Pharmacy Policy Bulletin: J-1044 Pylera (bismuth subcitrate potassium, metronidazole, tetracycline) – Commercial and Healthcare Reform	
Number: J-1044	**Category:** Prior Authorization
Line(s) of Business: ☒ Commercial ☒ Healthcare Reform ☐ Medicare	**Benefit:** **Commercial:** **Prior Authorization (1.):** **1.** Other Managed Prior Authorization = Yes w/ Prior Authorization **Healthcare Reform:** Not Applicable
Region(s): ☒ All ☐ Delaware ☐ New York ☐ Pennsylvania ☐ West Virginia	**Additional Restriction(s):** None
Version: J-1044-007	**Original Date:** 08/05/2020
Effective Date: 10/28/2024	**Review Date:** 10/02/2024

Drugs Product(s):	• Pylera (bismuth subcitrate potassium, metronidazole, tetracycline hydrochloride)
FDA-Approved Indication(s):	• In combination with omeprazole for the treatment of Helicobacter pylori (*H. pylori)* infection and duodenal ulcer disease (active or history of within the past 5 years) to eradicate *H. pylori.*

Background:	• Pylera is a combination of metronidazole, a nitroimidazole antimicrobial, tetracycline, a tetracycline class antimicrobial, and bismuth subcitrate potassium. Tetracycline hydrochloride interacts with the 30S subunit of the bacterial ribosome and inhibits protein synthesis. Metronidazole appears to selectively produce cytotoxic effects in anaerobes. The antibacterial action of bismuth salts is not well understood. • Helicobacter pylori (*H. pylori)* is the most prevalent chronic bacterial infection and is associated with peptic ulcer disease, chronic gastritis, gastric adenocarcinoma, and gastric mucosa associated lymphoid tissue (MALT) lymphoma. • All patients with evidence of active infection with *H. pylori* should be offered treatment. • Treatment of *H. pylori* is typically treated with combinations of 2-3 antibiotics along with a proton pump inhibitor (PPI). • The choice of initial antibiotic regimen to treat *H. pylori* should be guided by the presence of risk factors for macrolide resistance and the presence of a penicillin allergy. • For initial therapy in patients without risk factors for macrolide resistance, triple therapy with a PPI, clarithromycin, and amoxicillin or metronidazole for 14 days is recommended. For patients with a penicillin allergy, quadruple therapy with a PPI, bismuth, tetracycline, and a nitroimidazole for 10-14 days is recommended. • Success rate of triple therapy has declined due to the emergence of antibiotic antibiotic-resistant strains. The most effective treatment for *H. pylori* eradication is quadruple therapy (e.g., Pylera plus a PPI).

	• Factors associated with treatment failure include poor patient compliance and resistance of the patient's *H. pylori* strain to the prescribed antibiotics.
	• When a patient has been treated for *H. pylori* and the treatment has failed to eradicate the infection, the patient then requires salvage therapy. Antibiotics included in the initial regimen should generally be avoided; however, amoxicillin can be reused as resistance rarely develops.
	• Rifabutin-based triple therapy has the potential to increase the prevalence of rifabutin-resistant mycobacteria.
	• Reinfection with *H. pylori* following successful bacterial cure is unusual. Recurrence of infection most commonly represents recrudescence of the original bacterial strain.
	• Prescribing Considerations:
	  ○ Pylera has a black box warning for potential for carcinogenicity due to the metronidazole component.
	  ○ Safety and effectiveness of Pylera in pediatric patients infected with *H. pylori* have not been established.
	  ○ Pylera is contraindicated with concurrent usage of methoxyflurane, disulfiram usage within the last two weeks, alcoholic beverage consumption for at least 3 days during or after therapy, patients with Cockayne syndrome, severe renal impairment, and females who are pregnant.
	  ○ The package insert recommends to administer three Pylera capsules 4 times a day (after meals and at bedtime) for 10 days. Administer Pylera with omeprazole 20 mg twice daily (after the morning and evening meals). Guidelines recommend up to 14 days of treatment.
	  ○ Each capsule of Pylera contains 140 mg of bismuth subcitrate potassium, 125 mg of metronidazole, and 125 mg of tetracycline hydrochloride.
	  ○ Permanent discoloration of the tooth enamel may develop with use during tooth development (last half of pregnancy, infancy, and childhood to the age of 8 years) due to tetracycline component.
	  ○ To reduce the development of drug-resistant bacteria and maintain the effectiveness of Pylera and other antibacterial drugs, Pylera should be used only to treat or prevent infections that are proven or strongly suspected to be caused by bacteria.

Approval Criteria

I. Approval Criteria

When a benefit, coverage of Pylera (bismuth subcitrate potassium; metronidazole; tetracycline) may be approved when all of the following criteria are met **(A. through E.)**:

A. The member is 18 years of age or older.

B. The member has a diagnosis of *H. pylori* infection (ICD-10: B96.81) confirmed by one (1) of the following **(1. or 2.)**:
- **1.** Invasive techniques (e.g., endoscopic)
- **2.** Non-invasive techniques (e.g., urea breath test, stool antigen assay test).

C. The member meets one (1) of the following criteria **(1. or 2.)**:
- **1.** The member has previously been treated with all of the following components of a first-line treatment regimen and post-treatment testing has confirmed the treatments have failed to eradicate the *H. pylori* infection **(a., b., and c.)**:
  - **a.** lansoprazole **OR** omeprazole
  - **b.** amoxicillin **OR** metronidazole
  - **c.** clarithromycin
- **2.** The member has a clarithromycin allergy or prior exposure to macrolide therapy.

D. The member is concomitantly using omeprazole 20 mg twice daily (after the morning and evening meals) with Pylera therapy.

E. If the request is for brand Pylera, the member has experienced therapeutic failure or intolerance to generic bismuth subcitrate potassium; metronidazole; tetracycline hydrochloride capsules.

II. An exception to some or all of the criteria above may be granted for select members and/or circumstances based on state and/or federal regulations.

Limitations of Coverage

I. Coverage of drug(s) addressed in this policy for disease states outside of their FDA-approved indication should be denied based on the lack of clinical data to support their effectiveness and safety in other conditions unless otherwise noted in the approval criteria.
II. For Commercial or HCR members with a closed formulary, a non-formulary product will only be approved if the member meets the criteria for a formulary exception in addition to the criteria outlined within this policy.

Authorization Duration

- Commercial and HCR Plans: If approved, up to a 14 day authorization may be granted.

Automatic Approval Criteria

None

References:

1. Pylera [package insert]. Madison, NJ: Allergan USA, Inc.; July 2024.
2. Treatment Regimens for Helicobacter pylori. Available at: https://www.uptodate.com. Accessed July 16, 2024.
3. Chey, WD, et al. ACG Clinical Guideline: Treatment of Helicobacter pylori Infection. *Am J Gastroenterol.* 2017; 112:212-238.
4. Bacteriology and Epidemiology of the Helicobacter pylori infection. Available at: https://www.uptodate.com. Accessed July 16, 2024.
5. Godavarthy PK, Puli C. From antibiotic resistance to antibiotic Renaissance: A new era in helicobacter pylori treatment. *Cureus*. 2023.
6. DRUGDEX System (Micromedex 2.0). Greenwood Village, CO: Truven Health Analytics; 2024.

Pharmacy policies do not constitute medical advice, nor are they intended to govern physicians' prescribing or the practice of medicine. They are intended to reflect the plan's coverage and reimbursement guidelines. Coverage may vary for individual members, based on the terms of the benefit contract.

The plan retains the right to review and update its pharmacy policy at its sole discretion. These guidelines are the proprietary information of the plan. Any sale, copying or dissemination of the pharmacy policies is prohibited; however, limited copying of pharmacy policies is permitted for individual use.