Pharmacology Watch

Evidence-based updates in clinical pharmacology

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Review of Antibiotic Prescriptions Reignites Call for More Stewardship Programs

About one-third of outpatient antibiotic prescriptions may be inappropriate, according to a new study. CDC researchers used a national database of ambulatory visits in which oral antibiotics were prescribed for a number of outpatient conditions. Of the 184,000 visits, 12.6% received an antibiotic with the most common diagnosis of sinusitis, followed by otitis media and pharyngitis. Per thousand population, 506 antibiotic prescriptions were written, of which 353 were considered to be appropriate (pneumonia and urinary tract infections) and 149 were deemed inappropriate (acute bronchitis). Sinusitis and pharyngitis were considered indications for which antibiotics may be indicated. The authors concluded that these findings support the need for establishing outpatient antibiotic stewardship programs (*JAMA* 2016;315:1864-1873).

An accompanying editorial suggests that the number of inappropriate antibiotics may be underestimated because the authors did not count other encounters, such as telephone calls or practice sites such as urgent care clinics, retail pharmacies, and dentist offices, where antibiotics are frequently prescribed. Nonetheless, this new study "addresses an important area of uncertainty," and provides useful information for the White House National Action Plan for Combating Antibiotic-Resistant Bacteria, which calls for a reduction in inappropriate outpatient antibiotics by 50% by 2020 (*JAMA* 2016;315:1839-1841).

Study Scrutinizes Smoking Cessation Drug Risk

The neuropsychiatric risks of smoking cessation drugs may have been overstated, according to an FDA-requested study. Varenicline (Chantix) and bupropion (Wellbutrin) were compared to the nicotine patch and placebo with regard to efficacy and side effects. Of the more than 8,100 patients who were randomized, roughly half had a history of psychiatric disorders. In the non-psychiatric cohort, the rate of neuropsychiatric adverse events were 1.3%, 2.2%, 2.5%, and 2.4% in the varenicline, bupropion, nicotine, and placebo groups, respectively. The rates in the psychiatric group were 6.5%, 6.7%, 5.2%, and 4.9%, respectively. Varenicline was the most effective modality in achieving smoking abstinence. The authors concluded, "The study did not show a significant increase in neuropsychiatric adverse events attributable to varenicline or bupropion relative to nicotine patch or placebo." (*Lancet* published online April 22, 2016. doi: http://dx.doi.org/10.1016/S0140-6736(16)30272-0).

Clinical Brief Notes

Researchers may be closer to an Ebola vaccine as two vaccines showed promise in a recent clinical trial (*JAMA* 2016;315:1610-1623).

Diflucan, which is commonly prescribed to women for yeast infections, may increase the risk for miscarriage. The FDA advises caution in using the drug during pregnancy. (http://1.usa.gov/24C3wRr).

The DPP-4 inhibitors saxagliptin and sitagliptin do not increase the risk for heart failure relative to other diabetes medications (*Ann Intern Med* published online April 26, 2016. doi:10.7326/M15-2568).

Metformin is still a first-line therapy for type 2 diabetes mellitus as monotherapy or combination therapy because of its safety and beneficial effects, based on the findings of a large meta-analysis (*Ann Intern Med* published online April 19, 2016. doi: 10.7326/M15-2650).

FDA Actions

The FDA has approved the first biosimilar for infliximab (Remicade). Infliximab-dyyb is approved for the same indications as infliximab, which include Crohn's disease, ulcerative colitis in adults, rheumatoid arthritis (in combination with methotrexate), ankylosing spondylitis, psoriatic arthritis, and plaque psoriasis. The drug is the first biosimilar monoclonal antibody approved in the United States and the second approved biosimilar overall. Multiple biosimilars are approved in Europe and Asia. Because of the FDA's naming convention, biosimilars must bear a nonproprietary name that includes an FDA-designated four-digit suffix in lower case letters (in this case "dyyb"). The dose for the new biosimilar is the same as for infliximab. Infliximab-dyyb is marketed as Inflectra.

The FDA is warning that aripiprazole (Abilify), a commonly used antipsychotic drug, may be associated with compulsive or uncontrollable urges to "gamble, binge eat, shop, and have sex." The behavior stopped when the medication was discontinued or the dose was reduced. The agency states that these impulse control problems are rare but may result in patient harm if not recognized. The FDA recommends new drug labeling, which includes a warning regarding these behaviors.

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The FDA has announced that Brintellix, the brand name for the antidepressant vortioxetine, will be changed to avoid confusion with the antiplatelet drug ticagrelor, which is marketed as Brilinta. The FDA has received 50 reports of medication errors based on the name similarity, some of which reached the patient. As of June, vortioxetine will be known as Trintellix.

The FDA has approved pimavanserin to treat hallucinations and delusions in Parkinson's disease, the first drug approved for this indication. The drug was approved on the strength of one six-week clinical trial of 199 patients, which showed pimavanserin to be superior to placebo in decreasing the severity and/or frequency of hallucinations and delusions without worsening the primary motor symptoms of Parkinson's disease. Like other antipsychotics, the drug carries a boxed warning regarding an increased risk of death in patients with dementia-related psychosis. Pimavanserin is marketed as Nuplazid. The drug received "breakthrough therapy" designation and a priority review.

The FDA has approved the first generic version of rosuvastatin (Crestor). Prior to the approval, rosuvastatin was the last remaining brand name-only statin. It is also the most potent statin. Watson Pharmaceuticals has approval to market the first generic in multiple strengths. The indications are the same as for the brand name rosuvastatin.

The FDA has eased restrictions on metformin use in patients with mild renal impairment. The change in labeling is a result of a review of multiple studies suggesting metformin can be safely used in patients with mild renal impairment and in most patients with moderate chronic kidney disease. The FDA also recommends using estimated glomerular filtration rate (eGFR) as a measure of renal function rather than serum creatinine. The drug is contraindicated in patients with an eGFR < 30 mL and should not be initiated with an eGFR > 45 mL. If eGFR drops to 30-45 mL while on therapy, assess risks and consider benefits, but therapy may continue.

Two FDA advisory committees are recommending mandatory physician training regarding the risks of prescription opioids. A joint meeting of FDA's Drug Safety and Risk Management Advisory Committee and the Anesthetic and Analgesic Drug Products Advisory Committee resulted in a unanimous vote to require training for all prescribers of opioids. They further recommend that the training encompass the risk of immediate-release as well as extended-release and long-acting opioid preparations. Some panelists argue the training should focus on pain management and relate to recent CDC guidelines released in March. The FDA has yet to rule on the advisory committees' recommendations. ■