Clinical Policy: Ulcer Therapy Products

Reference Number: CP.PMN.277
Effective Date: 06.01.22
Last Review Date: 05.24
Line of Business: Commercial, HIM, Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

The following are ulcer therapy products that require prior authorization:

- Bismuth subcitrate potassium/metronidazole/tetracycline hydrochloride (Pylera®)
- Omeprazole/clarithromycin/amoxicillin (Omeclamox-Pak®)
- Rifabutin/omeprazole/amoxicillin (Talicia®)
- Vonoprazan (Voquezna®)
- Vonoprazan/amoxicillin/clarithromycin (Voquezna™ Triple Pak™)
- Vonoprazan/amoxicillin (Voquezna™ Dual Pak™)

FDA Approved Indication(s)

- Pylera is indicated for use, in combination with omeprazole, for the treatment of patients with *Helicobacter pylori* infection and duodenal ulcer disease (active or history of within the past 5 years) to eradicate *H. pylori*.*
- Talicia, Voquezna (in combination with amoxicillin, or with amoxicillin and clarithromycin), Voquezna Triple Pak, and Voquezna Dual Pak are indicated for the treatment of *Helicobacter pylori* infection in adults.*
- Omeclamox-Pak is indicated for the treatment of patients with *Helicobacter pylori* infection and duodenal ulcer disease (active or up to one-year history) to eradicate *H. pylori*.*
- Voquezna is additionally indicated:
  - For healing of all grades of erosive esophagitis and relief of heartburn associated with erosive esophagitis in adults.
  - To maintain healing of all grades of erosive esophagitis and relief of heartburn associated with erosive esophagitis in adults.

* *To reduce the development of drug-resistant bacteria and maintain the effectiveness of Pylera, Talicia, Omeclamox-Pak, Voquenza, Voquezna Triple/Dual Pak, and other antibacterial drugs, these products should be used only to treat or prevent infections that are proven or strongly suspected to be caused by bacteria.*

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Omeclamox-Pak, Pylera, Talicia, Voquezna, Voquezna Triple Pak, and Voquezna Dual Pak are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. *Helicobacter pylori* Infection (must meet all)**:**

1. Diagnosis of *H. pylori* infection;
2. Prescribed by or in consultation with a gastroenterologist or infectious disease specialist;
3. Age ≥ 18 years;
4. One of the following (a or b):
   a. For Omeclamox-Pak, Pylera, and Talicia requests, one of the following (i or ii):
      i. Member must instead use the individual components concurrently (i.e., for Talicia generic rifabutin, amoxicillin, omeprazole), unless contraindicated or clinically significant adverse effects are experienced;
      ii. Member must use generic Prevpac (lansoprazole, amoxicillin, clarithromycin), unless contraindicated or clinically significant adverse effects are experienced;
   b. For Voquezna and Voquezna Triple/Dual Pak requests, one of the following (i or ii):
      i. If *H. pylori* is clarithromycin- and amoxicillin-sensitive, member must use one of the following, unless clinically significant adverse effects are experienced or both regimens are contraindicated (1 or 2):
         1) Generic Prevpac (lansoprazole, amoxicillin, clarithromycin);
         2) Bismuth quadruple therapy;
      ii. If *H. pylori* is clarithromycin- or amoxicillin-resistant, member must use bismuth quadruple therapy, unless contraindicated or clinically significant adverse effects are experienced;
5. For Pylera requests, prescribed in combination with a proton pump inhibitor (PPI; e.g., omeprazole);
6. Dose does not exceed one of the following (a, b, c, d, e, or f):
   a. Omeclamox-Pak: two omeprazole capsules, two clarithromycin tablets, and four amoxicillin capsules per day for 10 days;
   b. Pylera: 12 capsules per day for 10 days;
   c. Talicia: 12 capsules per day for 14 days;
   d. Voquezna Triple Pak: two vonoprazan tablets, four amoxicillin capsules, and two clarithromycin tablets per day for 14 days;
   e. Voquezna Dual Pak: two vonoprazan tablets and six amoxicillin capsules per day for 14 days;
   f. Voquezna (i and ii):
      i. 40 mg per day for 14 days, in combination with amoxicillin with or without clarithromycin;
      ii. 2 tablets per day for 14 days.

Approval duration:
Omeclamox-Pak, Pylera – 10 days
Talicia, Voquezna, Voquezna Triple/Dual Pak – 14 days

B. Erosive Esophagitis (must meet all)**:**

1. Request is for Voquezna;
2. Diagnosis of erosive esophagitis;
3. Age ≥ 18 years;

4. Failure of ≥ 8 week trial of a PPI at up to maximally indicated doses, unless clinically significant adverse effects are experienced or all are contraindicated;
5. Dose does not exceed the following (a and b):
   a. One of the following (i or ii):
      i. For the healing of erosive esophagitis: 20 mg per day for 8 weeks;
      ii. For the maintenance of erosive esophagitis: 10 mg per day for 6 months;
   b. 1 tablet per day.

Approval duration: Up to 8 months

C. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. *Helicobacter pylori* Infection, Erosive Esophagitis

1. Re-authorization is not permitted. Members must meet the initial approval criteria.

Approval duration: Not applicable

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND

criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial, CP.PMN.53 for Medicaid, and HIM.PA.154 for health insurance marketplace, or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

FDA: Food and Drug Administration
PPI: proton pump inhibitor

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
clarithromycin triple regimen	***H. pylori* infection:** 14 days: PPI (standard or double dose) BID; Clarithromycin 500 mg BID; Amoxicillin 1,000 mg BID or metronidazole 500 mg TID (if penicillin allergy)	See dosing regimen
bismuth quadruple regimen	***H. pylori* infection:** 10-14 days: PPI (standard dose) BID; bismuth subcitrate (120-300 mg) or subsalicylate (300 mg) QID; tetracycline 500 mg QID; metronidazole 250 mg QID or 500 mg TID-QID	See dosing regimen
concomitant regimen	***H. pylori* infection:** 10-14 days: PPI (standard dose) BID; Clarithromycin 500 mg BID; Amoxicillin 1,000 mg BID; Metronidazole or tinidazole 500 mg BID	See dosing regimen
sequential regimen	***H. pylori* infection:** 5-7 days of BID PPI (standard dose) + amoxicillin 1,000 mg BID; followed by 5-7 days of BID PPI, clarithromycin 500 mg BID + metronidazole/tinidazole 500 mg BID	See dosing regimen
hybrid regimen	***H. pylori* infection:** 7 days of BID PPI (standard dose) + amoxicillin 1,000 mg BID; followed by 7 days of BID PPI,	See dosing regimen

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	amoxicillin 1,000 mg BID + clarithromycin 500 mg BID + metronidazole/tinidazole 500 mg BID	
levofloxacin triple regimen	***H. pylori* infection:** 10-14 days: PPI (standard dose) BID; levofloxacin 500 mg QD; amoxicillin 1,000 mg BID	See dosing regimen
levofloxacin sequential regimen	***H. pylori* infection:** 5-7 days of BID PPI (standard dose) + amoxicillin 1,000 mg BID; followed by 5-7 days of BID PPI, amoxicillin 1,000 mg BID + metronidazole/tinidazole 500 mg BID + QD levofloxacin 500 mg	See dosing regimen
rifabutin triple	***H. pylori* infection:** 10 days of BID PPI (standard dose) + amoxicillin 1,000 mg BID + rifabutin 300 mg QD	See dosing regimen
PPIs: lansoprazole, omeprazole, pantoprazole, rabeprazole, esomeprazole	***Erosive Esophagitis*** Varies	Varies

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s):
  - Omeclamox-Pak: known hypersensitivity to omeprazole, any macrolide antibiotic, any penicillin, or any component of the formulations, coadministration with pimozide, lurasidone, ergotamine or dihydroergotamine
  - Pylera: concurrent usage of methoxyflurane, disulfiram usage within the last two weeks, alcoholic beverage consumption for at least three days during or after therapy, patients with Cockayne syndrome, severe renal impairment, women who are pregnant, known hypersensitivity to product components
  - Talicia: hypersensitivity to the components of Talicia; patients receiving rilpivirine-containing products, delavirdine or voriconazole
  - Voquezna: known hypersensitivity to vonoprazan or any component of Voquezna; rilpivirine-containing products
  - Voquezna Triple Pak: known hypersensitivity to vonoprazan, amoxicillin or any other beta-lactams, clarithromycin or any other macrolide antimicrobial, or any component of Voquezna Triple Pak; rilpivirine-containing products; due to clarithromycin component: pimozide, lomitapide, lovastatin, simvastatin, ergot alkaloids (ergotamine or dihydroergotamine), colchicine in renal or hepatic impairment, history of cholestatic jaundice/hepatic dysfunction with use of clarithromycin, lurasidone

- Voquezna Dual Pak: known hypersensitivity to vonoprazan, amoxicillin or any other beta-lactams, or any component of Voquezna Dual Pak; rilpivirine-containing products

- Boxed warning(s):
  - Pylera: potential for carcinogenicity (metronidazole has been shown to be carcinogenic in mice and rats)

V. Dosage and Administration

Drug Name	Indication	Dosing Regimen	Maximum Dose
Omeprazole/ clarithromycin/amoxicillin (Omeclamox-Pak)	H. pylori	omeprazole 20 mg plus clarithromycin 500 mg plus amoxicillin 1,000 mg, each given PO BID for 10 days	See regimen
Bismuth subcitrate potassium/ metronidazole/tetracycline hydrochloride (Pylera)	H. pylori	Three capsules PO QID for 10 days with omeprazole 20 mg BID	See regimen
Rifabutin/omeprazole/amoxicillin (Talicia)	H. pylori	Four capsules PO TID (at least 4 hours apart) for 14 days	See regimen
Vonoprazan/amoxicillin/ clarithromycin (Voquezna Triple Pak)	H. pylori	Each of the following given BID for 14 days: vonoprazan 20 mg (2 tablets/day), amoxicillin 1,000 mg (4 capsules/day), and clarithromycin 500 mg (2 tablets/day)	See regimen
Vonoprazan/amoxicillin (Voquezna Dual Pak)	H. pylori	Vonoprazan 20 mg BID (2 tablets/day) and amoxicillin 1,000 mg TID a day (6 capsules/day) for 14 days	See regimen
Vonoprazan (Voquezna)	H. pylori	*Dual therapy*: 20 mg PO BID in combination with amoxicillin 1,000 mg PO TID for 14 days *Triple therapy*: 20 mg PO BID in combination with amoxicillin 1,000 mg and clarithromycin 500 mg PO BID for 14 days	20 mg/day for 14 days
	Erosive esophagitis	*Healing*: 20 mg PO QD for 8 weeks *Maintenance*: 10 mg PO QD for up to 6 months	See regimen

VI. Product Availability

Drug Name	Availability
Omeprazole/clarithromycin/ amoxicillin (Omeclamox-Pak)	Pack of 10 daily administration cards for morning and evening dosing, each containing: • Two 20 mg omeprazole delayed-release capsules • Two 500 mg clarithromycin tablets • Four 500 mg amoxicillin capsules
Bismuth subcitrate potassium/ metronidazole/tetracycline hydrochloride (Pylera)	Each capsule contains: 140 mg of bismuth subcitrate potassium, 125 mg metronidazole, 125 mg of tetracycline hydrochloride
Rifabutin/omeprazole/ amoxicillin (Talicia)	Delayed-release capsule: omeprazole 10 mg, (equivalent to 10.3 mg of omeprazole magnesium), amoxicillin 250 mg, and rifabutin 12.5 mg
Vonoprazan/amoxicillin/ clarithromycin (Voquezna Triple Pak)	Carton of 14 daily administration packs for morning and evening dosing, each containing the following three drug products: tablets: vonoprazan 20 mg, clarithromycin 500 mg; capsules: amoxicillin 500 mg
Vonoprazan/amoxicillin (Voquezna Dual Pak)	Carton of 14 daily administration packs for morning, mid-day and evening dosing, each containing the following two drug products: tablets: vonoprazan 20 mg; capsules: amoxicillin 500 mg
Vonoprazan (Voquenza)	Tablets: 10 mg, 20 mg

VII. References

1. Omeclamox-Pak Prescribing Information. Nashville, TN: Cumberland Pharmaceuticals Inc.; August 2023. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/050824s011s012lbl.pdf. Accessed January 10, 2024.
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9. Yadlapati R, Gyawali CP, Pandolfino JE, et al. AGA clinical practice update on the personalized approach to the evaluation and management of GERD: Expert review. Clinical Gastroenterology and Hepatology. 2022; 20(5): 984-994.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created per February SDC and prior clinical guidance (Talicia removed from CP.PMN.223).	02.17.22	05.22
RT4: added Voquezna Triple/Dual Pak to criteria with specific redirection based on *H. pylori* clarithromycin- and amoxicillin-sensitivity.	06.08.22	08.22
Template changes applied to other diagnoses/indications.	10.07.22	
2Q 2023 annual review: no significant changes; added boxed warning for Pylera to Appendix C; simplified dosing regimen for Talicia in initial criteria and dosing table; references reviewed and updated	02.02.23	05.23
RT4: added Voquezna with corresponding criteria set for erosive esophagitis; updated Appendix C with Voquezna Triple/Dual Pak contraindications; renamed policy from Ulcer Therapy Combinations to Ulcer Therapy Products.	11.15.23	02.24
2Q 2024 annual review: no significant changes; for Omeclamox-Pak updated contraindications to include coadministration with lurasidone per updated prescribing information; updated Talicia dosing in Section V; references reviewed and updated.	01.10.24	05.24

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions, and

limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members, and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.