Deoxycholic Acid (Kybella)

Manufacturer: Kythera Biopharmaceuticals Inc., Westlake Village, California

Date of Approval: April 29, 2015

Indication: Deoxycholic acid is indicated for improving the appearance of moderate-to-severe convexity or fullness associated with submental fat in adults.

It is contraindicated in the presence of infections at the injection sites.

Drug Class: Cytolytic drug that contains deoxycholic acid as the active ingredient

Uniqueness of Drug: When injected into tissue, this agent physically destroys the cell membrane, causing lysis.

Warnings and Precautions:

Marginal mandibular nerve injury. To avoid the potential for nerve injury, deoxycholic acid should not be injected into or in close proximity to the marginal mandibular branch of the facial nerve.

Dysphagia. Avoid use of deoxycholic acid in patients with dysphagia, as a current or prior history of dysphagia may exacerbate the condition.

Injection-site hematoma or bruising. Deoxycholic acid should be used with caution in patients who have bleeding abnormalities or who are currently being treated with anti-platelet or anticoagulant therapy because excessive bleeding or bruising in the treatment area may occur.

Risk of injecting in proximity to vulnerable anatomic structures. To avoid potential tissue damage, deoxycholic acid should not be injected into or in close proximity (1–1.5 cm) to salivary glands, lymph nodes, and muscles.

Dosage and Administration: Kybella is injected into subcutaneous fat tissue in the submental area using an area-adjusted dose of 2 mg/cm². A single treatment consists of a maximum of 50 injections. Up to six single treatments may be administered at intervals no less than one month apart.

Commentary: Kybella is a unique therapy designed to help patients manage the fat occurring below the chin area. Approval by the Food and Drug Administration (FDA) was based on data from two clinical trials including 1,022 adults with submental fat. These patients were randomly given treatment or placebo for up to six months. Efficacy results showed reductions in fat below the chin more frequently in patients receiving Kybella.

Sources: https://mykybella.com, www.fda.gov

Codeine Polistirex/Chlorpheniramine Polistirex

Extended-Release Oral Suspension (Tuzistra XR)

Manufacturers: Vernalis PLC, Winnersh, United Kingdom, and Tris Pharma, Inc., Monmouth Junction, New Jersey

Date of Approval: April 30, 2015

Indication: Tuzistra is indicated for the relief of cough and symptoms associated with upper respiratory allergies or a common cold in adults 18 years of age and older. It is contraindicated in:

- Postoperative pain management in children who have undergone tonsillectomy and/or adenoidectomy.
- Patients with known hypersensitivity to codeine, chlorpheniramine, or any of the medication’s inactive ingredients. Persons known to be hypersensitive to certain other opioids may exhibit cross-sensitivity to codeine.

Drug Class: Combination of an opiate agonist antitussive, codeine, and a histamine H₁ receptor antagonist (antihistamine), chlorpheniramine

Uniqueness of Drug: Codeine is a semisynthetic narcotic antitussive and analgesic with multiple actions qualitatively similar to those of morphine. The precise mechanism of action of codeine and other opiates is not known; however, codeine is believed to act centrally on the cough center.

Chlorpheniramine is a propylamine derivative antihistamine drug (H₁ receptor antagonist) that also possesses anticholinergic and sedative activity. It prevents released histamine from dilating capillaries and causing edema of the respiratory mucosa.

Warnings and Precautions:

Death related to ultra-rapid metabolism of codeine to morphine. When prescribing codeine-containing drugs, health care professionals should choose the lowest effective dose for the shortest period of time and inform patients and caregivers about these risks and the signs of morphine overdose.

Respiratory depression. If respiratory depression occurs, discontinue the medication. Use naloxone hydrochloride when indicated to antagonize the effect and use other supportive measures as necessary.

Drug dependence. Prescribe and administer Tuzistra XR with the same degree of caution appropriate to the use of other opioid drugs.

Head injury and increased intracranial pressure. The use of this medication should be avoided in patients with head injury, other intracranial lesions, or a pre-existing increase in intracranial pressure.

Activities requiring mental alertness. Advise patients to avoid engaging in hazardous tasks requiring mental alertness and motor coordination after ingestion of this agent. Concurrent use of the medication with alcohol or other central nervous system depressants should be avoided because additional impairment of central nervous system performance may occur.

Obstructive bowel disease. Use with caution in patients with underlying intestinal motility disorders.

Acute abdominal conditions. Tuzistra XR should be used with caution in patients with acute abdominal conditions because the administration of codeine may obscure the

Dr. Gohil is Central Services Manager with Medical Services at MediMedia Managed Markets in Yardley, Pennsylvania. His email address is kgohil@medimedia.com.
Ramucirumab (Cyramza)

Manufacturer: Eli Lilly and Company, Indianapolis, Indiana
Date of Indication Expansion: April 24, 2015
New Indication: Combination therapy with FOLFIRI for the treatment of patients with metastatic colorectal cancer (mCRC) with disease progression on or after prior therapy with bevacizumab, oxaliplatin, and a fluoropyrimidine

Drug Class: Ramucirumab is a recombinant human IgG1 monoclonal antibody that specifically binds to vascular endothelial growth factor (VEGF) receptor 2.

Uniqueness of Drug: As a VEGF receptor 2 antagonist, ramucirumab specifically bind VEGF receptor 2 and blocks binding of VEGF receptor ligands VEGF-A, VEGF-C, and VEGF-D. As a result, ramucirumab inhibits ligand-stimulated activation of VEGF receptor 2, thereby inhibiting ligand-induced proliferation and migration of human endothelial cells.

Warnings and Precautions:

Hemorrhage. Permanently discontinue ramucirumab in patients who experience severe bleeding.

Arterial thromboembolic events (ATEs). Permanently discontinue ramucirumab in patients who experience a severe ATE.

Hypertension. Temporarily suspend ramucirumab for severe hypertension until it is medically controlled. Permanently discontinue ramucirumab if medically significant hypertension cannot be controlled with antihypertensive therapy or in patients with hypertensive crisis or hypertensive encephalopathy.

Infusion-related reactions (IRRs). Monitor patients during the infusion for signs and symptoms of IRRs in a setting with available resuscitation equipment. Immediately and permanently discontinue ramucirumab for grade 3 or 4 IRRs.

Gastrointestinal (GI) perforations. Permanently discontinue ramucirumab in patients who experience a GI perforation.

Impaired wound healing. Withhold ramucirumab prior to surgery. Resume following the surgical intervention based on clinical judgment of adequate wound healing. If a patient develops wound-healing complications during therapy, discontinue ramucirumab until the wound is fully healed.

Clinical deterioration in patients with Child-Pugh B or C cirrhosis. Use ramucirumab in patients with Child-Pugh B or C cirrhosis only if the potential benefits of treatment are judged to outweigh the risks of clinical deterioration.

Reversible posterior leukoencephalopathy syndrome (RPLS). Confirm the diagnosis of RPLS with MRI and discontinue ramucirumab in patients who develop RPLS.

Proteinuria, including nephrotic syndrome. Withhold ramucirumab for urine protein levels of 2 g or more over 24 hours. Reinitiate ramucirumab at a reduced dose once the urine protein level returns to less than 2 g over 24 hours. Permanently discontinue ramucirumab for urine protein levels greater than 3 g over 24 hours or in the setting of nephrotic syndrome.

Thyroid dysfunction. Monitor thyroid function during treatment with ramucirumab.

Embryofetal toxicity. Advise pregnant women of the risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment with ramucirumab and for at least three months after the last dose of ramucirumab.

Dosage and Administration: The recommended dose of ramucirumab is 8 mg/kg every two weeks administered by intravenous infusion over 60 minutes prior to FOLFIRI administration. Continue ramucirumab until disease progression or unacceptable toxicity.

Commentary: This approval is based on results from a randomized, double-blind, multinational trial of 1,072 patients who received FOLFIRI with either placebo or ramucirumab. Overall survival (OS) improvement was observed in patients receiving FOLFIRI plus ramucirumab compared with placebo, with median OS at 13.3 and 11.7 months, respectively.

Sources: www.fda.gov, Cyramza prescribing information

Fluticasone Furoate/Vilanterol (Breo Ellipta)

Manufacturer: GlaxoSmithKline, Research Triangle Park, North Carolina
Date of Indication Expansion: April 30, 2015
New Indication: Breo Ellipta is a combination inhaled corticosteroid/long-acting beta agonist indicated for the once-daily treatment of asthma in patients 18 years of age and older. It is contraindicated in the following conditions:

• Primary treatment of status asthmaticus or other acute episodes of chronic obstructive pulmonary disease (COPD) or asthma where intensive measures are required
• Severe hypersensitivity to milk proteins or demonstrated hypersensitivity to fluticasone furoate, vilanterol, or any of the excipients

Drug Class: Breo Ellipta is a combination of inhalation powders for oral inhalation consisting of fluticasone furoate (an inhaled corticosteroid [ICS]) and vilanterol (a long-acting beta agonist [LABA]).

Uniqueness of Drug: The precise mechanism through
which fluticasone furoate affects COPD and asthma symptoms is not known.

**Warnings and Precautions:**

**Asthma-related death.** LABAs such as vilanterol increase the risk of asthma-related death. Once asthma control is achieved and maintained, assess the patient at regular intervals and step down therapy (e.g., discontinue fluticasone furoate/vilanterol) if possible without loss of asthma control; maintain the patient on a long-term asthma control medication, such as an ICS. Do not use fluticasone furoate/vilanterol for patients whose asthma is adequately controlled on low- or medium-dose ICSs.

**Deterioration of disease and acute episodes.** Fluticasone furoate/vilanterol should not be initiated in patients during rapidly deteriorating or potentially life-threatening episodes of COPD or asthma. Fluticasone furoate/vilanterol should not be used for the relief of acute symptoms, i.e., as rescue therapy for the treatment of acute episodes of bronchospasm.

**Excessive use of fluticasone furoate/vilanterol and use with other LABAs.** Fluticasone furoate/vilanterol should not be used more often than recommended, at higher doses than recommended, or in conjunction with other medicines containing a LABA, as an overdose may result.

**Local effects of ICSs.** Advise the patient to rinse his or her mouth with water without swallowing following inhalation to help reduce the risk of oropharyngeal candidiasis.

**Pneumonia.** Physicians should remain vigilant for the possible development of pneumonia in patients with COPD because the clinical features of such infections overlap with the symptoms of COPD exacerbations.

**Immunosuppression.** Persons who are using drugs that suppress the immune system are more susceptible to infections than healthy individuals. In such children or adults who have not had diseases like chickenpox and measles or who have not been properly immunized, particular care should be taken to avoid exposure.

**Transferring patients from systemic corticosteroid therapy.** Patients requiring oral corticosteroids should be weaned slowly from systemic corticosteroid use after transferring to fluticasone furoate/vilanterol. Prednisone reduction can be accomplished by reducing the daily prednisone dose by 2.5 mg on a weekly basis during therapy with fluticasone furoate/vilanterol.

**Hypercorticism and adrenal suppression.** Patients treated with fluticasone furoate/vilanterol should be observed carefully for any evidence of systemic corticosteroid effects. Particular care should be taken in observing patients postoperatively or during periods of stress for evidence of inadequate adrenal response.

**Drug interactions with strong cytochrome P450 3A4 inhibitors.** Caution should be exercised when considering the coadministration of fluticasone furoate/vilanterol with long-term ketoconazole and other known strong CYP3A4 inhibitors because increased systemic corticosteroid and cardiovascular adverse effects may occur.

**Paradoxical bronchospasm.** If paradoxical bronchospasm occurs following dosing with fluticasone furoate/vilanterol, it should be treated immediately with an inhaled, short-acting bronchodilator; fluticasone furoate/vilanterol should be dis-