NEW DRUG APPROVAL

Brand Name	Dartisla ODT
Generic Name	glycopyrrolate
Drug Manufacturer	Edenbridge Pharmaceuticals, LLC

New Drug Approval

FDA Approval Date: December 16, 2021

Review Designation: Standard

Type of Review: Type 3 - New Dosage Form; New Drug Application (NDA): 215019

Dispensing Restrictions: N/A

Place in Therapy

DISEASE DESCRIPTION & EPIDEMIOLOGY

Peptic ulcer disease (PUD) is characterized by discontinuation in the inner lining of the gastrointestinal (GI) tract because of gastric acid secretion or pepsin. It extends into the muscularis propria layer of the gastric epithelium. It usually occurs in the stomach and proximal duodenum. It may involve the lower esophagus, distal duodenum, or jejunum. Epigastric pain usually occurs within 15-30 minutes following a meal in patients with a gastric ulcer; on the other hand, the pain with a duodenal ulcer tends to occur 2-3 hours after a meal. Today, testing for Helicobacter pylori is recommended in all patients with peptic ulcer disease. Endoscopy may be required in some patients to confirm the diagnosis, especially in those patients with sinister symptoms. Today, most patients can be managed with a proton pump inhibitor (PPI) based triple-drug therapy.

In the United States, the prevalence of self-reported physician-diagnosed peptic ulcer disease was 10% in 1990, and the approximate incidence is about 500,000 new cases per a year. Overall, however, the risk of mortality and need for hospitalizations due to PUD has been decreasing worldwide. This is most likely secondary to a decline in *Helicobacter pylori (H. pylori)* infections due to treatment and improved hygiene. Increased use of prescription and over-the-counter acid-suppressing medications and greater caution with non-steroidal anti-inflammatory drugs (NSAIDs) may account partially for this trend as well. In the last five years in the United States, there has been a decline in the prevalence of *H.pylori* in all ages. Yet, there are differences based on ethnicity with rates of infection that are over 60% in Mexican Americans versus 30% in the non-Hispanic white population. There are differences based on ethnicity with rates of infection that are over 60% in Mexican Americans versus 30% in the non-Hispanic white population.

Efficacy

N/A

Safety

ADVERSE EVENTS

Common

- **Dermatologic:** Flushing (Oral, 30%)
- **Gastrointestinal:** Constipation (Oral, 35%), Vomiting (oral, 40%), Xerostomia (Oral, 40%).
- **Renal:** Urinary tract infectious disease (oral, less than 2%).

- **Respiratory:** Nasal congestion (Oral, up to 30%).

Serious

- **Cardiovascular:** Atrial fibrillation, Bradyarrhythmia, Cardiac arrest, Cardiac dysrhythmia, Tachycardia, Ventricular fibrillation.
- **Endocrine metabolic:** Heat exhaustion, Malignant hyperthermia.
- **Gastrointestinal:** Pseudo-obstruction of intestine.
- **Immunologic:** Hypersensitivity reaction.
- **Neurologic:** Nystagmus (Oral, less than 2%), Seizure (Oral, less than 2%), Somnolence.
- **Ophthalmic:** Angle-closure glaucoma.
- **Respiratory:** Paradoxical bronchospasm, Respiratory arrest.

Other: Angioedema.

WARNINGS & PRECAUTIONS

Precipitation of Acute Glaucoma: Glycopyrrolate may cause increased intraocular pressure in patients with glaucoma and reduce the effects of antiglaucoma agents. Instruct patients to discontinue Dartisla ODT and promptly seek medical care if they experience symptoms of acute angle closure glaucoma (pain and reddening of the eyes accompanied by dilated pupils).

Partial or Complete Mechanical Intestinal Obstruction: Dartisla ODT may worsen intestinal mechanical obstruction, and diarrhea may be an early symptom of incomplete intestinal obstruction, especially in patients with ileostomy or colostomy. If partial or complete intestinal obstruction is suspected, discontinue use of Dartisla ODT and evaluate for potential intestinal obstruction.

Gastrointestinal Adverse Reactions Due to Decreased Gastrointestinal Motility: Glycopyrrolate reduces gastrointestinal motility and may result in delayed gastric emptying, constipation, and intestinal pseudo-obstruction and may precipitate or aggravate paralytic ileus and toxic megacolon. The risk of gastrointestinal adverse reactions is further increased with use of other anticholinergics and other medications that decrease gastrointestinal peristalsis. Monitor patients for symptoms of decreased gastrointestinal motility. Concomitant use of Dartisla ODT and other anticholinergics or other medications that decrease GI peristalsis is not recommended.

Cognitive and Visual Adverse Reactions: Glycopyrrolate may produce drowsiness and blurred vision and impair the mental and/or physical abilities required for the performance of hazardous tasks such as driving a motor vehicle, operating machinery or performing other hazardous work. Concomitant use of other drugs that have anticholinergic properties may increase these effects.

Heat Prostration at High Environmental Temperatures: In the presence of a high environmental temperature, heat prostration resulting in fever and heat stroke can occur with use of Dartisla ODT due to decreased sweating, particularly in geriatric patients.

Other Conditions Exacerbated by Anticholinergic Adverse Reactions: Dartisla ODT is not recommended in patients with other conditions exacerbated by anticholinergic adverse reactions (e.g., autonomic neuropathy, hyperthyroidism, cardiac disease, and hiatal hernia associated with reflux esophagitis) and in patients taking other anticholinergic medications.

Increased Risk of Anticholinergic Adverse Reactions in Geriatric Patients: Geriatric patients 65 years of age and older are at increased risk of anticholinergic adverse reactions that may lead to complications of urinary retention, bowel obstruction, heat prostration, arrhythmias, delirium, and falls or fractures. Dartisla ODT is not recommended in geriatric patients and may be contraindicated in some geriatric patients with underlying medical conditions.

CONTRAINDICATIONS

Dartisla ODT is contraindicated in:

1. **Patients at risk for anticholinergic toxicity due to an underlying medical condition, including:**
   - Glaucoma
   - Obstructive uropathies including prostatic hypertrophy
   - Mechanical obstructive diseases of gastrointestinal tract (e.g., pyloroduodenal stenosis, strictures)
   - Gastrointestinal motility disorders (e.g., achalasia, paralytic ileus, intestinal atony)
   - Bleeding gastrointestinal ulcer
   - Active inflammatory or infectious colitis which can lead to toxic megacolon
   - History of or current toxic megacolon
   - Myasthenia gravis
2. **Patients with a hypersensitivity to glycopyrrolate or any of the inactive ingredients in Dartisla ODT**.

Clinical Pharmacology

MECHANISMS OF ACTION

Antimuscarinic anticholinergic agents inhibit the action of acetylcholine at autonomic effectors innervated by postganglionic cholinergic nerves and on smooth muscles that respond to acetylcholine but lack cholinergic innervation. The peripheral cholinergic receptors are present in the autonomic effector cells of smooth muscle, cardiac muscle, the sinoatrial node, the atrioventricular node, exocrine glands, and to a lesser degree, in the autonomic ganglia. Oral glycopyrrolate inhibits the action of acetylcholine on salivary glands thereby reducing the extent of salivation.

Dose & Administration

ADULTS

The recommended dosage is 1.7 mg given two or three times daily administered on top of the tongue; allow to disintegrate and swallow without water. Administer at least one hour before or two hours after food.

PEDIATRICS

Safety and effectiveness in pediatric patients have not been established.

GERIATRICS

N/A

RENAL IMPAIRMENT

N/A

HEPATIC IMPAIRMENT

N/A

Product Availability

DOSAGE FORM(S) & STRENGTH(S)

Orally Disintegrating Tablets: 1.7 mg of glycopyrrolate.