

## PRIOR AUTHORIZATION WITH STEP THERAPY POLICY

**POLICY:** Pulmonary – Roflumilast Prior Authorization with Step Therapy Policy

- Daliresp® (roflumilast tablets – Astra Zeneca, generic)

**REVIEW DATE:** 01/17/2024

---

### OVERVIEW

Roflumilast tablets (Daliresp, generic), a selective phosphodiesterase-4 inhibitor, is indicated as a treatment to reduce the risk of **chronic obstructive pulmonary disease (COPD)** exacerbations in patients with severe COPD associated with chronic bronchitis and a history of exacerbations.<sup>1</sup> Limitations of use: Roflumilast is not a bronchodilator and is not indicated for the relief of acute bronchospasm.

### Clinical Efficacy

Roflumilast has been studied in patients currently receiving treatment with bronchodilators (e.g., long-acting beta<sub>2</sub>-agonists [LABAs]) and inhaled corticosteroids (ICSs) with or without additional therapy with a long-acting muscarinic antagonist (LAMA).<sup>2-7</sup> Five placebo-controlled clinical trials evaluated the effect of roflumilast on COPD exacerbations.<sup>1-7</sup> Two of these studies initially included patients with severe COPD with chronic bronchitis and/or emphysema; in both studies, roflumilast did not demonstrate a significant reduction in COPD exacerbation rates. An exploratory analysis of these trials found that in the subgroup of patients with severe COPD who had chronic bronchitis and exacerbations within the previous year, roflumilast resulted in better exacerbation reduction than in the overall population. Two subsequent trials were conducted involving patients with severe COPD, chronic bronchitis, and at least one COPD exacerbation within the previous year. In both trials, roflumilast demonstrated a significant reduction in the rate of moderate or severe exacerbations compared to placebo.

### Guidelines

The Global Initiative for Chronic Obstructive Lung Disease guidelines for the diagnosis, management, and prevention of COPD (2024) recommend bronchodilators as initial pharmacologic treatment.<sup>8</sup> Following initiation, therapies should be adjusted as needed based on symptom severity and exacerbation risk. ICSs are recommended for patients who continue to experience COPD exacerbations and who have elevated blood eosinophils. Roflumilast is listed as a possible therapeutic option in patients with chronic bronchitis who are receiving triple therapy with an ICS/LAMA/LABA, who have a forced expiratory volume in 1 second (FEV<sub>1</sub>) < 50%, and who continue to experience exacerbations (especially if the patient has been hospitalized for one or more COPD exacerbations in the past year). This therapy is also recommended in patients who continue to experience exacerbations despite LAMA/LABA combination therapy and have a blood eosinophil level < 100 cells/microliter. Low blood eosinophils are predictive of an insufficient response to ICS therapy, thereby making roflumilast a more attractive option for add-on therapy.

### POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of roflumilast tablets (Daliresp, generic). This Prior Authorization Policy also contains a Step Therapy component. When clinically appropriate, the patient is directed to try generic roflumilast (Step 1) prior to brand Daliresp (Step 2). All approvals are provided for the duration noted below.

Automation: None.

### RECOMMENDED AUTHORIZATION CRITERIA

01/17/2024

© 2024. All Rights Reserved.

This document is confidential and proprietary. Unauthorized use and distribution are prohibited.

Coverage of roflumilast tablets (Daliresp, generic) is recommended in those who meet the following criteria:

### FDA-Approved Indication

1. **Chronic Obstructive Pulmonary Disease (COPD).** Approve for 1 year if the patient meets the following criteria (A, B, C, and D):
  - A) Patient has severe COPD or very severe COPD, according to the prescriber; AND
  - B) Patient has a of exacerbations; AND
  - C) Patient meets ONE of the following (i or ii):
    - i. Patient meets both of the following (a and b):
      - a) Patient has chronic bronchitis; AND
      - b) Patient has tried an inhaled long-acting beta<sub>2</sub>-agonist, an inhaled long-acting muscarinic antagonist, and an inhaled corticosteroid concomitantly; OR  
Note: Use of a combination inhaler containing multiple agents from the medication classes listed would fulfill the requirement. Refer to the [Appendix](#) for examples of inhaled therapies used for COPD.
    - ii. Patient meets both of the following (a and b):
      - a) Patient has a blood eosinophil level < 100 cells/microliter; AND
      - b) Patient has tried an inhaled long-acting muscarinic antagonist and long-acting beta<sub>2</sub>-agonist concomitantly.  
Note: Use of a combination inhaler containing multiple agents from the medication classes listed would fulfill the requirement. Refer to the [Appendix](#) for examples of inhaled therapies used for COPD.
  - D) If brand Daliresp is being requested, the patient meets both of the following criteria (i and ii):
    - i. Patient has tried generic roflumilast; AND
    - ii. Brand Daliresp is being requested due to a formulation difference in the inactive ingredient(s) [e.g., difference in dyes, fillers, preservatives] between the Brand and the corresponding generic product which, per the prescriber, would result in a significant allergy or serious adverse reaction.

### CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of roflumilast tablets (Daliresp, generic) is not recommended for the following situations:

1. **Asthma.** The efficacy of roflumilast (formulation not specified) in patients with asthma<sup>9-11</sup>, allergic asthma<sup>12,13</sup>, and exercise-induced asthma<sup>14</sup> has been evaluated. More data are needed to define the place in therapy of roflumilast in the treatment of asthma. Current asthma guidelines do not address roflumilast as a recommended therapy for asthma management.<sup>15,16</sup>
2. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

## REFERENCES

1. Daliresp® tablets [prescribing information]. Wilmington, DE: Astra Zeneca; January 2018.
2. Calverley PM, Rabe KF, Goehring UM, et al. Roflumilast in symptomatic chronic obstructive pulmonary disease: two randomized clinical trials. *Lancet*. 2009;374:685-694.
3. Fabbri LM, Calverley PMA, Izquierdo-Alonso JL, et al. Roflumilast in moderate-to-severe chronic obstructive pulmonary disease treated with long-acting bronchodilators: two randomized clinical trials. *Lancet*. 2009;374:695-703.
4. Calverley PM, Sanchez-Toril F, McIvor A, et al. Effect of 1-year treatment with roflumilast in severe chronic obstructive pulmonary disease. *Am J Respir Crit Care Med*. 2007;176:154-161.
5. Rennard SI, Sun SX, Tourkodimitris S, et al. Roflumilast and dyspnea in patients with moderate to very severe chronic obstructive pulmonary disease: a pooled analysis of four clinical trials. *Int J Chron Obstruct Pulmon Dis*. 2014;9:657-673.
6. Martinez FJ, Calverley PM, Goehring UM. Effect of roflumilast on exacerbations in patients with severe chronic obstructive pulmonary disease uncontrolled by combination therapy (REACT): a multicentre randomized controlled trial. *Lancet*. 2015;385:857-866.
7. Munoz-Esquerre M, Diez-Ferrer M, Monton C, et al. Roflumilast added to triple therapy in patients with severe COPD: a real life study. *Pulm Pharmacol Ther*. 2015;30:16-21.
8. Global Initiative for Chronic Obstructive Lung Disease. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease. National Institutes of Health, National Heart, Lung, and Blood Institute; 2024. Available at: <https://goldcopd.org/gold-reports/>. Accessed on January 9, 2024.
9. Bateman ED, Izquierdo JL, Harnest U, et al. Efficacy and safety of roflumilast in the treatment of asthma. *Ann Allergy Asthma Immunol*. 2006;96:679-686.
10. Bousquet J, Aubier M, Sastre J, et al. Comparison of roflumilast, an oral anti-inflammatory, with beclomethasone dipropionate in the treatment of persistent asthma. *Allergy*. 2006;61:72-78.
11. Bateman ED, Goehring UM, Watz RF, et al. Roflumilast combined with montelukast versus montelukast alone as add-on treatment in patients with moderate-to-severe asthma. *J Allergy Clin Immunol*. 2016;138(1):142-149.
12. Van Schalkwyk E, Strydom K, Williams Z, et al. Roflumilast, an oral, once-daily phosphodiesterase 4 inhibitor, attenuates allergen-induced asthmatic reactions. *J Allergy Clin Immunol*. 2005;116:292-298.
13. Gavreau GM, Boulet LP, Schmid-Wirlitsch C, et al. Roflumilast attenuates allergen-induced inflammation in mild asthmatic subjects. *Respir Res*. 2011;12:140-150.
14. Timmer W, Leclerc V, Birraux G, et al. The new phosphodiesterase 4 inhibitor roflumilast is efficacious in exercise-induced asthma and leads to suppression of LPS-stimulated TNF-alpha *ex vivo*. *J Clin Pharmacol*. 2002;42:297-303.
15. Global Initiative for Asthma. Global strategy for asthma management and prevention. Updated 2023. Available at: <http://www.ginasthma.org>. Accessed on January 9, 2024.
16. Holguin F, Cardet JC, Chung KF, et al. Management of severe asthma: a European Respiratory Society/American Thoracic Society guideline. *Eur Respir J*. 2020;55(1):1900588.

**APPENDIX**

LABA – Long-acting beta<sub>2</sub>-agonist; LAMA – Long-acting muscarinic antagonist; ICS – Inhaled corticosteroid.