Clinical Policy: Roflumilast (Daliresp)

Reference Number: CP.PMN.46
Effective Date: 11.01.11
Last Review Date: 08.19
Line of Business: Medicaid

Revision Log

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

Description
Roflumilast (Daliresp®) is a selective phosphodiesterase 4 inhibitor.

FDA Approved Indication(s)
Daliresp 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.

Limitation(s) of use:
- Daliresp is not a bronchodilator and is not indicated for the relief of acute bronchospasm.
- Daliresp 250 mcg is a starting dose for the first 4 weeks of treatment only and is not the effective (therapeutic) dose.

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 Daliresp is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Chronic Obstructive Pulmonary Disease (must meet all)**:**

1. Diagnosis of COPD;
2. Age ≥ 18 years;
3. Current (within the past 30 days) forced expiratory volume in one second (FEV_1) < 50% predicted;
4. Member meets one of the following (a or b):
   a. Failure of triple inhaled therapy consisting of a combination of a long-acting $beta_2$-agonist (LABA), long-acting antimuscarinic antagonist (LAMA), and inhaled corticosteroid (ICS) at up to maximally indicated doses;
   b. Both i and ii:
      i. Failure of dual inhaled therapy consisting of a combination of a LABA and LAMA at up to maximally indicated doses;
      ii. Current (within the past 30 days) blood eosinophil count < 100 cells/uL;
5. Daliresp is prescribed concurrently with a long-acting bronchodilator (i.e., LABA or LAMA);
6. Dose does not exceed 500 mcg per day (1 tablet per day).

Approval duration: 12 months

B. Other diagnoses/indications

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Chronic Obstructive Pulmonary Disease (must meet all)**:**

1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
2. Member is responding positively to therapy;
3. If request is for a dose increase, new dose does not exceed 500 mcg per day (1 tablet per day).

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.
   Approval duration: Duration of request or 12 months (whichever is less); or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.PMN.53 for Medicaid.

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.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

COPD: chronic obstructive pulmonary disease
FDA: Food and Drug Administration
FEV_1: forced expiratory volume in one second
ICS: inhaled corticosteroid
LABA: long-acting $beta_2$-agonist
LAMA: long-acting antimuscarinic antagonist

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
ICS/LABA Combinations		
fluticasone/salmeterol (Advair Diskus®)	Refer to prescribing information	

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Breo Ellipta® (fluticasone/ vilanterol)		Refer to prescribing information
Symbicort® (budesonide/ formoterol)		
Dulera®* (mometasone/ formoterol)	Doses of 10 mcg formoterol/400 mcg mometasone and 10 mcg formoterol/ 200 mcg mometasone, each inhaled BID, have been studied	The optimal dose has not been established
LABA/LAMA Combinations		
Bevespi Aerosphere® (formoterol/glycopyrrolate)	Refer to prescribing information	Refer to prescribing information
Utibron Neohaler® (indacaterol/glycopyrrolate)		
Anoro Ellipta® (vilanterol/umeclidinium)		
Stiolto Respimat® (olodaterol/tiotropium)		
LAMAs		
Tudorza Pressair® (aclidinium bromide)	Refer to prescribing information	Refer to prescribing information
Seebri Neohaler® (glycopyrrolate)		
Spiriva Respimat®/ HandiHaler® (tiotropium)		
Incruse Ellipta (umeclidinium)		
LABAs		
Brovana® (arformoterol)	Refer to prescribing information	Refer to prescribing information
Arcapta Neohaler® (indacaterol)		
Striverdi Respimat® (olodaterol)		
Serevent Diskus® (salmeterol)		
ICS/LABA/LAMA Combinations		
Trelegy™ Ellipta® (fluticasone/umeclidinium/ vilanterol)	1 inhalation by mouth QD	1 inhalation/day

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.
**Off-label*

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): moderate to severe liver impairment (Child-Pugh B or C)

- Boxed warning(s): none reported

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
COPD	500 mcg PO QD (starting treatment with 250 mcg QD for 4 weeks and increasing to 500 mcg QD thereafter may reduce the rate of discontinuation in some patients)	500 mcg/day

VI. Product Availability

Tablets: 250 mcg, 500 mcg

VII. References

1. Daliresp Prescribing Information. Wilmington, DE: AstraZeneca Pharmaceuticals; January 2018. Available at: https://www.daliresp.com/. Accessed April 23, 2019.
2. Global Initiative for Chronic Obstructive Lung Disease (GOLD): Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease (2019 report). Available from: http://www.goldcopd.org/. Accessed April 22, 2019.
3. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2019. Available at: http://www.clinicalpharmacology-ip.com/. Accessed April 23, 2019.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
No change.	12.14	12.14
Guideline converted to new template Modified criteria to require failure adherent use of ICS/LABA or anticholinergic with use for ≥ 3 months within the previous 6 months; Added criteria for concurrent use of a long acting bronchodilator; Added requirement that FEV1 must be within the last 30 days; Changed renewal criteria to only required concurrent use of a long acting bronchodilator	08.15	08.15
Removed option for contraindication to ICS/LABA and long acting anticholinergics as Daliresp should always be used in combination with at least one long-acting bronchodilator per GOLD guideline; Modified specific max quantity limit to generalized FDA max recommended dose and health plan approved QL statement; Modified continued approval to require claims of LABA and LANA or provider's documentation as evidence of concurrent use; Updated background section. Updated reference section to reflect current literature search.	05.16	08.16
Converted to new template. Initial: modified requirement related to failure of either a long-acting anticholinergic agent or ICS/LABA to failure of triple inhaled therapy consisting of a combination of long-acting beta$_2$-agonist	03.17	08.17

Reviews, Revisions, and Approvals	Date	P&T Approval Date
(LABA), long-acting antimuscarinic antagonist (LAMA), and inhaled corticosteroid (ICS) per GOLD 2017 guideline Removed age restriction as age is not an absolute contraindication and COPD does not normally occur in children per PI; updated generalized FDA max recommended dose and health plan approved QL statement to include specific max dose and QL; added documentation of positive response to therapy in continuation criteria. Updated references.		
3Q 2018 annual review: no significant changes; age restriction added, smoking cessation requirements removed as this cannot be enforced; initial approval duration increased from 6 to 12 months; references reviewed and updated.	04.09.18	08.18
3Q 2019 annual review: added an additional pathway to approval for members failing LABA/LAMA with blood eosinophil count < 100 cells/uL per GOLD 2019 guideline; removed trial duration and instead required that preferred drugs be tried at up to maximally indicated doses to align with approach for other COPD agents; references reviewed and updated.	05.07.19	08.19

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.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.