, leukopenia, neutropenia, aplastic anemia, and thrombocytopenia in patients receiving TNF blockers. Although no cases of severe cytopenias were noted in clinical trials of golimumab, caution should be exercised when a TNF blocker, including golimumab, is prescribed for patients with significant cytopenias.

**Dosage and Administration:** Golimumab 50 mg is administered by subcutaneous (SQ) injection once a month. For patients with RA, golimumab should be given with methotrexate. For patients with PsA or AS, golimumab may be given with or without methotrexate or other non-biologic disease-modifying antirheumatic drugs (DMARDs). For these patients, corticosteroids, non-biologic DMARDs, and/or nonsteroidal anti-inflammatory drugs (NSAIDs) may be continued during treatment with golimumab.

**Monitoring to assess safety.** Before and periodically during golimumab therapy, patients should be evaluated for active tuberculosis (TB) and should be tested for latent TB infection.

**General considerations.** Golimumab is intended for use under the guidance and supervision of a physician. After proper training in SQ injection technique, patients may use self-injection if the physician determines that it is appropriate. Patients should be instructed to follow the directions provided in the medication guide. The prefilled syringe or autoinjector should be allowed to sit at room temperature outside the carton for 30 minutes before the injection. Golimumab should not be warmed in any other way.

Before the solution is administered, it should be visually inspected for particles and discoloration through the viewing window. Golimumab should be clear to slightly opalescent and colorless to light yellow. The solution should not be used if it is discolored or cloudy or if foreign particles are present. Any leftover product remaining in the prefilled syringe or prefilled autoinjector should not be used. The needle cover on the prefilled syringe, as well as the prefilled syringe in the autoinjector, contains dry natural rubber (a derivative of latex), which should not be handled by persons sensitive to latex.

Injection sites should be rotated and should never be given into areas where the skin is tender, bruised, red, or hard.

**Dosage forms and strengths.** The product is available in an autoinjector and a prefilled syringe. Each single dose of the Simponi SmartJect Autoinjector contains a prefilled glass syringe that provides 50 mg of golimumab per 0.5 mL of solution.

**Commentary:** Golimumab is the first once-monthly SQ anti-TNF-α therapy approved for patients with moderately to severely active RA, active PsA, and active AS.

Although this TNF-α inhibitor enters a crowded market that includes adalimumab (Humira, Abbott), etanercept (Enbrel, Immunex/Wyeth/Amgen) and infliximab (Remicade, Centocor), it has two distinct advantages over the many “me-too” drugs. Golimumab is injected only once per month and is more convenient to use than other TNF-α inhibitors, which must be injected two to four times per month. This might not be a huge advantage—the first company to develop an oral drug that works well for RA should do extremely well—but the reduced number of injections needed will likely be a selling point.

Golimumab also works well for patients who have not...
responded to other TNF-α inhibitors. Because approximately 20% of patients do not respond to other available medications, there will likely be a place in the market for golimumab.

**Source:** www.simponi.com

**Benzyl Alcohol Lotion 5%**

**Manufacturer:** Sciele Pharma Inc., a subsidiary of Shionogi Co., Atlanta, Ga.

**Indication:** Benzyl alcohol lotion is prescribed for the topical treatment of head lice (*Pediculus capitis*)/infestation in patients six months of age and older. The lotion does not kill the eggs (nits) of the lice.

**Drug Class:** Benzyl alcohol, the active pharmaceutical ingredient, is a colorless liquid with a mild, pleasant aromatic odor. It is a useful solvent because of its polarity, low toxicity, and low vapor pressure. It is prepared by the hydrolysis of benzyl chloride via sodium hydroxide. Benzyl alcohol is produced naturally by many plants and is commonly found in fruits and teas. It is also found in a variety of essential oils, including jasmine, hyacinth, and ylang-ylang.

**Uniqueness of Product:** *In vitro* studies of the effect of the lotion on native, captured lice suggest that benzyl alcohol inhibits lice from closing their respiratory spiracles, allowing the vehicle to obstruct the spiracles and causing the lice to be asphyxiated. This is the first medication that kills head lice by asphyxiation without potential neurotoxic adverse effects.

**Warnings and Precautions:**

**Neonatal toxicity:** Intravenous (IV) administration of products containing benzyl alcohol has been associated with neonatal gasping syndrome consisting of severe metabolic acidosis; gasping respirations; progressive hypotension; seizures; central nervous system (CNS) depression; intraventricular hemorrhage; and death in preterm, low-birth-weight infants. Neonates younger than one month of age or preterm infants with a gestationally corrected age of less than 44 weeks can be at risk for gasping syndrome if they are treated with benzyl alcohol lotion.

**Eye irritation.** Exposure of the product to the eyes should be avoided because the lotion can cause eye irritation. If the lotion comes in contact with the eyes, they eyes should be flushed immediately with water. If irritation persists, a physician should be consulted.

**Contact dermatitis.** Benzyl alcohol lotion may cause allergic or irritant dermatitis.

**Use in children.** This lotion should be used only for children six months of age and older under the direct supervision of a physician.

**Dosage and Administration:** The lotion is applied to dry hair. The amount of lotion to be used is just enough to saturate the scalp and hair completely (Table 1). After 10 minutes, the head and scalp should be rinsed with water to wash off the solution. The treatment should be repeated in seven days.

**Adjunctive Measures:** Benzyl alcohol lotion should be used in the context of an overall lice-management program. All recently worn clothing and hats, used bedding, and towels should be washed in hot water or dry-cleaned. Personal-care items such as combs, brushes, and hair clips should be washed in hot water. A fine-tooth comb or special nit comb may be used to remove dead lice and eggs.

**Commentary:** Head lice are parasites that survive by injecting small amounts of saliva and removing small amounts of blood from the scalp every few hours. The parasites are an all-too-common and challenging medical problem that causes anxiety in families, schools, and summer camps. Generally found on the scalp, around the ears, and at the nape of the neck, the adult louse is about the size of a sesame seed and can be yellowish gray or reddish brown. The eggs are smaller and are silver. Each year, approximately six to 12 million children between 3 and 12 years of age are infested with head lice. To survive, lice breathe through sophisticated spiracles that close upon contact with most liquids, allowing them to go into suspended animation and survive for hours without respiration.

Benzyl alcohol lotion is considered an effective first-line treatment that eliminates lice infestation and minimizes disruption in the daily routines of family life. This product should fulfill the need for an effective treatment that does not contain a neurotoxic chemical and that addresses possible resistance.

**Source:** www.fda.gov

**Artemether/Lumefantrine (Coartem/Riamet) Tablets**

**Manufacturer:** Novartis, Florham Park, N.J.

**Indication:** Artemether/lumefantrine tablets are indicated for treating acute, uncomplicated malaria infections caused by *Plasmodium falciparum* in patients weighing 5 kg (11 pounds) or more. The tablets have been effective in geographical regions where resistance to chloroquine has been reported, but they should not be used to treat severe malaria or to prevent malaria.

**Drug Class:** As a methyl ether derivative of dihydroartemisinin, artemether is derived from artemisinin. Lumefantrine is a racemic 2,4,7,9-substituted fluorene derivative that conforms in structure, in physicochemical properties, and in mode of action to the aryl amino alcohol group of antimalarial agents that include quinine and mefloquine (Lariam, Hoffmann-LaRoche).

**Uniqueness of Drug:** The tablet is a fixed-dose combination of two antimalarial agents. It provides an effective three-day treatment with cure rates of more than 90% even in areas of multidrug resistance. After oral administration, artemether is absorbed relatively rapidly, with peak plasma concentrations occurring about one to two hours after it is given. Absorption of lumefantrine is slower, starting after a lag time of up to two hours and reaching peak plasma concentrations approximately six to eight hours after being administered.

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**Table 1 Recommendations for the Use of Benzyl Alcohol Lotion for Head Lice**

<table>
<thead>
<tr>
<th>Hair Length</th>
<th>Amount of Lotion per Treatment</th>
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<tbody>
<tr>
<td>Short hair</td>
<td>0–2 inches 4–6 oz. (0.5 to 0.75 bottle)</td>
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<tr>
<td></td>
<td>2–4 inches 6–8 oz. (0.75 to 1 bottle)</td>
</tr>
<tr>
<td>Medium hair</td>
<td>4–8 inches 8–12 oz. (1 to 1.5 bottles)</td>
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<tr>
<td></td>
<td>8–16 inches 12–24 oz. (1.5 to 3 bottles)</td>
</tr>
<tr>
<td>Long hair</td>
<td>16–22 inches 24–32 oz. (3 or 4 bottles)</td>
</tr>
</tbody>
</table>
Warnings and Precautions:  
**Prolongation of the QT interval.** Some antimalarial agents (e.g., halofantrine, quinine, quinidine), including this product, have been associated with a prolonged QT interval on electrocardiograms. Coartem/Riamet should be avoided in:

- patients with congenital prolongation of the QT interval or any other clinical condition known to prolong the corrected QT interval, such as patients with a history of symptomatic cardiac arrhythmias, clinically relevant bradycardia, or severe cardiac disease).
- patients with a family history of congenital prolongation of the QT interval or sudden death.
- patients with disturbances of electrolyte balance.
- patients receiving other medications that prolong the QT interval, such as:
  - class IA antiarrhythmic agents (quinidine, procainamide, disopyramide).
  - class III antiarrhythmic agents (amiodarone, sotalol).
  - antipsychotic medications (pimozide, ziprasidone).
  - antidepressants.
  - some antibiotics (macrolide antibiotics, fluoroquinolone antibiotics, imidazole, triazole antifungal agents).
  - some nonsedating antihistaminic agents (terfenadine, astemizole).
  - cisapride.
- patients using medications that are metabolized by the cytochrome P450 enzyme CYP 2D6 that also have cardiac effects ( flecainide, imipramine, amitriptyline, clomipramine).

**Use of QT-prolonging drugs and other antimalarial drugs.** Halofantrine (Halfan, SmithKline Beecham) and Coartem/Riamet should not be administered within one month of each other because of the long elimination half-life of lumefantrine (three to six days) and potential additive effects on the QT interval. As a result of limited safety data, antimalarial drugs should not be given concomitantly with Coartem/Riamet unless there is no other treatment option. Drugs that prolong the QT interval, including antimalarials such as quinine and quinidine, should be used cautiously after patients take Coartem/Riamet because of the long elimination half-life of lumefantrine and the potential for additive effects on the QT interval.

If mefloquine is taken immediately before a patient takes Coartem/Riamet, there may be a decreased exposure to lumefantrine, possibly as a result of a mefloquine-induced decrease in bile production. Therefore, patients should be monitored for decreased efficacy, and food consumption should be encouraged while they are taking Coartem/Riamet.

**Drug interactions with CYP 3A4.** When the tablets are administered with substrates of CYP 3A4, decreased concentrations of the substrate and a potential loss of substrate efficacy may result. When the tablets are given with an inhibitor of CYP 3A4, including grapefruit juice, increased concentrations of artemether or lumefantrine, as well as a prolonged QT interval, may result.

When the tablets are taken with inducers of CYP 3A4, decreased concentrations of artemether or lumefantrine, as well as a loss of antimalarial efficacy, may result.

Drugs that have a mixed effect on CYP 3A4, especially antiretroviral agents and medications that affect the QT interval, should be used with caution in patients who are taking Coartem/Riamet tablets.

**Drug interactions with CYP 2D6.** Administration of Coartem/Riamet with drugs that are metabolized by CYP 2D6 may significantly increase plasma concentrations of the co-administered drug and may increase the risk of adverse effects. Many of the drugs metabolized by CYP 2D6 (e.g., flecainide, imipramine, amitriptyline, and clomipramine) can prolong the QT interval and should not be given with Coartem/Riamet because of the potential additive effect on the QT interval.

**Recurdescence.** Food enhances the absorption of artemether and lumefantrine following their administration. Patients who remain averse to food during treatment should be closely monitored because the risk of recrudescence may be greater. If recrudescent *P. falciparum* infection occurs after treatment with Coartem/Riamet, patients should be given a different antimalarial drug.

**Hepatic and renal impairment.** Coartem/Riamet has not been studied for efficacy or safety in patients with severe hepatic or renal impairment.

**P. vivax infection.** In a limited study of only 43 patients, Coartem/Riamet has been effective in treating the erythrocytic stage of *P. vivax* infection. However, patients with relapsing malaria caused by *P. vivax* require additional treatment with other antimalarial agents to achieve radical cure, which consists of eradication of any hypnozoite forms that may remain dormant in the liver.

**Dosage and Administration:** Coartem/Riamet tablets should be taken with food, although patients with acute malaria are frequently averse to food. Patients should be encouraged to resume normal eating as soon as food can be tolerated because absorption of the active ingredients is enhanced.

For patients such as infants and children who might not be able to swallow tablets, the tablets may be crushed and mixed with one to two teaspoons of water in a clean container right before use. The container can be rinsed with more water, and the patient can swallow the contents. The crushed tablet preparation should be followed whenever possible by food or drink such as milk, formula, pudding, broth, or porridge. If the patient experiences vomiting within one to two hours after taking the drug, the dose should be repeated. If the second dose is vomited, the patient should be given an alternative antimalarial drug.

**Adults (16 years of age).** A three-day treatment schedule with a total of six doses is recommended for adults weighing 35 kg (77 pounds) or more: four tablets as a single initial dose, four tablets again after eight hours, then four tablets twice daily (morning and evening) for the following two days, for a total of 24 tablets.

**Pediatric patients.** A three-day treatment schedule with a total of six doses is recommended according to the patient’s weight:

- 5 kg to less than 15 kg (11 to 33 pounds): one tablet as an initial dose, one tablet again after eight hours, then one
tablet twice daily (morning and evening) for the following two days, for a total of six tablets

- 15 kg to less than 25 kg (11 to 55 pounds): two tablets as an initial dose, two tablets again after eight hours, then two tablets twice daily (morning and evening) for the following two days, for a total of 12 tablets

- 25 kg to less than 35 kg (55 to 77 pounds): three tablets as an initial dose, three tablets again after eight hours, then three tablets twice daily (morning and evening) for the following two days, for a total of 18 tablets

- 35 kg (77 pounds) and above: four tablets as a single initial dose, four tablets again after eight hours, then four tablets twice daily (morning and evening) for the following two days, for a total of 24 tablets

**Patients with hepatic or renal impairment.** No specific pharmacokinetic studies of Coartem/Riamet have been conducted in hepatically or renally impaired patients. Most patients with acute malaria have some degree of related hepatic or renal impairment. In clinical studies, the adverse-event profile did not differ in patients with mild or moderate hepatic or renal impairment compared with patients with normal hepatic function. No specific dose adjustments are needed for patients with mild or moderate hepatic or renal impairment. In clinical studies, few patients had severe renal impairment. Caution should be exercised for patients with severe hepatic or renal impairment.

**Dosage forms and strengths.** Coartem/Riamet tablets contain 20 mg of artemether and 120 mg of lumefantrine.

**Commentary:** Malaria is one of the most significant causes of morbidity and mortality worldwide, causing approximately 881,000 deaths every year. Current World Health Organization (WHO) guidelines recommend combinations of antimalarial drugs, in particular artemisinin-based combination therapies. Each year millions of Americans travel to malaria-endemic regions for business or pleasure, and this has led to a rise in cases of “travelers malaria.” Unlike patients in more than 80 countries, including Europe, patients in the U.S. have not had access to Coartem/Riamet. This drug is the first fixed-dose artemisinin-based combination therapy pre-qualified by WHO for efficacy, safety, and quality. Its two components have different modes of action that provide synergistic antimalarial activity. The tablets are indicated for infants, children, and adults with acute, uncomplicated malaria resulting from *P. falciparum*.

**Sources:** www.fda.com; www.drugs.com