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 $\geq 75$ 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 $\beta$-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. LABAs are used to treat chronic asthma and chronic obstructive pulmonary disease. Although they work primarily on $\beta_2$-receptors to promote bronchial dilation, LABAs can also stimulate, to a more limited degree, $\beta_1$-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- 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...