Clinical Policy: Ulcer Therapy Combinations

Reference Number: CP.PMN.277
Effective Date: 06.01.22
Last Review Date: 08.22
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 combination products that require prior authorization:

- Bismuth subcitrate potassium/metronidazole/tetracycline hydrochloride (Pylera®)
- Omeprazole/clarithromycin/amoxicillin (Omeclamox-Pak®)
- Rifabutin/omeprazole/amoxicillin (Talicia®)
- 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 Triple/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*.*

  ** To reduce the development of drug-resistant bacteria and maintain the effectiveness of Pylera/Talicia/Omeclamox-Pak/ 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, and Voquezna Triple/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 Triple/Dual Pak, 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 (e.g., omeprazole);
6. Dose does not exceed one of the following (a, b, c, d, or e):
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: 150 mg rifabutin (12 capsules) per day for 14 days;
d. Voquezna Triple Pak: two vonoprazan tablets, four amoxicillin capsules, and 2 clarithromycin tablets per day for 14 days;
e. Voquezna Dual Pak: two vonoprazan tablets, six amoxicillin capsules per day for 14 days.

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

B. Other diagnoses/indications
1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, CP.PMN.53 for Medicaid, and HIM.PA.154 for health insurance marketplace.

II. Continued Therapy

A. *Helicobacter pylori* Infection
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. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.
Approval duration: Duration of request or 12 months (whichever is less); or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is

NOT authorized): CP.CPA.09 for commercial, CP.PMN.53 for Medicaid, and HIM.PA.154 for health insurance marketplace.

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

LAC: lansoprazole, amoxicillin, clarithromycin

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

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, 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
- Boxed warning(s): none reported

V. Dosage and Administration

Drug Name	Dosing Regimen	Maximum Dose
Omeprazole/clarithromycin/amoxicillin (Omeclamox-Pak)	omeprazole 20 mg plus clarithromycin 500 mg plus amoxicillin 1000 mg, each given PO BID for 10 days	See dosing regimen
Bismuth subcitrate potassium/metronidazole/tetracycline hydrochloride (Pylera)	Three capsules PO QID for 10 days with omeprazole 20 mg BID	See dosing regimen
Rifabutin/ omeprazole/ amoxicillin (Talicia)	Four capsules PO Q8H for 14 days	150 mg rifabutin (12 capsules)/day

Drug Name	Dosing Regimen	Maximum Dose
Voquezna Triple Pak (vonoprazan, amoxicillin, clarithromycin)	Each of the following given twice daily for 14 days: vonoprazan 20 mg (2 tablets/day), amoxicillin 1,000 mg (4 capsules/day), clarithromycin 500 mg (2 tablets/day)	See dosing regimen
Voquezna Dual Pak (vonoprazan, amoxicillin)	Vonoprazan 20 mg twice daily (2 tablets/day), amoxicillin 1,000 mg three times a day (6 capsules/day) for 14 days	See dosing 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
Voquezna Triple Pak (vonoprazan, amoxicillin, clarithromycin)	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
Voquezna Dual Pak (vonoprazan, amoxicillin)	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

VII. References

1. Omeclamox-Pak Prescribing Information. Nashville, TN: Cumberland Pharmaceuticals Inc.; November 2020. Available at: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=9e52c29a-fdbe-4a4d-b280-d700eba5b94f. Accessed February 21, 2022.

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3. Talicia Prescribing Information. Raleigh, NC: RedHill Biopharma Inc.; October 2021. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/213004s002lbl.pdf. Accessed February 21, 2022.
4. Voquezna Triple Pak, Voquezna Dual Pak Prescribing Information. Buffalo Grove, IL: Phanthom Pharmaceuticals; May 2022. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/215152s000,215153s000lbl.pdf. Accessed June 7, 2022.
5. Chey WD, Leontiadis GI, Howden CW, et al. ACG Clinical Guideline: Treatment of Helicobacter pylori Infection. American Journal of Gastroenterology: 2017 January 10; doi: 10.1038/ajg.2016.563.
6. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2022. Available at: http://www.clinicalpharmacology-ip.com/. Accessed February 21, 2022.

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

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.