Drug Coverage Policy

Effective Date.....5/1/2025
Coverage Policy Number.....IP0609
Policy Title..... Roflumilast for Individual and Family Plans

Pulmonary – Roflumilast for Individual and Family Plans

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

INSTRUCTIONS FOR USE
The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Each coverage request should be reviewed on its own merits. Medical directors are expected to exercise clinical judgment where appropriate and have discretion in making individual coverage determinations. Where coverage for care or services does not depend on specific circumstances, reimbursement will only be provided if a requested service(s) is submitted in accordance with the relevant criteria outlined in the applicable Coverage Policy, including covered diagnosis and/or procedure code(s). Reimbursement is not allowed for services when billed for conditions or diagnoses that are not covered under this Coverage Policy (see "Coding Information" below). When billing, providers must use the most appropriate codes as of the effective date of the submission. Claims submitted for services that are not accompanied by covered code(s) under the applicable Coverage Policy will be denied as not covered. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Cigna Healthcare Coverage Policy

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.[1]

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$_2$-agonists [LABAs]) and inhaled corticosteroids (ICSs) with or without additional therapy with a long-acting muscarinic antagonist (LAMA).[2-7] Five placebo-controlled clinical trials evaluated the effect of roflumilast on COPD exacerbations.[1-7] 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 (2025) recommend bronchodilators as initial pharmacologic treatment.[8] 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 a recommended therapy option in patients who continue to experience exacerbations despite inhaled therapy in patients who have symptoms of chronic bronchitis, who have a forced expiratory volume in 1 second (FEV_1), and who have a history of a prior severe exacerbation. It is recommended in addition to ICS/LAMA/LABA therapy or in addition to LAMA/LABA therapy in patients who 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.

Medical Necessity Criteria

Policy Statement
Prior Authorization is recommended for prescription benefit coverage of roflumilast tablets (Daliresp, generic). All approvals are provided for the duration noted below. In cases where the approval is authorized in months, 1 month is equal to 30 days. Because of the specialized skills required for evaluation and diagnosis of patients treated with roflumilast tablets (Daliresp, generic) as well as the monitoring required for adverse events and long-term efficacy, approval requires roflumilast tablets (Daliresp, generic) to be prescribed by a physician who has consulted with or who specializes in the condition.

Roflumilast tablets (Daliresp, generic) is considered medically necessary when the following criteria are met:

FDA-Approved Indication

1. **Chronic Obstructive Pulmonary Disease (COPD).** Approve for the duration noted if the patient meets ONE of the following (A or B):
   - **A)** Initial Therapy. Approve for 6 months if the patient meets the following (i, ii, iii, iv, and v):
     - **i.** Patient has a forced expiratory volume in 1 second (FEV_1) < 50% predicted; AND
     - **ii.** Patient has a history of two or more moderate COPD exacerbations or one or more severe COPD exacerbations, according to the prescriber; AND
       Note: A moderate COPD exacerbation is an exacerbation that required treatment with a short-acting bronchodilator and a systemic corticosteroid. A severe COPD exacerbation is an exacerbation that required hospitalization or an Emergency Department visit.
     - **iii.** Patient has chronic bronchitis; AND
     - **iv.** Patient meets ONE of the following (a or b):
       1. Patient has tried an inhaled long-acting $beta_2$-agonist, an inhaled long-acting muscarinic antagonist, and an inhaled corticosteroid concomitantly; OR
          Note: Use of single-entity inhalers or 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.
       - **b)** Patient meets both of the following (1 and 2):
         a. Patient has a blood eosinophil level < 100 cells/microliter; AND
         b. Patient has tried an inhaled long-acting muscarinic antagonist and long-acting $beta_2$-agonist concomitantly; AND
            Note: Use of single-entity inhalers or 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.
     - **v.** If brand Daliresp is being requested, the patient meets both of the following criteria (a and b):
       - **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; OR
   - **B)** Patient is Currently Receiving Roflumilast (Daliresp, generic). Approve for 1 year if the patient meets the following (i, ii, and iii):
     - **i.** If brand Daliresp is being requested, the patient meets both of the following criteria (a and b):
       - **a)** Patient has tried generic roflumilast; AND
       - **b)** 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; AND
     - **ii.** Patient continues to receive combination therapy with an inhaled long-acting $beta_2$-agonist and a long-acting muscarinic antagonist; AND

Note: Use of single-entity inhalers or 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.

iii. Patient has experienced a beneficial clinical response, defined by ONE of the following (a, b, c, d, or e):
- **a)** Reduced COPD symptoms; OR
- **b)** Reduced COPD exacerbations; OR
- **c)** Reduced COPD-related hospitalizations; OR
- **d)** Reduced emergency department or urgent care visits; OR
- **e)** Improved lung function parameters.

C. Preferred product criteria are met for the product(s) as listed in the below table(s):

Product	Criteria
Daliresp (roflumilast)	Trial of **roflumilast tablets** (the bioequivalent generic product) AND cannot take due to a formulation difference in the inactive ingredient(s) which would result in a significant allergy or serious adverse reaction

Roflumilast tablets (Daliresp, generic) for any other use is considered not medically necessary, including the following (this list may not be all inclusive; criteria will be updated as new published data are available):

1. **Asthma.** The efficacy of roflumilast (formulation not specified) in patients with asthma[9-11], allergic asthma[12,13], and exercise-induced asthma[14] 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.[15,16]

References

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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 2024. Available at: http://www.ginasthma.org. Accessed on January 29, 2025.
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Revision Details

Type of Revision	Summary of Changes	Date
New	New policy	05/01/2024
Annual Revision	**Chronic Obstructive Pulmonary Disease.** The following changes were made: **Criteria were divided into Initial and Continuation criteria**. Initial approval duration was updated to 6 months if the patient meets the existing criteria. The requirement that the patient have severe COPD or very severe COPD, according to the prescriber was changed to require the patient have a forced expiratory volume in 1 second (FEV_1) < 50% predicted. **The requirement that the patient have a history of exacerbations** was updated to require the patient to have a history of two or more moderate COPD exacerbations or one or more severe COPD exacerbations, according to the prescriber. A Note was added to clarify that a moderate COPD exacerbation is an exacerbation that required treatment with a short-acting bronchodilator and a systemic corticosteroid. A severe COPD exacerbation is an exacerbation that required hospitalization or an Emergency Department visit. **The requirement that the patient has chronic bronchitis** was changed to apply to all patients. Previously, this requirement only applied to patients who were receiving inhaled therapy with a long-	5/1/2025

	acting beta$_2$-agonist, a long-acting muscarinic antagonist, and an inhaled corticosteroid. **The Notes regarding other therapies tried** were updated to clarify that use of single-entity inhalers, as well as a combination inhaler fulfills the requirement. Previously, the Notes stated that a combination inhaler fulfilled the requirement. **Continuation criteria** were added to approve roflumilast (Daliresp, generic) for 1 year if the patient has tried generic roflumilast (if brand Daliresp is requested), if the patient continues to receive combination therapy with an inhaled long-acting beta$_2$-agonist and a long-acting muscarinic antagonist, and the patient has experienced a beneficial clinical response as defined by reduced COPD symptoms, exacerbations, hospitalizations, emergency department or urgent care visits, or improved lung function parameters.	

The policy effective date is in force until updated or retired.

Appendix

Brand (Generic Name)	Mechanism of Action
Serevent® Diskus® (salmeterol xinafoate inhalation powder)	LABA
Striverdi® Respimat® (olodaterol inhalation spray)	LABA
Brovana® (arformoterol tartrate inhalation solution, generic)	LABA
Perforomist® (formoterol fumarate inhalation solution, generic)	LABA
Incruse® Ellipta® (umeclidinium inhalation powder)	LAMA
Spiriva® HandiHaler® (tiotropium bromide inhalation powder, generic)	LAMA
Spiriva® Respimat® (tiotropium bromide inhalation spray)	LAMA
Tudorza® Pressair® (aclidinium bromide inhalation powder)	LAMA
Lonhala® Magnair® (glycopyrrolate inhalation solution) [discontinued]	LAMA
Yupelri® (revefenacin inhalation solution)	LAMA
Alvesco® (ciclesonide inhalation aerosol)	ICS
ArmonAir® Digihaler® (fluticasone propionate inhalation powder) [discontinued]	ICS
Arnuity® Ellipta® (fluticasone furoate inhalation powder)	ICS
Asmanex® HFA (mometasone inhalation aerosol)	ICS
Asmanex® Twisthaler® (mometasone inhalation powder)	ICS
Flovent® Diskus® (fluticasone propionate inhalation powder, generic) [brand discontinued]	ICS
Flovent® HFA (fluticasone propionate inhalation aerosol, generic) [brand discontinued]	ICS
Pulmicort Flexhaler® (budesonide inhalation powder)	ICS
Qvar® RediHaler® (beclomethasone HFA inhalation aerosol)	ICS
Pulmicort Respules® (budesonide inhalation suspension, generic)	ICS
Advair Diskus® (fluticasone propionate/salmeterol inhalation powder, generic [including Wixela Inhub®])	ICS/LABA
Breo® Ellipta® (fluticasone furoate/vilanterol inhalation powder, generic)	ICS/LABA
Symbicort® (budesonide/formoterol fumarate inhalation aerosol, generic [including Breyna®)	ICS/LABA
Anoro® Ellipta® (umeclidinium and vilanterol inhalation powder)	LAMA/LABA
Bevespi Aerosphere® (glycopyrrolate and formoterol fumarate inhalation aerosol)	LAMA/LABA
Duaklir® Pressair® (aclidinium bromide and formoterol fumarate inhalation powder)	LAMA/LABA
Stiolto® Respimat® (tiotropium bromide and olodaterol inhalation spray)	LAMA/LABA
Breztri Aerosphere® (budesonide, glycopyrrolate, and formoterol fumarate inhalation aerosol)	ICS/LAMA/LABA
Trelegy® Ellipta® (fluticasone furoate, umeclidinium, and vilanterol inhalation powder)	ICS/LAMA/LABA

LABA – Long-acting beta$_2$-agonist; LAMA – Long-acting muscarinic antagonist; ICS – Inhaled corticosteroid.