NEW HYPOTENSION TREATMENT FOR SEPTIC SHOCK

- Giapreza, an exogenous form of angiotensin II, has been approved to treat hypotension in adults with septic or other distributive shock. It should be added to the vasopressors used in the standard treatment of hypotension and shock.
- Giapreza use can cause thrombotic and thromboembolic events. Patients receiving the drug require prophylaxis with anticoagulants.

The Food and Drug Administration (FDA) has approved Giapreza, an exogenous form of angiotensin II, to increase blood pressure in adults with septic or other distributive shock. The drug should be added to the vasopressors used in the standard treatment of hypotension and shock. Angiotensin II is a potent endogenous vasoconstrictor; it also increases aldosterone release.

Giapreza was approved under a priority review, which the FDA gives to drugs it considers likely to "significantly improve the safety or effectiveness of treating, diagnosing or preventing a serious condition." A priority review guarantees that the FDA will make a decision on a drug application within six months. In a double-blind clinical trial of 321 patients with critical hypotension, significantly more patients responded positively to Giapreza added to conventional treatments than to placebo. The median time it took for patients to achieve the mean target arterial pressure of ≥ 75 mmHg was five minutes.

The most common serious adverse effects of Giapreza use, occurring in more than 10% of those receiving the drug, are thrombotic and thromboembolic events, which can occur in both veins and arteries. Patients who take Giapreza also require standard prophylaxis with anticoagulants. There are two main drug interactions noted in the drug's labeling: angiotensin-converting enzyme inhibitors may increase, and angiotensin II receptor blockers may decrease, the response to Giapreza.

Giapreza must be diluted with normal saline and administered as an IV infusion. Nurses should confirm with the prescriber that the patient has been placed on anticoagulant prophylaxis before administering the drug. Giapreza should be added to other, traditional vasopressor treatments, not used as monotherapy. It is not necessary to wait until other drugs are at maximum dosage to begin Giapreza. Careful assessment of the patient for thrombotic and thromboembolic events is needed. For complete Giapreza prescribing information, see www.accessdata.fda.gov/drugsatfda_docs/label/2017/209360s000lbl.pdf.

MAJOR CHANGE IN WARNING FOR ASTHMA DRUGS

- The Food and Drug Administration has removed the black box warning from the labeling of combination long-acting β-agonists (LABAs) and corticosteroids used in asthma treatment. The warning stated that these combination drugs may increase the risk of serious asthma-related events such as hospitalization, intubation, or death.
- Single-ingredient LABAs will continue to receive this black box warning.

The Food and Drug Administration (FDA) has removed the black box warning from the labeling of combination long-acting β-agonists (LABAs) and corticosteroids used in the treatment of asthma. The warning stated that these combination drugs may increase the risk of serious asthma-related events such as hospitalization, intubation, or death. LABAs are used to treat chronic asthma and chronic obstructive pulmonary disease. Although they work primarily on β_2-receptors to promote bronchial dilation, LABAs can also stimulate, to a more limited degree, β_1-receptors in the heart, increasing heart rate and force of contraction. Inhaled corticosteroids decrease inflammation in the lungs.

Black box warnings for LABAs originated in 2006—after the Salmeterol Multicenter Asthma Research Trial found they increased the risk of asthma-related death—and were placed on both single-ingredient and combination drugs. The decision to remove the warnings was based on a review of findings from four clinical trials. The FDA required drug manufacturers to conduct these trials in 2011 to obtain more safety information on the drug combinations.

The four clinical trials involved 41,297 patients. Three of the trials included patients ages 12 years and older, and one trial included exclusively pediatric patients ages four to 11 years. Different inhaled LABA-corticosteroid combination drugs were used in each trial. The FDA examined data from these trials in a meta-analysis, the results of which indicated that inhaled LABA-corticosteroid combination therapy does not significantly increase the risk of serious asthma events compared with inhaled corticosteroid monotherapy. The data also indicated that the LABA-corticosteroid combination is more effective than inhaled corticosteroid monotherapy.

The use of LABA monotherapy increases the risk of asthma-related deaths, and single-ingredient LABA medications will continue to receive

the black box warning related to this risk.

Examples of combination LABAs and corticosteroids are salmeterol–fluticasone (Advair Diskus, Advair HFA, Airduo Respiclick), vilanterol–fluticasone (Breo Ellipta), formoterol–mometasone (Dulera), and formoterol–budesonide (Symbicort). Nurses and NPs should review the revised labels of these asthma drugs (go to www.accessdata.fda.gov/scripts/cder/daf/index.cfm) and discuss the revised warnings with patients. To read the *FDA Drug Safety Communication* regarding LABA-corticosteroid combination inhalers, see www.fda.gov/Drugs/DrugSafety/ucm589587.htm.

NEW FDA WEB PAGE ON ANTIMICROBIAL RESISTANCE

- A new Food and Drug Administration web page provides fast, up-to-date information on the resistance and susceptibility of bacterial and fungal infections to antimicrobials. The web page streamlines the previous process of updating this information.

The Food and Drug Administration (FDA) has created a new web page to help NPs and other health care providers make timely and appropriate decisions regarding antimicrobial prescribing.

Bacterial and fungal organisms can mutate, minimizing or even eliminating the effectiveness of antimicrobial therapy. Historically, providing updated information on an organism's susceptibility to various drug therapies was a multistep process that took considerable time, as each organism's susceptibility test interpretive criteria (or "breakpoints") had to be reviewed and updated as needed.

The new web page was created to fulfill the requirements of the 21st Century Cures Act, which authorized the FDA to simultaneously update the breakpoints for all drugs with the same active ingredient. Further streamlining the process, the drug manufacturer will no longer need to revise a product's label to update breakpoints, but can just reference the FDA web page.

To access the new web page, go to www.fda.gov/Drugs/DevelopmentApprovalProcess/DevelopmentResources/ucm410971.htm. NPs should continue to read the entire drug label for complete information on the prescribing of antimicrobials to treat infection.

NEW ROUTE FOR BUPRENORPHINE ADMINISTRATION

- Buprenorphine, used to treat opioid use disorder, is now available in a once-monthly injectable form and sold under the trade name Sublocade. It can be initiated after the patient has received and tolerated a consistent dose of a transmucosal buprenorphine–naloxone product for at least a week.
- Sublocade must be administered by a health care professional. Nurses and NPs who administer the drug must confirm they are injecting it into the subcutaneous tissue, as injection into a vessel could lead to serious harm or death.

Sublocade is the first once-monthly injectable form of buprenorphine approved for the treatment of moderate-to-severe opioid use disorder. The patient can be transitioned to Sublocade after receiving a stable dose of a transmucosal buprenorphine–naloxone product for at least a week. The drug must be administered subcutaneously by a health care professional. A depot is created from the injection that slowly releases the drug. Sublocade must be prescribed as part of a Risk Evaluation and Mitigation Strategy (REMS) to ensure that it is not distributed directly to patients. The drug should be used in conjunction with counseling and psychosocial supportive therapy.

Two clinical studies of Sublocade were conducted in 848 adults diagnosed with moderate-to-severe opioid use disorder who had been stabilized on buprenorphine–naloxone sublingual film. Patients treated with Sublocade remained opioid free longer than patients who did not receive the drug. No one younger than 18 or older than 65 was included in the clinical trials. Postmarketing trials will determine if Sublocade can be given without a dose stabilization period of sublingual buprenorphine.

The most common adverse effects of Sublocade include nausea, vomiting, headache, drowsiness, injection site pain, injection site pruritus, and abnormal liver function tests. Most of these are similar to the adverse effects of other forms of buprenorphine. Other warnings and precautions are also similar to those of other buprenorphine products.

Sublocade should not be started in patients with moderate-to-severe hepatic disease. These patients do not metabolize Sublocade normally; therefore, the half-life of the drug is longer in these patients, and circulating levels of the drug are higher.

Nurses or NPs who administer Sublocade should confirm they are injecting it into the subcutaneous tissue. Accidental administration into a vessel will cause the depot that forms to block blood flow. Serious harm, including occlusion, local tissue damage, thromboembolic events, or death could result from this blockade.

For complete prescribing information for Sublocade, see www.accessdata.fda.gov/drugsatfda_docs/label/2017/209819s000lbl.pdf. ▼

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