Pharmacy & Therapeutics Update

From the November meeting of the SHC Pharmacy and Therapeutics Committee
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Added to the formulary:

- **Pembrolizumab (Keytruda®)** is a monoclonal antibody that binds to the PD-1 receptor and blocks its interaction with PD-L1 and PD-L2, releasing the PD-1 pathway-mediated inhibition of the immune response, including the anti-tumor immune response. In syngeneic mouse tumor models, blocking PD-1 activity resulted in decreased tumor growth. It is approved for the FDA-approved indication of treatment of patients with unresectable or metastatic melanoma and disease progression following ipilimumab and, if BRAF V600 mutation positive, a BRAF inhibitor. The recommended dosing for the FDA-approved indication is 2 mg/kg IV administered over 30 minutes every 3 weeks until disease progression or unacceptable toxicity. The most common adverse reactions (greater than 20% of patients) in patients receiving pembrolizumab include fatigue, nausea, constipation, diarrhea, cough, pruritis, rash, decreased appetite, and arthralgia. No formal pharmacokinetic drug interaction studies have been conducted with pembrolizumab.
- **Lubiprostone (Amitiza®)** is a locally acting chloride channel activator that enhances chloride-rich intestinal fluid secretion without altering sodium and potassium concentrations in the serum. It acts by specifically activating CIC-2, which is a normal constituent of the apical membrane of the human intestine. It has been approved for the FDA-approved indication of treatment of chronic idiopathic constipation; treatment of opioid-induced constipation with chronic non-cancer pain; or treatment of irritable bowel syndrome with constipation in adult women. The recommended dosing varies per indication:
    - Chronic idiopathic constipation: Oral: 24 mcg twice daily
    - Irritable bowel syndrome with constipation: Females ≥18 years: Oral: 8 mcg twice daily
    - Opioid-induced constipation: Oral: 24 mcg twice daily

  The most common adverse reactions (>10%) include headache, nausea, and diarrhea. No in vivo drug-drug interaction studies have been performed with lubiprostone. There is low likelihood of drug-drug interactions based upon results of in-vitro human microsome studies as cytochrome P450 isoenzymes are not involved in the metabolism of lubiprostone. There may be a potential interaction with diphenylheptane opioids (e.g. methadone) where non-clinical studies have shown opioids of the diphenylheptane chemical class to dose-dependently reduce the activation of ClC-2 by lubiprostone in the gastrointestinal tract.

Removed from the formulary:

- None