DEPARTMENT OF VETERANS AFFAIRS VETERAN HEALTH ADMINISTRATION (VHA)
PHARMACY BENEFITS MANAGEMENT SERVICES (PBM) & MEDICAL ADVISORY PANEL (MAP)
VA CENTER FOR MEDICATION SAFETY (VAMedSAFE)

NATIONAL PBM COMMUNICATION · March 9 , 2010

Use of Long-Acting Beta-Agonists (Formoterol and Salmeterol) and Their Safety in Patients with Asthma

- The question regarding use of long-acting beta-agonists [LABAs] (formoterol and salmeterol) and their safety in patients with asthma has been in the news for several years.
- In 2006, labeling for these drugs was changed to include a boxed warning regarding the increased risk of asthma-related death associated with LABA use. This warning recommends that LABAs be reserved for additional therapy in asthma patients with suboptimal control on other asthma-controller medications or whose disease severity necessitates combination treatment.[1-2]
- Asthma-controller medications refer to maintenance therapies that typically include low to medium dose inhaled corticosteroids (preferred based on current evidence).
- In February 2010, FDA concluded that among pediatric and adult patients using LABAs for the treatment of asthma, there is an increased risk for severe exacerbation of asthma symptoms leading to hospitalizations, as well as death, in some patients. FDA is requiring a Risk Evaluation and Mitigation Strategy (REMS) and class-labeling changes to the drug labels to ensure safe use of these agents.
- FDA's new recommendations only apply to LABA use for asthma and include[3]:
    - *The use of LABAs is contraindicated without the use of an asthma controller medication, typically an inhaled corticosteroid. Single-ingredient LABAs should only be used in combination with an asthma controller medication; they should not be used alone.*
    - *LABAs should only be used long-term in patients whose asthma cannot be adequately controlled on asthma controller medication, typically an inhaled corticosteroid.*
    - *LABAs should be used for the shortest duration of time required to achieve control of asthma symptoms and discontinued, if possible, once asthma control is achieved. Patients should then be maintained on an asthma controller medication, typically an inhaled corticosteroid.*
    - *Pediatric and adolescent patients who require the addition of a LABA to an inhaled corticosteroid should use a combination product containing both an inhaled corticosteroid and a LABA, to ensure compliance with both medications.*
- Consistent with the NHLBI Guidelines for the Diagnosis and Treatment of Asthma and the Global Initiative for Asthma (GINA) Guidelines, inhaled steroids (plus a short-acting beta-agonist for as needed use) remain the first line drugs for treatment of asthma. The long-acting beta-agonists are only considered as add-on drugs to inhaled steroids and should not be used alone.
- This recommendation does not apply to patients with COPD. Long-acting bronchodilators such as formoterol and salmeterol may continue to be used with or without an inhaled corticosteroid in patients with COPD. However, in light of this new warning from the FDA Advisory Committee, clinicians may want to reassess the appropriateness of LABA monotherapy for individual patients.
- VA performed an evaluation in 2006 of long-acting beta-agonist (LABA) monotherapy in asthmatics in response to a Public Health Advisory released by the FDA in November 2005 that warned of the increase in severe asthma episodes and death associated with the use of this drug class. The previous efforts were able to reduce LABA monotherapy use in asthmatic patients, and PBM periodically monitors this issue to ensure the downward trend in use continues. Providers interested in additional information please see the APPENDIX posted on the PBM Intranet website under the *"VAMedSAFE Project Results (Select)"* link on the Quick Launch bar.
- Providers must emphasize the importance of regular and proper use of inhaled corticosteroids in their patients with asthma.

REFERENCES

1. Serevent Diskus® (salmeterol xinafoate inhalation powder) [package insert]. Research Triangle Park, NC: GlaxoSmithKline; March 2008.
2. Foradil Aerolizer® (formoterol fumarate inhalation powder) [package insert]. Kenilworth, NJ: Schering Corporation; June 2006.
3. FDA Drug Safety Communiaction. http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm200776.htm. Accessed March 2, 2010.

ACTIONS

- ***Facility Director*** *(or physician designee): Forward this document to the Facility Chief of Staff (COS).*
- ***Facility COS and Chief Nurse Executives:*** *Forward this document to all appropriate providers who prescribe these medications (e.g.,* ***primary care providers****,* ***pulmonary specialists****, including contract providers, etc.). In addition, forward to the Associate Chief of Staff (ACOS) for Research and Development (R&D). Forward to other VA employees as deemed appropriate.*
- ***ACOS for R&D:*** *Forward this document to Principal Investigators (PIs) who have authority to practice at the facility and to your respective Institutional Review Board (IRB).*