

Clinical Policy: Roflumilast (Daliresp, Zoryve)

Reference Number: CP.PMN.46

Effective Date: 11.01.11

Last Review Date: 02.24

Line of Business: Commercial, HIM, Medicaid

[Revision Log](#)

See [Important Reminder](#) at the end of this policy for important regulatory and legal information.

Description

Roflumilast (Daliresp[®], Zoryve[®]) 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.

Zoryve cream is indicated for topical treatment of plaque psoriasis, including intertriginous areas, in patients 6 years of age and older.

Zoryve foam is indicated for the treatment of seborrheic dermatitis in adult and pediatric patients 9 years of age and older.

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 and Zoryve are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

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

1. Request is for roflumilast tablet (Daliresp);
2. Diagnosis of COPD;
3. Age \geq 18 years;
4. Current (within the past 30 days) forced expiratory volume in one second (FEV₁) < 50% predicted;
5. Member meets one of the following (a or b):
 - a. Failure of triple inhaled therapy consisting of a combination of a long-acting beta₂-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;
6. Daliresp is prescribed concurrently with a long-acting bronchodilator (i.e., LABA or LAMA);
7. For brand Daliresp requests, member must use generic roflumilast, unless contraindicated or clinically significant adverse effects are experienced;
8. Dose does not exceed both of the following (a and b):
 - a. 500 mcg per day;
 - b. 1 tablet per day.

Approval duration: 12 months

B. Plaque Psoriasis (must meet all):

1. Request is for roflumilast cream (Zoryve);
 2. Diagnosis of plaque psoriasis with body surface area involvement $\leq 20\%$;
 3. Prescribed by or in consultation with a dermatologist or rheumatologist;
 4. Age ≥ 6 years;
 5. Member meets one of the following (a or b):
 - a. Failure of both (i and ii) used concurrently, unless clinically significant adverse effects are experienced or all are contraindicated:
 - i. Medium to ultra-high potency topical corticosteroid (*see Appendix B*);
 - ii. Calcipotriene, calcitriol, or tazarotene;
 - b. For face or intertriginous areas (e.g., genitals, armpits, forearms, and groin): Failure of a topical calcineurin inhibitor* (*see Appendix B*), unless contraindicated or clinically adverse effects are experienced;
- *Prior authorization may be required for topical calcineurin inhibitors*
6. Request does not exceed 1 tube per month.

Approval duration: 12 months

C. Seborrheic Dermatitis (must meet all):

1. Request is for roflumilast foam (Zoryve);
2. Diagnosis of seborrheic dermatitis with body surface area involvement $\leq 20\%$;
3. Prescribed by or in consultation with a dermatologist;
4. Age ≥ 9 years;
5. Failure of both of the following (a and b), unless clinically significant adverse effects are experienced or all are contraindicated:
 - a. Topical antifungal (*see Appendix B*);
 - b. Topical corticosteroid (*see Appendix B*);
6. Request does not exceed 1 can per month.

Approval duration: 12 months

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

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):

- a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
 - b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

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

1. Member meets one of the following (a or b):
 - a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
 - b. Member is receiving benefit from the referenced states for the applicable product and regulation (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B*);
2. Request is for roflumilast tablet (Daliresp);
3. Member is responding positively to therapy;
4. For brand Daliresp requests, member must use generic roflumilast, unless contraindicated or clinically significant adverse effects are experienced;
5. If request is for a dose increase, new dose does not exceed both of the following (a and b):
 - a. 500 mcg per day;
 - b. 1 tablet per day.

Approval duration: 12 months

B. Plaque Psoriasis (must meet all):

1. Member meets one of the following (a or b):
 - a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
 - b. Member is receiving benefit from the referenced states for the applicable product and regulation (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B*);
2. Request is for roflumilast cream (Zoryve);
3. Member is responding positively to therapy;
4. If request is for a dose increase, new dose does not exceed 1 tube per month.

Approval duration: 12 months

C. Seborrheic Dermatitis (must meet all):

1. Member meets one of the following (a or b):

- a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
 - b. Member is receiving benefit from the referenced states for the applicable product and regulation (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B*);
2. Request is for roflumilast foam (Zoryve);
 3. Member is responding positively to therapy;
 4. If request is for a dose increase, new dose does not exceed 1 can per month.

Approval duration: 12 months

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

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
 - a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
 - b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and 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.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and 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

FEV₁: forced expiratory volume in one second

ICS: inhaled corticosteroid

LABA: long-acting beta₂-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.

COPD		
Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
<i>ICS/LABA Combinations</i>		
fluticasone/salmeterol (Advair Diskus [®])	Refer to prescribing information	Refer to prescribing information
Breo Ellipta [®] (fluticasone/ vilanterol)		
budesonide/formoterol (Symbicort [®])		
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
<i>LABA/LAMA Combinations</i>		
Bevespi Aerosphere [®] (formoterol/glycopyrrolate)	Refer to prescribing information	Refer to prescribing information
Utibron Neohaler [®] (indacaterol/glycopyrrolate)		
Anoro Ellipta [®] (vilanterol/umeclidinium)		
Stiolto Respimat [®] (olodaterol/tiotropium)		
<i>LAMAs</i>		
Tudorza Pressair [®] (aclidinium bromide)	Refer to prescribing information	Refer to prescribing information
Seebri Neohaler [®] (glycopyrrolate)		
Spiriva Respimat [®] / HandiHaler [®] (tiotropium)		
Incruse Ellipta (umeclidinium)		
<i>LABAs</i>		
Brovana [®] (arformoterol)	Refer to prescribing information	Refer to prescribing information
Arcapta Neohaler [®] (indacaterol)		
Striverdi Respimat [®] (olodaterol)		
Serevent Diskus [®] (salmeterol)		
<i>ICS/LABA/LAMA Combinations</i>		
Trelegy [™] Ellipta [®] (fluticasone/umeclidinium/ vilanterol)	1 inhalation by mouth QD	1 inhalation/day

Plaque Psoriasis		
Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
calcipotriene (Dovonex [®]) cream, ointment, solution	Apply topically to the affected area(s) BID	100 g/week
calcitriol (Vectical [™]) ointment	Apply topically to the affected area(s) BID	200 g/week
tazarotene (Tazorac [®]) gel, cream	Apply topically to the affected area(s) QHS	Once daily application
Ultra-High Potency Topical Corticosteroids		
augmented betamethasone dipropionate 0.05% (Diprolene [®] , Alphatrex [®]) ointment, gel	Apply topically to the affected area(s) BID	Should not be used for longer than 2 consecutive weeks
clobetasol propionate 0.05% (Temovate [®] , Temovate E [®]) cream, ointment, gel, solution		
diflorasone diacetate 0.05% (Apexicon [®]) ointment		
halobetasol propionate 0.05% (Ultravate [®]) cream, ointment		
High Potency Topical Corticosteroids		
augmented betamethasone dipropionate 0.05% (Diprolone [®] , Diprolene [®] AF) cream, lotion	Apply topically to the affected area(s) BID	Should not be used for longer than 2 consecutive weeks
betamethasone dipropionate 0.05% ointment		
desoximetasone (Topicort [®]) 0.25%, 0.05% cream, ointment, gel		
diflorasone 0.05% (Apexicon E [®]) cream		
fluocinonide acetone 0.05% cream, ointment, gel, solution		
triamcinolone acetone 0.5% (Aristocort [®] , Kenalog [®]) cream, ointment		
Medium/Medium to High Potency Topical Corticosteroids		
betamethasone dipropionate 0.05% cream	Apply topically to the affected area(s) BID	Should not be used for longer

Plaque Psoriasis		
Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
desoximetasone 0.05% (Topicort [®]) cream, ointment, gel		than 2 consecutive weeks
fluocinolone acetonide 0.025% (Synalar [®]) cream, ointment		
fluticasone propionate 0.05% (Cutivate [®]) cream		
mometasone furoate 0.1% (Elocon [®]) cream, lotion, ointment		
triamcinolone acetonide 0.1%, 0.25%, 0.5% (Aristocort [®] , Kenalog [®]) cream, ointment		
Combination Corticosteroid + (Vitamin D Analog or Retinoid)		
Enstilar [®] (calcipotriene 0.005% and betamethasone dipropionate 0.064%) foam	Apply topically to affected areas QD for up to 4 weeks. Avoid use on face, groin, axillae, skin treatment site with atrophy present, or with occlusive dressing unless directed by a healthcare provider	60 g/4 days
Duobrii [®] (halobetasol propionate 0.01% and tazarotene 0.045%) lotion	Apply a thin layer of lotion once daily to affected areas until control is achieved	50 g/week
Topical Calcineurin Inhibitors		
tacrolimus (Protopic [®]) (off-label)	Apply twice daily to psoriatic lesions of the face and intertriginous areas	2 applications/day
pimecrolimus (Elidel [®]) (off-label)	Apply twice daily to affected intertriginous areas	2 applications/day
Seborrheic Dermatitis		
Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Topical Antifungal		
ketoconazole (Nizoral [®] A-D, Extina [®] , Ketodan [®] , Xolegel [™]) 1-2% shampoo, 1-2% cream, foam, gel	Refer to prescribing information	Refer to prescribing information
ciclopirox 1-1.5% shampoo, 0.77% gel, 1% cream		
miconazole 2% solution		

Plaque Psoriasis		
Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
clotrimazole (Lotrimin [®]) 1% cream, ointment, solution		
econazole (Ecoza [®]) 1% cream, foam		
luliconazole (Luzu [®]) 1% cream		
oxiconazole (Oxistat [®]) 1% cream, lotion		
sulconazole (Exelderm [®]) 1% cream, solution		
Topical Corticosteroids		
betamethasone dipropionate 0.05% cream, gel, lotion, spray; betamethasone valerate 0.12% foam, 0.1% cream, lotion	Refer to prescribing information	Refer to prescribing information
clobetasol propionate (Temovate [®] , Temovate E [®]) 0.05% cream, ointment, gel, solution, shampoo		
desonide (Desowen [®] , Tridesilon [®] , Verdeso [®]) 0.05% cream, foam, gel, lotion, ointment		
hydrocortisone (NuZon [®] , NuCort [®]) 0.5-2.5% cream, ointment, lotion		
fluocinolone (Synalar [®]) 0.01% shampoo, lotion, cream		

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

Drug Name	Indication	Dosing Regimen	Maximum Dose
Daliresp	COPD	500 mcg PO QD (starting treatment with 250 mcg QD for 4 weeks and increasing to 500	500 mcg/day

Drug Name	Indication	Dosing Regimen	Maximum Dose
		mcg QD thereafter may reduce the rate of discontinuation in some patients)	
Zoryve	Plaque psoriasis	Apply cream to affected areas once daily	Once daily application
	Seborrheic dermatitis	Apply foam to affected areas once daily	Once daily application

VI. Product Availability

Drug Name	Availability
Daliresp	Tablets: 250 mcg, 500 mcg
Zoryve	Cream (0.3%): 60 g tube Foam (0.3%): 60 g can

VII. References

1. Daliresp Prescribing Information. Wilmington, DE: AstraZeneca Pharmaceuticals; March 2020. Available at: <https://www.daliresp.com/>. Accessed April 18, 2023.
2. Zoryve Cream Prescribing Information. Westlake Village, CA: Arcutis Biotherapeutics, Inc; October 2023. Available at <https://www.zoryvehcp.com/>. Accessed October 17, 2023.
3. Zoryve Foam Prescribing Information. Westlake Village, VA: Arcutis Biotherapeutics, Inc; December 2023. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/217242s000lbl.pdf. Accessed December 27, 2023.
4. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2023. Available at: <http://www.clinicalpharmacology-ip.com/>. Accessed May 16, 2023.
COPD
5. Global Initiative for Chronic Obstructive Lung Disease (GOLD): Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease (2023 report). Available from: <http://www.goldcopd.org/>. Accessed May 16, 2023.
Psoriasis
6. Elmets CA, Korman NJ, Prater EF, et al. Joint AAD-NPF Guidelines of care for the management and treatment of psoriasis with topical therapy and alternative medicine modalities for psoriasis severity measures. *J Am Acad Dermatol* 2021;84(2):432-70.
7. Menter A, Cordoro KM, Davis DMR, et al. Joint AAD-NPF Guidelines of care for the management and treatment of psoriasis in pediatric patients. *J Am Acad Dermatol* 2020;82(1):161-201.
Seborrheic Dermatitis
8. Borda LJ and Wikramanayake TC. Seborrheic dermatitis and dandruff: A comprehensive review. *J Clin Investig Dermatol*. 2015 December; 3(2):1-22.
9. Dall'Oglio F, Nasca MR, Gerbino C and Micali G. An overview of the diagnosis and management of seborrheic dermatitis. *Clinical, Cosmetic and Investigational Dermatology* 2022;15 1537-1548.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
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
3Q 2020 annual review: no significant changes; references reviewed and updated.	04.15.20	08.20
3Q 2021 annual review: no significant changes; added Commercial line of business; references reviewed and updated.	03.17.21	08.21
3Q 2022 annual review: no significant changes; references reviewed and updated.	03.30.22	08.22
RT4: added criteria for newly FDA-approved dosage form (Zoryve cream) and indication of plaque psoriasis.	08.08.22	11.22
Template changes applied to other diagnoses/indications and continued therapy section.	11.07.22	
3Q 2023 annual review: no significant changes; added HIM line of business; added redirection to generic roflumilast for brand Daliresp requests; references reviewed and updated.	04.18.23	08.23
RT4: updated age requirement from 12 to 6 years per updated pediatric extension on Zoryve label.	10.17.23	
RT4: added criteria for newly FDA-approved dosage form (Zoryve topical foam) and indication of seborrheic dermatitis.	01.16.24	02.24

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.

©2011 Centene Corporation. All rights reserved. All materials are exclusively owned by Centene Corporation and are protected by United States copyright law and international copyright law. No part of this publication may be reproduced, copied, modified, distributed, displayed, stored in a retrieval system, transmitted in any form or by any means, or otherwise published without the prior written permission of Centene Corporation. You may not alter or remove any trademark, copyright or other notice contained herein. Centene[®] and Centene Corporation[®] are registered trademarks exclusively owned by Centene Corporation.