PHARMACOLOGY WATCH

Evidence-based updates in clinical pharmacology

FDA Greenlights Biosimilars

In one of the most important decisions of the past 5 years, the FDA has given the greenlight to the first biosimilar drug with the approval of Sandoz's filgrastim-sndz, a copy of Amgen's multibillion dollar drug filgrastim (Neupogen). Biosimilars are drugs that are derived from living organisms and thus cannot be exact copies of the original compounds. They are different from generics in this respect. But the FDA has agreed to approve biologic copies that are "highly similar to another, already FDA-approved biologic (known as the reference product)."

The approval process verifies that there are no clinically meaningful differences between the biosimilar and the reference product, and the strength, dosage, form, and route of administration are the same. The FDA followed the advice of its Oncologic Drugs Approval Committee in approving filgrastim-sndz after the committee unanimously concluded that it was not clinically different from filgrastim. The new biosimilar is approved for the same indications as the parent drug, to treat cancer patients on myelosuppressive chemotherapy, patients with acute myeloid leukemia receiving induction or consolidation chemotherapy, cancer patients undergoing bone marrow transplantation, patients undergoing autologous peripheral blood progenitor cell collection and therapy, and patients with severe chronic neutropenia.

The naming convention of biosimilars is still be debated. Currently the original drug name will be used with a clear identification that it is a biosimilar (e.g., filgrastim-sndz). The FDA has indicated that this may not be the final naming convention for all biosimilars to follow. Biosimilars have been in wide use in Europe for 7 years. Filgrastim-sndz is manufactured by Sandoz, a Novartis company, and will be marketed as Zarxio.

Trimethoprim-sulfamethoxazole (TMP-SMX) and clindamycin were both effective in treating uncomplicated skin infections in younger patients who had a high rate of MRSA. Researchers randomized 524 patients to TMP-SMX or clindamycin, including 155 children. About 30% had an abscess, about 50% had cellulitis, and the rest had mixed infections.

S. aureus was isolated from 41%, of which the majority were MRSA (77%). The proportion of patients cured was similar in both groups in the intention-to-treat population (80.3% clindamycin vs 77.7% TMP-SMX; 95%CI, -10.2 to 4.9 for percentage difference; $P = 0.52$). In the group that could be evaluated, the cure rates were also similar, at nearly 90% for both drugs. There was no difference in effectiveness of the two drugs with regard to age or infection type. Adverse events were similar and there were no *C. difficile* infections. The authors conclude that both drugs are equally effective for the treatment of uncomplicated skin infections (*N Engl J Med* 2015;372:1093-1103).

An accompanying editorial points out that treatment for abscesses is primarily incision and

This supplement was written by William T. Elliott, MD, FACP, Chair, Formulary Committee, Kaiser Permanente, California Division; Assistant Clinical Professor of Medicine, University of California-San Francisco. In order to reveal any potential bias in this publication, we disclose that Dr. Elliott reports no consultant, stockholder, speaker's bureau, research, or other financial relationships with companies having ties to this field of study. For questions and comments, please e-mail: leslie.hamlin @ahcmedia.com.

drainage, and treatment of cellulitis should be directed primarily at beta-hemolytic strep, so a first-generation cephalosporin or dicloxacillin is a good choice. When there is concern for MRSA, however, this study shows that TMP-SMX or clindamycin are both good choices, although clindamycin also has activity against strep (*N Engl J Med* 2015;372:1164-1165).

The newly recommended 13-valent polysaccharide conjugate vaccine (PCV13 [Prevnar-13]) is highly effective in preventing pneumonia in adults in an industry-sponsored study. Nearly 85,000 Dutch adults age 65 or older were randomized to PCV13 or placebo with follow-up for about 4 years. During that timeframe, community-acquired pneumonia caused by vaccine-type strains occurred in 49 persons in the PCV13 group and 90 persons in the placebo group (vaccine efficacy, 45.6%; 95.2% CI, 21.8-62.5), non-bacteremic and noninvasive community-acquired pneumonia occurred in 33 persons in the PCV13 group and 60 persons in the placebo group (vaccine efficacy 45.0%; 95.2% CI, 14.2-65.3), and invasive pneumococcal disease occurred in 7 persons in the PCV13 group and 20 persons in the placebo group (vaccine efficacy 75.0%, 95% CI, 41.4-90.8).

Overall rates of community-acquired pneumonia, however, were similar in both groups, and there was no difference in overall mortality. There were more local reactions in the PCV13 group but, otherwise, serious adverse events were similar. The authors conclude that PCV13 is effective in preventing vaccine-type pneumococcal, bacteremic, and nonbacteremic community-acquired pneumonia and vaccine-type invasive pneumococcal disease, but not in preventing communitty-acquired pneumonia from any cause (*N Engl J Med* 2015;375:1114-1125). Prevnar 13 is now a CDC-recommended vaccine for adults along with the 23-valent pneumonia vaccine (Pneumovax). ■

FDA Actions

The FDA has approved afibercept for the treatment of diabetic retinopathy in patients with diabetic macular edema. It is the second drug to be approved for this indication this year after ranibizumab (Lucentis). Alfibercept is an inhibitor or vascular endothelial growth factor. The drug is injected into the eye once a month for 5 months then once every 2 months. Approval was based on two studies of 679 patients who were randomized to afibercept or macular laser photocoagulation. At week 100, afibercept patients showed significant improvement in their diabetic retinopathy compared to patients who did not receive the injections. The drug was approved with breakthrough therapy designation. It was previously approved for the treatment of wet age-related macular degeneration and diabetic macular edema secondary to retinal vein occlusion. Alfibercept is marketed by Regeneron Pharmaceuticals as Eylea.

The FDA has added a new warning to the label of the smoking deterrent drug varenicline (Chantix) regarding potential adverse reactions with alcohol. The FDA reports that there have been almost 50 adverse events reported with the drug involving alcohol since the drug was approved in 2006. These events include increased intoxicating effects of alcohol sometimes associated with aggressive behavior and/or amnesia. There also have been more than 60 cases of seizures, mostly occurring in patients without seizure history. The drug also has a black box warning regarding neuropsychiatric changes. With this new warning, the FDA recommends weighing the potential risk of seizures against the potential benefit, and also recommends cutting back on alcohol intake when initiating the medication (www.FDA.gov/Safety/MedWatch/).

The FDA has approved isavuconazonium sulfate, a new azole antifungal for the treatment of adults with invasive aspergillosis and invasive mucormycosis. The drug is available in oral and intravenous formulations. It was approved as a "Qualified Infectious Disease Product," the sixth such improved antibacterial or antifungal to receive this designation. Approval was based on a clinical trial of more than 500 patients randomly assigned to receive isavuconazonium or voriconazole, which showed equivalent outcomes and safety. Isavuconazonium is marketed by Astellas Pharma as Cresemba. ■