# PRIOR AUTHORIZATION CRITERIA

**BRAND NAME***
**(generic)**

**PULMICORT RESPULES 1MG ONLY**
**(budesonide)**

***Status: CVS Caremark Criteria***
***Type: Post Limit Prior Authorization*** ***Ref # 2495-J***

**Drugs that are listed in the target drug box include both brand and generic and all dosage forms and strengths unless otherwise stated. OTC products are not included unless otherwise stated.*

## FDA-APPROVED INDICATIONS

Pulmicort Respules is indicated for the maintenance treatment of asthma and as prophylactic therapy in children 12 months to 8 years of age.

Limitations of Use:
Pulmicort Respules is NOT indicated for the relief of acute bronchospasm.

Off-Label / Rare Disease / Orphan Drug Uses
Eosinophilic Esophagitis[2-8]

## COVERAGE CRITERIA

The requested drug will be covered with prior authorization when the following criteria are met:

- The patient has the diagnosis of eosinophilic esophagitis (EoE)

**AND**

- The request is for continuation of therapy with Pulmicort (budesonide) Respules at a dose of 1mg twice daily (2mg daily), and the patient has been evaluated for improvement or relapse in symptoms or inflammation

**OR**

- The patient had all of the following: A) Eosinophil-predominant inflammation on biopsy, B) Trial of a proton pump inhibitor (PPI), C) Secondary causes of esophageal eosinophilia were ruled out

Quantity Limits apply.

## RATIONALE

The intent of the criteria is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. Pulmicort Respules is indicated for the maintenance treatment of asthma and as prophylactic therapy in children 12 months to 8 years of age.[1] The Initial Limits (Ref# 158-H) cover a quantity sufficient for the maintenance treatment of asthma and as prophylactic therapy.

Guidelines from the American College of Gastroenterology (ACG) state that although there are limited data supporting management decisions, clinical parameters are needed to guide the care of patients with eosinophilic-esophageal disorders.[4] Esophageal eosinophilia alone does not define eosinophilic esophagitis (EoE). Esophageal eosinophilia is most commonly found in three clinical conditions: gastroesophageal reflux disease (GERD), EoE, and proton-pump inhibitor-responsive esophageal eosinophilia (PPI-REE). A number of other diseases with distinct clinical and histologic features have also been associated with eosinophilic gastrointestinal disorders. Isolated esophageal eosinophilia must be distinguished from a more generalized disease such as eosinophilic gastroenteritis or hypereosinophilic syndrome.[3-5,7] The International Consensus Diagnostic Criteria (Dellon E 2018) states that EoE and PPI-REE share similar clinical, endoscopic, histologic, immunologic, and molecular features.[8] Therefore, diagnosis of EoE should be confirmed and other eosinophilic esophageal disorders should be ruled out.

The ACG guidelines state that EoE is diagnosed by clinicians taking into consideration both clinical and pathologic information without either of these parameters interpreted in isolation, and defined by the following criteria[3-5]:
• Symptoms related to esophageal dysfunction
• Eosinophil-predominant inflammation on esophageal biopsy, characteristically consisting of a peak value of ≥ 15 eosinophils per high-power field (eos/hpf)
• Mucosal eosinophilia is isolated to the esophagus and persists after a PPI trial
• Secondary causes of esophageal eosinophilia excluded
• A response to treatment (dietary elimination; topical corticosteroids) supports, but is not required for, diagnosis
The International Consensus Diagnostic Criteria (Dellon E 2018) states that EoE should be diagnosed when there are symptoms of esophageal dysfunction and at least 15 eosinophils per high-power field (or approximately 60 eosinophils per $mm^2$) on esophageal biopsy and after a comprehensive assessment of non-EoE disorders that could cause or potentially contribute to esophageal eosinophilia. The evidence suggests that PPIs are better classified as a treatment for esophageal eosinophilia that may be due to EoE than as a diagnostic criterion.[8]

Regarding the diagnosis and management of eosinophilic esophagitis (EoE), the ACG guidelines recommend that oral administration of topical corticosteroids (i.e., fluticasone or budesonide[3-6], swallowed rather than inhaled , for an initial duration of 8 weeks), be considered as first-line therapy in adults and children.[3-6] Additionally, swallowed topical glucocorticosteroids were the only therapy to receive a strong recommendation in the AGA Institute and the Joint Task Force on Allergy Immunology Practice Parameters Guidelines for the Management of Eosinophilic Esophagitis.[9] The ACG guidelines recommend dosage in children be determined by age, height, or weight.[4] A possible starting dose for maintenance therapy in adults would be 1mg per day of budesonide, with lower doses in children, and with doses titrated to provide the best clinical response at the lowest achievable dose. The recommended initial dosing for children is 1mg per day, and the initial dosing for adults and older children is 2mg per day, typically in a divided dose. In children, aqueous budesonide has been mixed with a sugar substitute to create a slurry. In a trial for adults, budesonide was nebulized and then swallowed.[3-5]

Pulmicort Respules are available in three strengths: 0.25mg/2mL, 0.5mg/2mL, and 1mg/2mL. Each dosage strength is supplied as 2mL single-dose ampules in a carton containing 30 Respule ampules.

If the Post Limit criteria are met, then the post limit quantity for approval will be 2 packages/60 respules of the Pulmicort Respules 1mg strength per month to accommodate higher dosages of 2mg daily, with divided dosing. The Initial Limit (Ref# 158-H) quantity for the Pulmicort Respules 0.5mg strength, (2 packages/60 respules per month), is sufficient for the recommended starting maintenance dose for EoE at 1mg/day, with divided dosing. The Initial Limit (Ref# 158-H) quantity for Pulmicort Respules 0.25mg strength, (3 packages/90 respules per month), accommodates the EoE referenced use of twice daily dosing.[4-6] Therefore, Pulmicort Respules 0.25mg and 0.5mg strengths are not included in this Post Limit criteria.

The guidelines also recommend a possible starting dose for maintenance therapy in adults of 880 mcg/day of fluticasone, with lower doses in children. The recommended initial dosing for children is 88-440mcg per day in a divided dose. The recommended initial dosing for adults is 440-1760mcg per day in a divided dose. For using fluticasone, the patient is directed to puff the inhaler into the mouth during a breath hold, and then to swallow it.[4-6] The Initial Limit (Ref#158-H) quantity for Flovent HFA, (2 packages/240 inhalations per month), is sufficient for the recommended dosing for EoE, up to 1760mcg/day, with divided dosing and for the maintenance treatment of asthma as prophylactic therapy. Therefore, Flovent HFA will not be included in this Post Limit criteria.

The ACG guidelines state that patients without symptomatic and histologic improvement after topical steroids might benefit from a longer course of topical steroids, higher doses of topical steroids, systemic steroids, elimination diet, or esophageal dilation. Symptoms often recur upon discontinuation, and steroid resistance has been reported. Maintenance therapy with topical corticosteroids and/or dietary restriction should be considered for all patients, but particularly in those with severe dysphagia or food impaction, high-grade esophageal stricture, and rapid symptomatic/histologic relapse following initial therapy.[3-5] Therefore, for continuation of therapy, patients must be evaluated for improvement or relapse in symptoms or inflammation.

Per guidelines, in the coming years there will be shifts in recommendations, as new data emerge concerning noninvasive diagnostic strategies with biomarkers or genetic analysis, novel treatment modalities, non-endoscopic methods to monitor treatment response, and long-term outcomes.[3-5,7,9] Also, the guidelines reference one maintenance study for 50 weeks and states that long-term safety data are not yet available for growth rates or bone density.[5] Therefore, to accommodate

initial treatment with a longer course and take into consideration future treatment updates, the approval duration will be set at 6 months for initial therapy and 12 months for continuation of therapy.

## REFERENCES


1. Pulmicort Respules [package insert]. Wilmington, DE: AstraZeneca LP; October 2019.
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4. Dellon E, Gonsalves N, Hirano I, et al. ACG Clinical Guideline: Evidenced Based Approach to the Diagnosis and Management of Esophageal Eosinophilia and Eosinophilic Esophagitis (EoE). *Am J Gastroenterol* 2013; 108:679–692.
5. Liacouras C, Furuta G, Hirano I, et al. Eosinophilic esophagitis: Updated Consensus Recommendations for Children and Adults *J Allergy Clin Immunol* 2011;128:3-20.
6. FDA. Orphan Drug Designations and Approvals. Available at: https://www.accessdata.fda.gov/scripts/opdlisting/oopd/listResult.cfm. Accessed August 2020.
7. Chenga K, Gupta S, Kantorc S, et al. Creating a Multi-center Rare Disease Consortium – the Consortium of Eosinophilic Gastrointestinal Disease Researchers (CEGIR). *Translational Science of Rare Diseases* 2 (2017) 141–155.
8. Dellon E, Liacouras C, Molina-Infante J, et al. Updated International Consensus Diagnostic Criteria for Eosinophilic Esophagitis: Proceedings of the AGREE Conference. *Gastroenterology* 2018;155:1022–1033.
9. 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.


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| Reviewed: | Medical Affairs: (AN) 02/2018; (CHART) 09/26//2019, 09/24/2020, 09/30/2021<br>External Review: 05/2018, 02/2019, 12/2019, 12/2020, 12/2021 |

## CRITERIA FOR APPROVAL

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| 1 | Does the patient have the diagnosis of eosinophilic esophagitis (EoE)?<br>[If no, then no further questions.] | Yes | No |
| 2 | Is this request for continuation of therapy with Pulmicort (budesonide) Respules at a dose of 1mg twice daily (2mg daily)?<br>[If no, then skip to question 4.] | Yes | No |
| 3 | Has the patient been evaluated for improvement or relapse in symptoms or inflammation?<br>[No further questions.] | Yes | No |
| 4 | Has the patient had all of the following: A) Eosinophil-predominant inflammation on biopsy, B) Trial of a proton pump inhibitor (PPI), C) Secondary causes of esophageal eosinophilia were ruled out?<br>[If no, then no further questions.] | Yes | No |
| 5 | Does the patient require more than the plan allowance of 2 packages/60 respules per month? | Yes | No |

[RPh Note: If yes, then deny and enter a partial approval for 120 mL (2 packages of 30 respules each) / 25 days, or 360 mL (6 packages of 30 respules each) / 75 days of Pulmicort (budesonide) 1mg Respules.]

| Mapping Instructions | | | |
|---|---|---|---|
| | **Yes** | **No** | **DENIAL REASONS – DO NOT USE FOR MEDICARE PART D** |
| 1. | Go to 2 | Deny | You do not meet the requirements of your plan. Your plan covers additional quantities of this drug when you have eosinophilic esophagitis (EoE). Your request has been denied based on the information we have. [Short Description: No approvable diagnosis] |
| 2. | Go to 3 | Go to 4 | |
| 3. | Approve, 12 months, Pulmicort (budesonide) 1mg Respules: 120 mL (2 packages of 30 respules each) / 25 days* or 360 mL (6 packages of 30 respules each) / 75 days* | Deny | You do not meet the requirements of your plan. Your plan covers additional quantities of this drug when you meet these conditions: - You need to continue therapy of 1mg two times a day - You were checked for improvement or relapse Your request has been denied based on the information we have. [Short Description: Continuation of therapy, No evaluation for response to treatment or relapse] |
| 4. | Go to 5 | Deny | You do not meet the requirements of your plan. Your plan covers additional quantities of this drug when you meet all of these conditions: - Swelling with eosinophils on biopsy - Trial of a proton pump Inhibitor (PPI) - Other causes were ruled out Your request has been denied based on the information we have. [Short Description: No symptoms or confirmation of diagnosis] |
| 5. | Deny | Approve, 6 months, Pulmicort (budesonide) 1mg Respules: 120 mL (2 packages of 30 respules each) / 25 days* or 360 mL (6 packages of 30 respules each) / 75 days* | You have requested more than the maximum quantity allowed by your plan. Current plan approved criteria cover up to 2 packages/60 respules per month of Pulmicort (budesonide) 1mg Respules. Your request has been partially approved. You have been approved for the maximum quantity that your plan covers for a duration of 6 months. Your request for additional quantities of the requested drug and strength has been denied. [Short Description: Over max quantity] |

**The duration of 25 days is used for a 30-day fill period and 75 days is used for a 90-day fill period to allow time for refill processing.*