Focus on Diabetes Care

Advising on this article: Charles Ponte

December 1, 2015

Diabetes: New recommendations push for earlier screening

Key Point

As part of a cardiovascular risk assessment, the U.S. Preventive Services Task Force (USPSTF) advises that adults 40 to 70 years of age who are overweight or obese and asymptomatic should be screened for abnormal blood glucose levels, according to newly revised recommendations. This guidance differs from current American Diabetes Association (ADA) recommendations that support screening at age 45 and for those with multiple risk factors.

Source URL:

Updated Beers Criteria: Drugs, interactions to avoid in older adults

Key Point

The American Geriatrics Society (AGS) released the second revision of the Beers Criteria in early October, which contains new information on drug–drug interactions, medications to avoid or to be dose modified in those with impaired renal function, and several new classes of medications to avoid in older patients.

Source URL:

http://www.aphadruginfoline.com/gastroenterology/updated-beers-criteria-drugs-interactions-avoid-older-adults
Focus on Asthma Care

Advising on this article: Devra K. Dang

December 8, 2015

New strategies to improve asthma control in children

Key Point

A new review focuses on strategies to improve asthma control in children, such as electronic monitoring devices to improve adherence, on-demand dosing of inhaled corticosteroids (ICSs), a potential role for tiotropium (Spiriva—Boehringer Ingelheim), and new biologics in development.

Source URL:

http://www.aphadruginfoline.com/focus-asthma-care/new-strategies-improve-asthma-control-children
Peripheral thermometers: Not so hot for detecting fever

Key Point

Peripheral thermometers, such as tympanic membrane, temporal artery, axillary, or oral thermometers, lack clinical accuracy and should not be used when precise measurement of core body temperature will influence clinical decisions, according to results of a new systematic review and meta-analysis published in the Annals of Internal Medicine.

Source URL:

http://www.aphadruiginfoline.com/otc-medicines-corner/peripheral-thermometers-not-so-hot-detecting-fever
Focus on Lipids Care

Advising on this article: Amber Briggs

December 15, 2015

Statins, fibrates for primary prevention of stroke in older adults

Key Point

Use of lipid-lowering drugs, such as statins and fibrates, was associated with an approximately 30% decrease in the incidence of stroke in adults 65 years of age and older with no known history of vascular events, according to results of an observational study published in The British Medical Journal.

Source URL:

Lower systolic BP better in those at increased risk for cardiac events

Key Point

Lowering systolic blood pressure (BP) to less than 120 mm Hg in patients at increased cardiovascular (CV) risk who did not have diabetes or a history of stroke led to a 25% decrease in the relative risk of select CV events and a 27% decrease in all-cause mortality, according to results of the landmark SPRINT (Systolic Blood Pressure Intervention Trial) Study.

Source URL:

http://www.aphadruginfoline.com/cardiology/lower-systolic-bp-better-those-increased-risk-cardiac-events
New breast cancer screening guidelines released

Key Point

For women at average risk, the American Cancer Society (ACS) has released updated breast cancer screening guidelines that increase the initial age for regular screening from 40 to 45 years old, recommend biennial screening for those 55 years of age and older, and no longer recommend clinical breast examinations for women of any age.

Source URL:
Cholecalciferol

(Vitamin D3—Glades Drugs)

Compounded multivitamins contain potentially toxic amounts of Vitamin D3

FDA is alerting health professionals and patients of a voluntary recall of compounded multivitamin capsules containing high amounts of cholecalciferol (Vitamin D3), distributed nationwide by Glades Drugs in Pahokee, Florida. FDA has received reports of several adverse events potentially associated with these compounded capsules.

Consumption of this product may result in vitamin D toxicity, which may be severe and lead to life-threatening outcomes if left untreated. Patients experiencing adverse effects from high Vitamin D levels may not initially show symptoms. Therefore, patients who have received these compounded capsules should stop taking this medication and immediately seek medical attention.

Symptoms of short-term vitamin D toxicity are due to high calcium levels and include confusion, increased urination, increased thirst, loss of appetite, vomiting, and muscle weakness. Acute hypercalcemia may intensify tendencies for heart arrhythmias and seizures and may increase the effects of certain heart drugs. Long-term toxicity may cause kidney failure, increase in calcium deposits in the blood and soft tissue, bone demineralization, and pain. Patients with conditions such as liver disease or chronic kidney failure may be at increased risk for developing vitamin D toxicity.

Health care providers should quarantine and return any products subject to this recall to the company at Glades Drugs, 109 S. Lake Ave., Pahokee, FL 33476. Glades Drugs sent recall letters to patients, attempted to contact them by phone, and called prescribing physicians.

Source URL:

Elotuzumab
*(Empliciti—Bristol-Myers Squibb)*

New immune-stimulating therapy treats multiple myeloma

FDA granted approval for elotuzumab in combination with two other therapies (lenalidomide and dexamethasone) to treat people with multiple myeloma who have received one to three prior medications.

It is the second monoclonal antibody approved to treat patients with multiple myeloma and works with another approved therapy to provide additional benefit. Daratumumab, approved earlier this month, is the only other FDA-approved monoclonal antibody for the treatment of patients with multiple myeloma.

Safety and efficacy of elotuzumab were tested in a randomized, open-label clinical study of 646 participants whose multiple myeloma came back after treatment or did not respond to previous treatment. Those taking elotuzumab plus lenalidomide and dexamethasone experienced a delay in the amount of time before their disease worsened (19.4 months) compared with participants taking only lenalidomide and dexamethasone (14.9 months).

In addition, 78.5% of those taking elotuzumab with lenalidomide and dexamethasone saw a complete or partial shrinkage of their tumors compared with 65.5% in those only taking lenalidomide and dexamethasone.

The most common adverse effects of elotuzumab are fatigue, diarrhea, fever, constipation, cough, peripheral neuropathy, nasopharyngitis, upper respiratory tract infection, decreased appetite, and pneumonia.


**New Drug Approvals**

<table>
<thead>
<tr>
<th>Generic Name (Trade Name—Company)</th>
<th>Uses/Notes</th>
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<tbody>
<tr>
<td>Mepolizumab</td>
<td>FDA approved mepolizumab for use with other asthma medicines for the maintenance treatment of asthma in patients aged 12 years and older who have a history of severe asthma attacks despite receiving their current asthma medicines.</td>
</tr>
</tbody>
</table>

The agent, a humanized interleukin-5 antagonist monoclonal antibody produced by recombinant DNA technology in Chinese hamster ovary cells, treats severe asthma attacks by reducing the levels of blood eosinophils, a type of white blood cell that contributes to the development of asthma.

The medication is administered by a health professional once every 4 weeks by subcutaneous injection into the upper arm, thigh, or abdomen.

Safety and efficacy were established in three double-blind, randomized, placebo-controlled trials in patients with severe asthma on currently available therapies. Mepolizumab or a placebo was administered to patients every 4 weeks as an add-on asthma treatment.

Compared with placebo, patients with severe asthma receiving mepolizumab had fewer exacerbations requiring hospitalization and/or emergency department visits and a longer time to the first exacerbation. In addition, patients with severe asthma receiving mepolizumab experienced greater reductions in their daily maintenance oral corticosteroid dose while maintaining asthma control, compared with patients receiving placebo.

Treatment with mepolizumab did not result in a significant improvement in lung function, as measured by the volume of air exhaled by patients in one second.

Common adverse effects include headache, injection site reactions, back pain, and weakness (fatigue).

Hypersensitivity reactions can occur within hours or days of being treated with mepolizumab, including swelling of the face, mouth, and tongue; fainting, dizziness, or
lightheadedness; hives; breathing problems; and rash. Herpes zoster infections have occurred in patients receiving mepolizumab.

Source URL:
### Alerts and Recalls

<table>
<thead>
<tr>
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<tr>
<td>Sodium-glucose cotransporter-2 inhibitors</td>
<td><strong>An FDA safety review</strong> has resulted in adding warnings to the labels of sodium-glucose cotransporter-2 (SGLT2) inhibitors about the risks of too much acid in the blood and of serious urinary tract infections (UTIs). Both conditions can result in hospitalization.</td>
</tr>
<tr>
<td><strong>(Multiple trade names—Multiple companies)</strong></td>
<td><strong>Revised labels include warnings about too much acid in the blood, serious UTIs</strong></td>
</tr>
<tr>
<td><strong>December 14, 2015</strong></td>
<td><strong>Patients should stop taking their SGLT2 inhibitor and seek medical attention immediately if they have any symptoms of ketoacidosis, which include nausea, vomiting, abdominal pain, tiredness, and trouble breathing. Patients should also be alert for signs and symptoms of a UTI and contact a health professional if they experience any of these symptoms.</strong></td>
</tr>
<tr>
<td><strong>Revised labels include warnings about too much acid in the blood, serious UTIs</strong></td>
<td><strong>Health professionals should assess for ketoacidosis and urinary tract infections in patients taking SGLT2 inhibitors who present with suggestive symptoms. Ketoacidosis associated with the use of SGLT2 inhibitors can occur even if the blood glucose level is not very high. If ketoacidosis is suspected, the SGLT2 inhibitor should be discontinued and treatment instituted promptly.</strong></td>
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**Source URL:**

### New Drug Approvals

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<tr>
<td><strong>December 14, 2015</strong></td>
<td><strong>FDA approved sebelipase alfa</strong> as the first treatment for patients with a rare disease known as lysosomal acid lipase (LAL) deficiency.</td>
</tr>
<tr>
<td><strong>Sebelipase alfa</strong> <em>(Kanuma—Alexion Pharmaceuticals)</em></td>
<td>Patients with LAL deficiency (also known as Wolman disease and cholesteryl ester storage disease [CESD]) have no or little LAL enzyme activity. This results in a build-up of fats within the cells of various tissues that can lead to liver and cardiovascular disease and other complications.</td>
</tr>
<tr>
<td><strong>First drug approved to treat rare enzyme disorder</strong></td>
<td>Wolman disease often presents during infancy (around 2 to 4 months of age) and is a rapidly progressive disease. Patients with Wolman disease rarely survive beyond the first year of life. CESD is a milder, later-onset form of LAL deficiency and presents in early childhood or later. Life expectancy of patients with CESD depends on the severity of the disease and associated complications. Wolman disease affects one to two infants per million births, and CESD affects 25 individuals per million births.</td>
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<td></td>
<td>Treatment is provided via I.V. infusion once weekly in patients with rapidly progressive LAL deficiency presenting in the first 6 months of life, and once every other week in all other patients.</td>
</tr>
<tr>
<td></td>
<td>Common adverse effects observed in patients treated with sebelipase alfa are diarrhea, vomiting, fever, rhinitis, anemia, cough, headache, constipation, and nausea.</td>
</tr>
</tbody>
</table>

**Source URL:**

Alerts and Recalls

Generic Name (Trade Name—Company)  Uses/Notes

December 14, 2015

Baclofen active pharmaceutical ingredient

(Multiple trade names—Taizhou)

APIs may be contaminated with particulates

FDA is alerting drug compounders that certain lots of baclofen active pharmaceutical ingredient (API) manufactured by Taizhou Xinyou Pharmaceutical & Chemical Co., Ltd. (Taizhou), Taizhou City, Zhejiang Province, China, may be at risk for contamination with particulates and should not be used to compound sterile injectable drugs.

Taizhou manufactures APIs for repackagers and distributors, some of which sell these products to compounding facilities in the United States. FDA contacted Taizhou through its U.S. agent, and the company confirmed that, due to the level of controls in the manufacturing process, the baclofen API it manufactures is not suitable for use in injectable drugs.

Based on available information, the affected API may potentially pose serious safety risks for U.S. patients who use or receive injectable drug products compounded with the affected baclofen, especially when administered directly into the spinal column. For example, use of baclofen API contaminated with particulate matter can result in serious injury if injected directly into the spinal column and may also clog pumps used to administer the medication.

There is also a potential risk that the baclofen API may be contaminated by endotoxin or microorganisms. FDA is continuing to investigate this incident.

Source URL:

http://www.aphadruginfoline.com/alerts-and-recalls/apis-may-be-contaminated-particulates
<table>
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<tbody>
<tr>
<td>Uridine triacetate (Vistogard—Wellstat Therapeutics Corp.)</td>
<td><strong>First emergency treatment approved for overdose of certain types of chemotherapy</strong></td>
</tr>
</tbody>
</table>

**Uses**

FDA approved uridine triacetate for the emergency treatment of adults and children who receive an overdose of the cancer treatment fluorouracil or capecitabine, or who develop certain severe or life-threatening toxicities within 4 days of receiving these cancer treatments.

Fluorouracil (taken by infusion) and capecitabine (taken orally) are similar types of chemotherapy that have been used for decades to treat several types of cancer, including breast and gastrointestinal cancers. An overdose of fluorouracil or capecitabine is rare, but when it occurs, the effects are serious and can be fatal.

**Uridine triacetate**, taken orally, blocks cell damage and cell death caused by fluorouracil chemotherapy. Patients should take uridine triacetate as soon as possible after the overdose (whether or not they have symptoms) or early-onset (within 4 days) of severe or life-threatening toxicity. The patient’s health care provider will determine when he or she should return to the prescribed chemotherapy after treatment with uridine triacetate.

**Uridine triacetate** is not recommended for treating nonemergency adverse reactions associated with fluorouracil or capecitabine because it may lessen the efficacy of these drugs. The safety and efficacy of uridine triacetate initiated more than 96 hours following the end of treatment with fluorouracil or capecitabine have not been established.

The most common adverse effects of treatment were diarrhea, vomiting, and nausea.

**Source URL:**

Alectinib

(Alecensa—Genentech)

New oral therapy treats ALK-positive lung cancer

FDA approved alectinib to treat people with advanced (metastatic) ALK-positive non–small cell lung cancer (NSCLC) whose disease has worsened after treatment with crizotinib (Xalkori) or who could not tolerate treatment with that agent.

Alectinib is an oral medication that blocks the activity of the ALK protein, which may prevent NSCLC cells from growing and spreading.

Its most common adverse effects are fatigue, constipation, edema, and muscle pain. Possible serious adverse effects include liver problems, severe or life-threatening inflammation of the lungs, very slow heartbeats, and severe muscle problems. Treatment may cause sunburn when patients are exposed to sunlight.
FDA approved sugammadex injection to reverse the effects of neuromuscular blockade induced by rocuronium bromide and vecuronium bromide, which are used during certain types of surgery in adults.

Rocuronium bromide and vecuronium bromide are neuromuscular blocking drugs that cause temporary paralysis by interfering with the transmission of nerve impulses to the muscle and are used to paralyze the vocal cords when patients require tracheal intubation. They can also be used to prevent patients from moving during surgery while they are receiving general anesthesia. Neuromuscular blocking drugs are also sometimes used to prevent the body from breathing automatically when a patient has to be placed on a ventilator.

Safety and efficacy of sugammadex injection were evaluated in three Phase 3 clinical trials involving 456 participants. The return to recovery time was faster overall for the sugammadex treatment groups compared with the comparator groups, with most participants recovering within 5 minutes of routine use of sugammadex.

Because of concerns about the nature and frequency of anaphylaxis (severe, potentially life-threatening allergic reaction) and hypersensitivity reactions reported in the clinical trials, sugammadex injection was further evaluated in a randomized, double-blind, parallel-group, repeat-dose trial. Of the 299 participants treated with sugammadex injection, one person had an anaphylactic reaction. Clinicians should be aware of the possibility of a hypersensitivity reaction or anaphylaxis and should intervene as appropriate.

Cases of marked bradycardia (abnormally slow heart action), some of which have resulted in cardiac arrest, have been observed within minutes after the administration of sugammadex injection. Patients should be closely monitored for hemodynamic changes during and after reversal of neuromuscular blockade, and treatment with anticholinergic agents, such as atropine, should be administered if clinically significant.
bradycardia is observed.

The most common adverse reactions reported in clinical trials included vomiting, low blood pressure, pain, headache and nausea. Doctors should also advise women using hormonal contraceptives that sugammadex injection may temporarily reduce the contraceptive effect, so they must use an alternate method of birth control for a period of time.

Source URL:
Selexipag
(Upravi—Actelion)

New orphan drug treats pulmonary arterial hypertension

FDA approved selexipag tablets to treat adults with pulmonary arterial hypertension (PAH), a chronic, progressive, and debilitating rare lung disease that can lead to death or the need for transplantation.

Selexipag belongs to a class of drugs called oral IP prostacyclin receptor agonists. The drug acts by relaxing muscles in the walls of blood vessels to dilate blood vessels and decrease the elevated pressure in the vessels supplying blood to the lungs.

Safety and efficacy of the drug were established in a long-term clinical trial of 1,156 participants with PAH. Selexipag was shown to be effective in reducing hospitalization for PAH and reducing the risks of disease progression compared with placebo. Participants were exposed to selexipag in this trial for a median duration of 1.4 years.

Common adverse effects observed in those treated with selexipag in the trial include headache, diarrhea, jaw pain, nausea, muscle pain, vomiting, pain in an extremity, and flushing.

Selexipag was granted orphan drug designation, which provides incentives such as tax credits, user fee waivers, and eligibility for exclusivity to assist and encourage the development of drugs for rare diseases.

Source URL:
## Supplemental Approvals

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<tr>
<th>Generic Name (Trade Name—Company)</th>
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<tr>
<td>December 22, 2015</td>
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<tr>
<td><strong>Pembrolizumab</strong></td>
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<tr>
<td><em>(Keytruda—Merck Sharp &amp; Dohme)</em></td>
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**Drug now approved for initial treatment of unresectable or metastatic melanoma**

FDA expanded the approval of pembrolizumab for the initial treatment of patients with unresectable or metastatic melanoma.

In 2014 pembrolizumab received accelerated approval based on a clinically meaningful, durable objective response rate in patients with unresectable or metastatic melanoma and disease progression following ipilimumab and, if BRAF V600 mutation positive, a BRAF inhibitor. Two new clinical trials verified the clinical benefit of the drug.

The recommended dose and schedule for pembrolizumab is 2 mg/kg Q3W administered as an I.V. infusion every 3 weeks until disease progression or unacceptable toxicity.

**Source URL:**

http://www.aphadruginfoline.com/supplemental-approvals/drug-now-approved-initial-treatment-unresectable-or-metastatic-melanoma
Alerts and Recalls

Multiple generic names

(Smart Lipo—Smart Lipo 365)

Dietary supplement contains undeclared drug ingredients

SmartLipo365 is voluntarily recalling all lots of Smart Lipo capsules to the consumer level because an FDA analysis found that the product contains undeclared sibutramine, desmethylsibutramine, and phenolphthalein. These undeclared ingredients make the product an unapproved new drug for which safety and efficacy have not been established. The product may also interact in life-threatening ways with other medications a patient may be taking.

Smart Lipo is marketed as a dietary supplement and is packaged in bottles of 30 capsules in 800 mg, 900 mg, and 950 mg per capsule.

Smart Lipo 365 has not received any complaints associated with this product to date.

The company is notifying its distributors and customers by e-mail and letter and will not continue distribution of the product.

Source URL:
