Eohilia Prior Authorization with Quantity Limit Program Summary

This program applies to FlexRx Closed, FlexRx Open, FocusRx, GenRx Closed, GenRx Open, Health Insurance Marketplace, and KeyRx formularies.

This is a FlexRx Standard and GenRx Standard program.

The BCBS MN Step Therapy Supplement also applies to this program for all Commercial/HIM lines of business.

POLICY REVIEW CYCLE

Effective Date	Date of Origin
10-01-2024	10-01-2024

FDA LABELED INDICATIONS AND DOSAGE

Agent(s)	FDA Indication(s)	Notes	Ref#
Eohilia™ (budesonide) Oral suspension	Treatment of eosinophilic esophagitis (EoE) for 12 weeks in adult and pediatric patients aged 11 years and older Limitations of use: • Eohilia has not been shown to be safe and effective for the treatment of EoE for longer than 12 weeks		1

See package insert for FDA prescribing information: https://dailymed.nlm.nih.gov/dailymed/index.cfm

CLINICAL RATIONALE

Eosinophilic Esophagitis	Eosinophilic Esophagitis (EoE) is an allergen/immune-mediated disease characterized by symptoms of esophageal dysfunction and marked eosinophilic inflammation of the esophageal mucosa in the absence of secondary causes. EoE has dramatically increased in prevalence over the years. EoE is characterized by symptoms related to esophageal dysfunction and histologically with eosinophil-predominant inflammation (a peak count of greater than or equal to 15 eosinophils per high-power field on esophageal biopsy). Atopic and allergic inflammatory conditions commonly occur concomitantly with EoE.(2) The symptoms of EoE are age dependent. Young children may refuse to eat, have decreased appetite, recurring abdominal pain, trouble swallowing, and vomiting. Young adults and adults have the same symptoms, but often struggle to swallow dry or dense, solid foods due to inflammation. Food impaction is a common cause for emergency room visits in patients with EoE. Patients may also have concurrent gastroesophageal reflux disease (GERD). EoE is a progressive disease if left untreated. The chronic inflammation can lead to tissue fibrosis and strictures in the esophagus that require esophageal dilation.(3) The diagnosis of EoE is suspected on the basis of chronic symptoms such as dysphagia, food impaction, food refusal, failure to progress with food introduction, heartburn, regurgitation, vomiting, chest pain, odynophagia, abdominal pain, and malnutrition. Due to the wide range of chronic symptoms, the diagnosis should be highly considered in the presence of concomitant atopic conditions and if there are endoscopic findings. Endoscopic findings associated with EoE include esophageal rings, longitudinal furrows, exudates, edema, strictures, or narrow caliber esophagus. Assessment of non-EoE disorders and esophageal biopsy are required to confirm the

	diagnosis of EoE, with at least 15 eosinophils (eos)/ high-power field (hpf) present on esophageal biopsy.(4) Nonpharmacological treatment of EoE includes dilation and diet. Dilation is only conditionally recommended for patients with dysphagia associated with strictures due to EoE, noting that the dilation does not address the underlying inflammation.(5) Both elemental and elimination diets have been shown to be effective, however, barriers of adherence and cost make this treatment modality feasible only for select patients.(5,6) Proton pump inhibitors (PPIs) are a first line treatment option for patients with EoE, and PPI monotherapy is widely used in practice. PPIs have a longstanding safety profile and have shown to be effective based on symptom response and histological remission. The 2020 American Gastroenterological Association (AGA) and the Joint Task Force on Allergy-Immunology Practice Parameters (JTF) guidelines conditionally recommend their use while the 2022 British Society of Gastroenterology (BSG) and British Society of Pediatric Gastroenterology, Hepatology and Nutrition (BSPGHAN) guidelines strongly recommend their use.(5,6) The AGA/JTF and BSG/BSPGHAN both strongly recommend the use of topical glucocorticoids for the treatment of EoE. Studies showed that topical (swallowed) budesonide or topical fluticasone induced histological remission significantly better than placebo and had similar adverse events to placebo. Due to the chronic nature of the disease and the risk of progression, topical corticosteroids may be continued as maintenance therapy after remission with short term use. A clinical review of the patient should guide this decision based on preference to avoid long term adverse effects of topical steroids, or to prevent undesirable outcomes of the disease itself.(5,6)
Efficacy	The efficacy and safety of Eohilia 2 mg twice daily were evaluated in two multicenter, randomized, double-blind, parallel-group, placebo-controlled 12-week studies (Study 1 [NCT02605837] and Study 2 [NCT01642212]). Eligible subjects in both studies had esophageal inflammation defined as greater than or equal to 15 eosinophils/high-power field (hpf) from at least 2 levels of the esophagus at baseline following a treatment course of a proton pump inhibitor (PPI) either prior to or during screening and at least 4 days of dysphagia as measured by the Dysphagia Symptom Questionnaire (DSQ) over a 2-week period prior to randomization. Concomitant use of stable doses of inhaled or intranasal steroids (for conditions other than EoE), PPIs, H2-receptor antagonists, antacids, antihistamines or anti-leukotrienes, and maintenance immunotherapy was allowed. In Study 1, subjects were enrolled after maintaining a stable diet for at least 3 months prior to screening and were instructed to maintain a stable diet throughout the study. Subjects were excluded if they were on a full liquid or 6-food elimination diet. In Study 2, subjects were instructed to maintain a stable diet throughout the study. In both studies, subjects were instructed to not eat or drink for 30 minutes after taking the drug and then to rinse their mouth with water and spit out the contents without swallowing prior to resuming normal oral intake.(1) A total of 318 subjects (277 adults and 41 pediatric subjects) were randomized and received at least one dose of study drug (Eohilia or placebo) in Study 1. The mean age of the study population was 34 years (range 11 to 56 years). Over 80% of the subjects were on concomitant PPI. The mean (SD) DSQ combined scores at baseline were 30.3 (13.9) and 30.4 (13.1) in the EOHILIA and placebo groups, respectively.(1) A total of 92 subjects (58 adults and 34 pediatric subjects) were randomized and received at least one dose of study drug (Eohilia or placebo) in Study 2. The mean age of the study population was 22 years (range 11 to 42 years). Over 65% of the subjects were on concomitant PPI. The mean (SD) DSQ combined scores at baseline were 30.7 (16.0) and 29.0 (13.5) in the EOHILIA and placebo groups, respectively.(1) Efficacy endpoints for both studies were the proportion of patients with a histologic response (defined as a peak eosinophil count of less than or equal to 6/hpf across all available esophageal levels) and the absolute change from baseline in subject-

reported DSQ combined score after 12 weeks of treatment. Results are shown in the table below:(1)

	Study 1			Study 2		
Efficacy Endpoints	**Eohilia 2mg twice daily (n=213)**	**Placebo (n=105)**	**Treatment difference and 95% CI**	**Eohilia 2mg twice daily (n=50)**	**Placebo (n=42)**	**Treatment difference and 95% CI**
Proportion of subjects achieving histological remission (peak esophageal intraepithelial eosinophil count ≤6 eos/hpf)	53.1%	1.0%	52.4% (43.3,59.1)	38.0%	2.4%	35.8% (17.2,50.0)
Absolute change from baseline in DSQ combined score (0-84*), LS mean (SE)	-10.2 (1.5)	-6.5 (1.8)	-3.7 (-6.8,-0.6)	-14.5 (1.8)	-5.9 (2.1)	-8.6 (-13.7,-3.5)

*Total biweekly DSQ scores range from 0 to 84, higher scores indicate greater frequency and severity of dysphagia

In both studies, during the last 2 weeks of the 12-week treatment periods, a greater proportion of subjects randomized to Eohilia experienced no dysphagia or only experienced dysphagia that "got better or cleared up on its own" compared to placebo, as measured by the subject-reported DSQ.(1)

In Study 1, 48 subjects from the Eohilia treatment arm entered a double-blind randomized withdrawal extension study and either received Eohilia 2mg twice daily or placebo for up to an additional 36 weeks. No statistically significant difference was demonstrated between the two groups based on eosinophil count and/or clinical symptoms measured by the DSQ at Week 36.(1)

Safety	Eohilia is contraindicated in patients with hypersensitivity to budesonide. Serious hypersensitivity reactions, including anaphylaxis, have occurred with oral budesonide products.(1)

REFERENCES

Number	Reference
1	Eohilia prescribing information. Takeda Pharmaceuticals America, Inc. February 2024.

Number	Reference
2	O'Shea K, Aceves SS, Dellon ES, et al. Pathophysiology of Eosinophilic Esophagitis. *Gastroenterology*. 2018;154(2):333-345. doi:10.1053/j.gastro.2017.06.065
3	The American Academy of Allergy, Asthma & Immunology. Eosinophilic Esophagitis: Symptoms, Diagnosis & Treatment. https://www.aaaai.org/conditions-treatments/related-conditions/eosinophilic-esophagitis. Last revised May 1, 2023.
4	Dellon ES, Liacouras CA, Molina-Infante J, et al. Updated International Consensus Diagnostic Criteria for Eosinophilic Esophagitis: Proceedings of the AGREE Conference. *Gastroenterology*. 2018;155(4):1022-1033.e10. doi:10.1053/j.gastro.2018.07.009
5	Hirano I, Chan ES, Rank MA, et al. AGA Institute and the Joint Task Force on Allergy-Immunology Practice Parameters Clinical Guidelines for the Management of Eosinophilic Esophagitis. Gastroenterology. 2020;158(6):1776-1786. doi:10.1053/j.gastro.2020.02.038
6	Dhar A, Haboubi H, Attwood S, et al. British Society of Gastroenterology (BSG) and British Society of Paediatric Gastroenterology, Hepatology and Nutrition (BSPGHAN) joint consensus guidelines on the diagnosis and management of eosinophilic oesophagitis in children and adults. *Gut*. May 2022:gutjnl-327326. doi:10.1136/gutjnl-2022-327326

POLICY AGENT SUMMARY PRIOR AUTHORIZATION

Target Brand Agent(s)	Target Generic Agent(s)	Strength	Targeted MSC	Available MSC	Final Age Limit	Preferred Status
Eohilia	budesonide oral suspension	2 MG/10ML	M ; N ; O ; Y	N		

POLICY AGENT SUMMARY QUANTITY LIMIT

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	QL Amount	Dose Form	Day Supply	Duration	Addtl QL Info	Allowed Exceptions	Targeted NDCs When Exclusions Exist
Eohilia	budesonide oral suspension	2 MG/10ML	1800	mLs	90	DAYS			

CLIENT SUMMARY – PRIOR AUTHORIZATION

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Eohilia	budesonide oral suspension	2 MG/10ML	FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx

CLIENT SUMMARY – QUANTITY LIMITS

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Eohilia	budesonide oral suspension	2 MG/10ML	FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ; Health Insurance

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
			Marketplace/BasicRx ; KeyRx

PRIOR AUTHORIZATION CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
PA	**Target Agent(s)** will be approved when ALL of the following are met: 1. The patient has a diagnosis of eosinophilic esophagitis (EoE) AND the patient's diagnosis was confirmed by ALL of the following: A. Chronic symptoms of esophageal dysfunction **AND** B. Greater than or equal to 15 eosinophils per high-power field on esophageal biopsy **AND** C. Other causes that may be responsible for or contributing to symptoms and esophageal eosinophilia have been ruled out **AND** 2. ONE of the following: A. The patient is currently being treated with the requested agent as indicated by ALL of the following: 1. A statement by the prescriber that the patient is currently taking the requested agent **AND** 2. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on requested agent **AND** 3. The prescriber states that a change in therapy is expected to be ineffective or cause harm **OR** B. The patient has tried and had an inadequate response to ONE standard corticosteroid therapy used in the treatment of EoE (i.e., budesonide oral suspension, swallowed budesonide, nebulizer suspension, swallowed fluticasone MDI) **OR** C. The patient has an intolerance or hypersensitivity to standard corticosteroid therapy used in the treatment of EoE **OR** D. The patient has an FDA labeled contraindication to ALL standard corticosteroid therapies used in the treatment of EoE **OR** E. The prescriber has provided documentation that ALL standard corticosteroid therapies used in the treatment of EoE cannot be used due to a documented medical condition or comorbid condition that is likely to cause an adverse reaction, decrease ability of the patient to achieve or maintain reasonable functional ability in performing daily activities or cause physical or mental harm **OR** F. The patient has tried and had an inadequate response to ONE proton pump inhibitor (PPI) used in the treatment of EoE **OR** G. The patient has an intolerance or hypersensitivity to PPI therapy used in the treatment of EoE **OR** H. The patient has an FDA labeled contraindication to ALL PPI therapies used in the treatment of EoE **OR** I. The prescriber has provided documentation that ALL PPI therapies used in the treatment of EoE cannot be used due to a documented medical condition or comorbid condition that is likely to cause an adverse reaction, decrease ability of the patient to achieve or maintain reasonable functional ability in performing daily activities or cause physical or mental harm **AND** 3. If the patient has an FDA labeled indication, then ONE of the following: A. The patient's age is within FDA labeling for the requested indication for the requested agent **OR** B. There is support for using the requested agent for the patient's age for the requested indication **AND** 4. The prescriber is a specialist in the area of the patient's diagnosis (e.g., gastroenterologist, allergist, immunologist) or the prescriber has consulted with a specialist in the area of the patient's diagnosis **AND** 5. The patient does NOT have any FDA labeled contraindications to the requested agent **AND** 6. ONE of the following:

Module	Clinical Criteria for Approval
	A. The patient has not previously been treated with a course of therapy (12 weeks) with the requested agent **OR** B. The patient has previously been treated with a course of therapy with the requested agent, AND there is support for an additional course of therapy with the requested agent **Length of Approval:** 3 months NOTE: If Quantity Limit applies, please refer to Quantity Limit Criteria.

QUANTITY LIMIT CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
QL	**Quantity limit for the Target Agent(s)** will be approved when ONE of the following is met: 1. The requested quantity (dose) does NOT exceed the program quantity limit **OR** 2. The requested quantity (dose) exceeds the program quantity limit AND ONE of the following: A. BOTH of the following: 1. The requested agent does NOT have a maximum FDA labeled dose for the requested indication **AND** 2. There is support for therapy with a higher dose for the requested indication **OR** B. BOTH of the following: 1. The requested quantity (dose) does NOT exceed the maximum FDA labeled dose for the requested indication **AND** 2. There is support for why the requested quantity (dose) cannot be achieved with a lower quantity of a higher strength that does NOT exceed the program quantity limit **OR** C. BOTH of the following: 1. The requested quantity (dose) exceeds the maximum FDA labeled dose for the requested indication **AND** 2. There is support for therapy with a higher dose for the requested indication **Length of Approval:** up to 3 months