APhA DrugInfoLine®

July 2018

Cardiology

Advising on this article: Eric MacLaughlin

July 2, 2018

Self-monitoring results in better BP control than clinic-based monitoring

Key Point

Results of a large, 12-month, open-label, multicenter trial in patients with uncontrolled hypertension showed that self-monitoring (SM) of blood pressure (BP) with or without telemonitoring (TM) resulted in better BP control compared with clinic-based BP monitoring. Primary care clinicians were better able to titrate antihypertensive medications to meet recommended goals.

Source URL:

http://www.aphadruginfoline.com/cardiology/self-monitoring-results-better-bp-control-clinic-based-monitoring

Gastroenterology

Advising on this article: C. Wayne Weart

July 2, 2018

Corticosteroids for severe alcoholic hepatitis improves short-term outcomes

Key Point

According to a study published in Gastroenterology, use of corticosteroids in patients with severe alcoholic hepatitis significantly reduced the risk of death within 28 days when compared with controls or pentoxifylline. However, no difference was seen in 6-month mortality for any treatment or controls.

Source URL:

http://www.aphadruginfoline.com/gastroenterology/corticosteroids-severe-alcoholic-hepatitis-improves-short-term-outcomes

Focus on Immunizations

Advising on this article: John D. Grabenstein

July 9, 2018

Communication strategies to improve HPV vaccination rates

Key Point

Providers with a persistent communication style that focuses on the benefits of HPV vaccine and a strong recommendation to accept vaccination resulted in much higher same-day vaccination rates compared with acquiescence and agreement to defer the vaccination, according to a study published in Pediatrics.

Source URL:

http://www.aphadruginfoline.com/focus-immunizations/communication-strategies-improve-hpv-vaccination-rates

Cardiology

Advising on this article: Eric MacLaughlin

July 9, 2018

Vitamins and mineral supplements have little benefit on CV outcomes

Key Point

No significant benefits were observed with use of multivitamins, vitamin D, calcium, or vitamin C on cardiovascular (CV) outcomes or all-cause mortality. Only low- to moderate-quality evidence supports use of folic acid to reduce CV disease and folic acid and B vitamins to reduce the risk of stroke, according to results of systematic reviews and meta-analyses published in the Journal of the American College of Cardiology.

Source URL:

http://www.aphadruginfoline.com/cardiology/vitamins-and-mineral-supplements-have-little-benefit-cv-outcomes

Alerts and Recalls

Generic Name (Trade Name—Company)	**Uses**/Notes
July 9, 2018	
Celecoxib	FDA approved a labeling supplement for celecoxib, a COX-2 selective NSAID, to include results from a postmarketing cardiovascular outcomes trial that found that at the lowest dose, cardiovascular safety of celecoxib was similar to that of moderate doses of naproxen and ibuprofen. Concerns about the cardiovascular thrombotic risk of COX-2 selective NSAIDs emerged in the early 2000s. Following an FDA Advisory Committee meeting held in 2005, which considered data from large clinical outcome trials in a wide range of indications and epidemiology studies of several individual NSAIDs, FDA concluded that the risk for cardiovascular thrombotic events was present for both COX-2 selective NSAIDs and nonselective NSAIDs. The Prospective Randomized Evaluation of Celecoxib Integrated Safety vs Ibuprofen or Naproxen (PRECISION) trial was conducted to address the remaining concerns about the relative cardiovascular safety of COX-2 selective NSAIDS and nonselective NSAIDs. PRECISION was a large, randomized, double-blind controlled trial that began in 2006. Ninety percent of the patients enrolled in the trial had osteoarthritis, and the remaining 10% had rheumatoid arthritis. Results of the PRECISION trial demonstrated that celecoxib at the lowest approved dose of 100 mg twice daily is noninferior to (or no worse than) ibuprofen dosed in the range of 600 mg to 800 mg three times daily or naproxen dosed in the range of 375 mg to 500 mg twice daily on a composite cardiovascular endpoint consisting of cardiovascular death, nonfatal myocardial infarction, and nonfatal stroke. In an ambulatory blood pressure monitoring study that was part of the larger PRECISION trial, celecoxib dosed at 100 mg twice daily showed little effect on average 24-hour systolic blood pressure (SBP), whereas ibuprofen dosed in the range of 600 mg to 800 mg three times daily and naproxen dosed in the range of 375 mg to 500 mg twice daily increased average 24-hour SBP

(Celebrex—Pfizer)	by 3.7 mmHg and 1.6 mmHg, respectively.
At lowest dose, CV safety similar to moderate doses of naproxen, ibuprofen	Too few patients received higher doses of celecoxib to evaluate the risk of cardiovascular events or the effect on blood pressure for doses greater than 100 mg twice daily. The cardiovascular risks of the NSAID class are dose dependent; therefore, the results for celecoxib 100 mg twice daily on the composite cardiovascular endpoint and the lack of effect on SBP cannot be extrapolated to dosing regimens using the higher strengths of celecoxib (200 mg or 400 mg). Patients with recent cardiovascular events such as acute MI, coronary revascularization, or coronary stent placement were not studied in the PRECISION trial. NSAID class labeling warns against use of NSAIDs in such patients.

Source URL:

http://www.aphadruginfoline.com/alerts-and-recalls/lowest-dose-cv-safety-similar-moderate-doses-naproxen-ibuprofen

Alerts and Recalls

Generic Name (Trade Name—Company)	**Uses**/Notes
July 9, 2018	
Neostigmine methylsulfate 5-mL syringes ***(No trade names—Fagron Sterile Services)*** **Two lots of recalled syringe units may be incorrectly labeled**	Fagron Sterile Services is voluntarily recalling two lots of neostigmine methylsulfate 5-mL syringes because some syringe units containing 1 mg/mL, 5 mg per 5mL, are incorrectly labelled as 1 mg/mL, 3 mg per 3mL. Secondary packages are properly labelled as neostigmine methylsulfate 1 mg/mL, 5 mg per 5mL. If 5 mL rather than the intended 3mL is administered to a patient, adverse events overdosage can range from nausea, vomiting, diarrhea, excessive salivation and sweating, increased bronchial secretions, miosis, bradycardia or tachycardia, cardiospasm, bronchospasm, incoordination, muscle cramps, fasciculation, and paralysis, to cholinergic crisis resulting in death. To date, Fagron has not received any reports of adverse events or injuries related to this recall. Neostigmine methylsulfate injection is a cholinesterase inhibitor indicated for reversal of the effects of nondepolarizing neuromuscular blocking agents after surgery.

Source URL:

http://www.aphadruginfoline.com/alerts-and-recalls/two-lots-recalled-syringe-units-may-be-incorrectly-labeled

Alerts and Recalls

Generic Name (Trade Name—Company)	**Uses**/Notes
July 9, 2018	
Kratom products ***(Blissful Remedies—World Organix LLC)*** **Recalled kratom products are contaminated with high counts of bacteria**	FDA is advising consumers not to use kratom products sold by World Organix LLC, Las Vegas, NV. FDA laboratory analysis found that the products are contaminated with high counts of various bacteria that can cause infections, including salmonella, *Clostridium difficile, Klebsiella pneumoniae,* and *Pseudomonas aeruginosa.* The products were recalled on June 30, 2018; however, FDA is concerned this recall does not include all lot numbers of the affected products. FDA has received reports of adverse events associated with kratom products. The agency strongly discourages the public from consuming kratom, as there are no proven medical uses for kratom, an inherently addictive product that can cause harm.

Source URL:

http://www.aphadruginfoline.com/alerts-and-recalls/recalled-kratom-products-are-contaminated-high-counts-bacteria

Supplemental Approvals

Generic Name (Trade Name—Company)	**Uses**/Notes
July 9, 2018	
Encorafenib, binimetinib ***(Braftovi, Mektovi—Array BioPharma)*** **Agents approved in combination for unresectable or metastatic melanoma with BRAF mutations**	FDA approved encorafenib and binimetinib in combination for patients with unresectable or metastatic melanoma with a *BRAF V600E* or *V600K* mutation, as detected by an FDA-approved test. Approval was based on a randomized, active-controlled, open-label, multicenter trial in 577 patients with *BRAF V600E* or *V600K* mutation-positive unresectable or metastatic melanoma. Patients were randomized (1:1:1) to receive binimetinib 45 mg twice daily plus encorafenib 450 mg once daily, encorafenib 300 mg once daily, or vemurafenib 960 mg twice daily. Treatment continued until disease progression or unacceptable toxicity. The major efficacy measure was progression-free survival (PFS) using RECIST 1.1 response criteria and assessed by blinded independent central review. The median PFS was 14.9 months for patients receiving binimetinib plus encorafenib and 7.3 months for the vemurafenib monotherapy arm (hazard ratio 0.54 [95% CI 0.41–0.71], $P < 0.0001$). Overall response rates assessed by central review were 63% and 40%, respectively. Median response duration was 16.6 months vs. 12.3 months, respectively. The most common (?25%) adverse reactions in patients receiving the combination were fatigue, nausea, diarrhea, vomiting, abdominal pain, and arthralgia. Discontinuation of therapy due to adverse reactions occurred in 5% of patients receiving the combination; the most common reasons were hemorrhage and headache. FDA also granted approval of the THxID BRAF Kit (bioMérieux) as a companion diagnostic for these therapeutics. The recommended doses are binimetinib 45 mg orally twice daily and encorafenib 450 mg orally once daily.

Source URL:

http://www.aphadruginfoline.com/supplemental-approvals/agents-approved-combination-unresectable-or-metastatic-melanoma-braf

New Drug Approvals

Generic Name (Trade Name—Company)	**Uses**/Notes
July 9, 2018	
Glycopyrronium ***(Qbrexza—Dermira)*** **FDA approves first once-daily, topical prescription for excessive underarm sweating**	Dermira announced FDA approval of glycopyrronium cloth, an anticholinergic indicated for topical treatment of primary axillary hyperhidrosis in adult and pediatric patients aged 9 years and older. Commonly known as excessive underarm sweating, primary axillary hyperhidrosis is a chronic medical skin condition that results in sweating beyond what is needed for normal body temperature regulation. The exact cause is unknown, but it affects nearly 10 million people in the United States, with both men and women having similar prevalence. Approved under the trade name Qbrexza (pronounced kew brex' zah), it is applied directly to the skin and is designed to block sweat production by inhibiting sweat gland activation. Approval was based on results from two Phase III clinical trials, ATMOS-1 and ATMOS-2, which evaluated the efficacy and safety of Qbrexza in patients with primary axillary hyperhidrosis. Both trials assessed the absolute change from baseline in sweat production (the weight or amount of sweat a patient produced) following treatment with Qbrexza and the proportion of patients who achieved at least a four-point improvement from baseline in their sweating severity, as measured by the Axillary Sweating Daily Diary (ASDD), Dermira's proprietary patient-reported outcome (PRO) instrument. The most common adverse effects observed following topical application of Qbrexza to the underarms were dry mouth, dilated pupil, sore throat, headache, urinary hesitation, blurred vision, dry nose, dry throat, dry eye, dry skin, and constipation. The most common local skin reactions were erythema, burning/stinging, and pruritus. Qbrexza is expected to be available nationwide in pharmacies beginning in October 2018. For more information, visit www.qbrexza.com.

Source URL:

http://www.aphadruginfoline.com/new-drug-approvals/fda-approves-first-once-daily-topical-prescription-excessive-underarm-sweating

Supplemental Approvals

Generic Name (Trade Name—Company)	**Uses**/Notes
July 9, 2018	
Incobotulinumtoxin A ***(Xeomin—Merz North America)*** **First neurotoxin approved for chronic sialorrhea, or excessive drooling**	FDA approved incobotulinumtoxinA to treat chronic sialorrhea, or excessive drooling, in adult patients. It is the first and only neurotoxin with this approved indication in the United States. Sialorrhea is a common symptom among patients who have neurological disorders such as Parkinson disease, amyotrophic lateral sclerosis, or cerebral palsy or who have had a stroke. The condition can occur from difficulty retaining saliva inside the mouth, from issues with swallowing, and from problems controlling facial muscles. Approval for this indication was based on a Phase III, randomized, double-blind, placebo-controlled, multicenter trial involving 184 patients in which both coprimary endpoints were successfully achieved. Study participants received placebo (n = 36), incobotulinumtoxinA 75 U (n = 74), or incobotulinumtoxinA 100 U (n = 74). Overall frequency of adverse events was similar between placebo and treatment groups, with no new or unexpected adverse events reported. This is the fourth neurological indication for the neurotoxin, which was first approved by FDA in 2010 to treat cervical dystonia and blepharospasm (in patients previously treated with onabotulinumtoxinA) in adult patients and later in 2015 for upper limb spasticity in adult patients.

Source URL:

http://www.aphadruginfoline.com/supplemental-approvals/first-neurotoxin-approved-chronic-sialorrhea-or-excessive-drooling