PHARMACOLOGY WATCH

Evidence-based updates in clinical pharmacology

CDC Panel Publishes New Vaccine Recommendations

In this issue: Panel Publishes Flu Vaccine Recommendations; High-dose Flu Vaccine in Older Adults; Pneumonia Vaccine in Older Adults; and FDA Actions.

Panel Publishes Flu Recommendations

The Centers for Disease Control and Prevention's (CDC) Advisory Committee on Immunization Practices (ACIP) has published its recommendations for the coming 2014-2015 influenza season. This year's vaccine will be identical to the 2013-2014 vaccine. The trivalent vaccine will again contain the H1N1 strain, as well as one additional influenza A antigen and one influenza B antigen. The quadrivalent vaccine adds an additional B antigen. The ACIP is recommending that children aged 6 months through 8 years receive two vaccinations administered ≥ 4 weeks apart if they did not receive last year's vaccine. Since the vaccine is identical this flu season, a second vaccination is not needed if they were vaccinated last year. Children should preferentially receive the live attenuated influenza vaccine (Flumist) since it has been shown to be more effective in children. If Flumist is unavailable, children should receive the inactivated influenza injection. Flumist has been shown to be of similar efficacy to the standard vaccine in adults, so either vaccine is acceptable in anyone over the age of 8. The ACIP recommends that health care providers get the vaccine early — preferably in October. The vaccine should be available to patients as long as flu is circulating in the community. There is some evidence that antibody levels drop in the elderly 6 months after vaccination, but the ACIP does not recommend delaying vaccination in this group because of the risk of missed opportunities to vaccinate (*MMWR Morb Mortal Wkly Rep* 2014;63:691-697). ■

High-dose Flu Vaccine in Older Adults

Next year, the ACIP may be recommending high-dose flu vaccine for those ≥ 65 years of age, based on the results of a new study. High-dose trivalent inactivated vaccine was compared to standard-dose inactivated vaccine to evaluate flu protection in those ≥ 65 years of age. The high-dose strain has four times the antigen of the standard dose. Nearly 32,000 adults in the United States and Canada were randomized to standard-dose or high-dose trivalent flu vaccine. In the intention-to-treat analysis, 1.4% of high-dose recipients and 1.9% of low-dose recipients developed laboratory-confirmed influenza (relative efficacy, 24.2%; 95% confidence interval, 9.7-36.5). Antibody titers were significantly higher in the high-dose group, and adverse events were slightly higher in the high-dose group. The authors conclude that among those ≥ 65 years, high-dose trivalent flu vaccine induced higher antibody responses and better protection against laboratory-confirmed influenza compared to standard-dose vaccine (*N Engl J Med* 2014;371:635-645). ■

Pneumonia Vaccine in Older Adults

The ACIP is also recommending the 13-valent pneumococcal vaccine (Prevnar) for those ≥ 65 years of age regardless of whether they have already been immunized with the 23-valent vaccine (Pneumovax). Results from the CAPiTA trial

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showed a significant reduction in pneumococcal disease with the 13-valent vaccine. The new recommendation states that unvaccinated older adults should receive Prevnar-13 first followed some time later by a dose of Pneumovax. Those adults who have already been vaccinated with Pneumovax should receive a dose of Prevnar-13. The need for both vaccines will be reevaluated by the ACIP and the CDC in 2018. The CDC has not officially endorsed this recommendation yet and Medicare does not have the mechanism to pay for the new vaccine recommendation until at least 2015. ■

FDA Actions

As anticipated, the FDA and the Drug Enforcement Administration (DEA) have moved hydrocodone-combination products (Vicodin, Lortab, Norco, and others) from Schedule III to the more restrictive Schedule II category with an implementation date of early October. The move puts hydrocodone products in the same category as morphine, oxycodone, fentanyl, dilaudid, and methadone. This action was taken to counter the growing problem of prescription opioid abuse and overdoses, which has reached epidemic proportions in the United States in recent years. Non-combination hydrocodone is already Schedule II. Among other changes, the new rule will require a written, tamper-proof prescription for every fill of hydrocodone-combination products. No phone prescriptions will be allowed and refills are not allowed. The new category also strengthens penalties for diversion and requires increased security for storage in pharmacies. The new rule is expected to put pressure on physicians who treat pain patients as well as pharmacies that dispense these drugs — dramatically increasing foot traffic and visits. Some patient advocates argued that chronic pain patients will also be affected by the new rule.

The FDA has approved apixaban (Eliquis) for the treatment of deep venous thrombosis (DVT) and pulmonary embolism (PE) and for the reduction in the risk of recurrent DVT and PE after initial therapy. The drug is already approved for stroke prevention in patients with non-valvular afib as well as for prophylaxis of DVT and PE in patients who have undergone hip or knee replacement surgery. The other drugs in this category — rivaroxaban (Xarelto) and dabigatran (Pradaxa) — are already approved for this indication.

The FDA has approved a novel new drug to treat insomnia. Suvorexant is an antagonist of orexin receptors, which regulate sleep-wake cycles. Approval was based on three clinical trials of more than 500 patients. The drug was associated with falling asleep faster and longer time asleep compared to placebo. The drug is Schedule IV and comes with a warning regarding daytime somnolence, including impaired driving, especially with higher doses. It should be taken at bedtime with at least 7 hours before planned awakening. There is also a warning regarding dependence and complex behaviors while not fully awake including driving, preparing food, making phone calls, or having sex. The drug is supplied in 5, 10, 15, and 20 mg strengths with the lowest effective dose recommended. Suvorexant is made by Merck, Sharpe & Dohme Corporation and marketed as Belsomra.

The FDA has approved oritavancin, the third new antibiotic to treat skin and skin structure infections caused by susceptible bacteria including *Staphylococcus aureus* (including methicillin-susceptible and methicillin-resistant strains), *Streptococcus* species and *Enterococcus faecalis*. Oritavancin is administered intravenously as a single 3-hour infusion. The single-dose regimen was compared to intravenous vancomycin for 7-10 days and was shown to be of equal efficacy. Oritavancin is the third new antibiotic approved for this indication after dalbavancin (Dalvance) and tedizolid (Sivextro). All three were approved as qualified infectious disease products, and hence given a priority review and an additional 5 years of market exclusivity beyond the normal patent life. Oritavancin is marketed by The Medicines Company as Orbactiv.

The FDA has approved the third inhibitor of sodium-glucose transport protein (SGLT2) for the treatment of type 2 diabetes. Empagliflozin follows canagliflozin (Invokana) and dapagliflozin (Farxiga) in this class of antidiabetic drugs that block glucose reabsorption in the kidneys, allowing glucose to be eliminated in the urine, thus lowering blood sugar levels. The drug can be used alone or in combination with other antidiabetic medications. The drug was approved on the strength of seven clinical trials of nearly 4500 patients with type 2 diabetes which showed that the drug modestly lowered HbA1c levels. Empagliflozin is not for treatment of type 1 diabetics. The FDA is requiring postmarketing studies on cardiovascular outcomes as well as use in children. The most common side effects are urinary tract infections and female genital infections. Empagliflozin is manufactured by Boehringer Ingelheim as Jardiance. ■