Clinical Policy: Crofelemer (Mytesi)

Reference Number: CP.CPA.32
Effective Date: 11.16.16
Last Review Date: 08.23
Line of Business: Commercial

Revision Log

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

Description

Crofelemer (Mytesi®) is an anti-diarrheal.

FDA Approved Indication(s)

Mytesi is indicated for the symptomatic relief of non-infectious diarrhea in adult patients with human immunodeficiency virus/acquired immune deficiency syndrome (HIV/AIDS) on anti-retroviral therapy.

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 Mytesi is **medically necessary** when the following criteria are met.

I. Initial Approval Criteria

A. Non-Infectious Diarrhea in HIV/AIDS (must meet all)**:**

1. Diagnosis of HIV/AIDS;
2. Age ≥ 18 years;
3. Member has non-infectious diarrhea;
4. Member is currently receiving anti-retroviral therapy as evidenced by claims history;
5. Failure of an antidiarrheal medication (e.g., loperamide, diphenoxylate/atropine, bismuth subsalicylate), unless clinically significant adverse effects are experienced or all are contraindicated;
6. Dose does not exceed 250 mg (2 tablets) per day.

Approval duration: 6 months

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; 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; 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.

II. Continued Therapy

A. Non-Infectious Diarrhea in HIV/AIDS (must meet all)**:**

1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B);*
2. Member is responding positively to therapy;
3. If request is for a dose increase, new dose does not exceed 250 mg (2 tablets) per day.

Approval duration: 12 months

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; 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; 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.

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 or evidence of coverage documents;

B. Irritable bowel syndrome with diarrhea.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

AIDS: acquired immune deficiency syndrome
FDA: Food and Drug Administration
HIV: human immunodeficiency virus

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
loperamide (Imodium®)	2 mg PO after each loose stool	16 mg/day
diphenoxylate/atropine (Lomotil®)	2 tablets (5-0.05 mg) PO QID	20 mg/day (diphenoxylate)
bismuth subsalicylate (PeptoBismol®)	Regular strength: 524 mg PO every 0.5-1 hour as needed Extra strength: 1,050 mg PO every 1 hour as needed	Regular strength: 4,192 mg/day (8 doses/24 hours) Extra strength: 4,200 mg/day (4 doses/24 hours)

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
None reported

Appendix D: General Information
- Mytesi was known by the trade name Fulyzaq until October 2016.
- In a 12-week, double-blind, placebo-controlled trial evaluating 3 doses (125 mg, 250 mg, 500 mg BID) of Mytesi in 242 patients with diarrhea-predominant irritable bowel syndrome, Mytesi did not produce significant improvement in stool consistency, the primary endpoint.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Non-infectious diarrhea in HIV/AIDS	One 125 mg tablet PO BID	250 mg/day

VI. Product Availability
Delayed-release tablet: 125 mg

VII. References
1. Mytesi Prescribing Information. San Francisco, CA: Napo Pharmaceuticals, Inc.; November 2020. Available at: www.mytesi.com. Accessed May 8, 2023.
2. Mangel AW, Chaturvedi P. Evaluation of crofelemer in the treatment of diarrhea-predominant irritable bowel syndrome patients. Digestion. 2008; 78(4): 180-186.
3. Micromedex® Healthcare Series [Internet database]. Greenwood Village, Colo: Thomson Healthcare. Updated periodically. Accessed May 8, 2023.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
3Q 2019 annual review: no significant changes; references reviewed and updated.	05.21.19	08.19
3Q 2020 annual review: no significant changes; references reviewed and updated.	04.20.20	08.20
3Q 2021 annual review: no significant changes; references reviewed and updated.	03.18.21	08.21
3Q 2022 annual review: no significant changes; references reviewed and updated.	03.29.22	08.22
Template changes applied to other diagnoses/indications and continued therapy section.	09.23.22	
3Q 2023 annual review: no significant changes; references reviewed and updated.	04.18.23	08.23

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.

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