Zoryve (roflumilast) Prior Authorization Program Summary

This program applies to FlexRx Closed, FlexRx Open, FocusRx, GenRx Closed, GenRx Open, Health Insurance Marketplace, and KeyRx formularies.

This is a FlexRx Standard and GenRx Standard program.

The BCBS MN Step Therapy Supplement also applies to this program for all Commercial/HIM lines of business.

POLICY REVIEW CYCLE

Effective Date	Date of Origin
06-01-2024	04-01-2023

FDA APPROVED INDICATIONS AND DOSAGE

Agent(s)	FDA Indication(s)	Notes	Ref#
Zoryve® (roflumilast) Cream	Treatment of plaque psoriasis, including intertriginous areas, in patients 6 years of age and older		1
Zoryve® (roflumilast) Foam	Treatment of seborrheic dermatitis in adult and pediatric patients 9 years of age and older		7

See package insert for FDA prescribing information: https://dailymed.nlm.nih.gov/dailymed/index.cfm

CLINICAL RATIONALE

Psoriasis (PS)	Psoriasis (PS) is a chronic inflammatory skin condition that is often associated with systemic manifestations, especially arthritis. Diagnosis is usually clinical, based on the presence of typical erythematous scaly patches, papules, and plaques that are often pruritic and sometimes painful. Treatment goals for psoriasis include improvement of skin, nail, and joint lesions plus enhanced quality of life.(2)
	
	The American Academy of Family Physicians (AAFP) categorizes psoriasis severity into mild to moderate (less than 5% of body surface area [BSA]) and moderate to severe (5% or more of BSA). The AAFP psoriasis treatment guidelines recommend basing treatment on disease severity:(2)
	
	• Mild to moderate (less than 5% of BSA and sparing the genitals, hands, feet, and face):
	  ○ Candidate for intermittent therapy: topical corticosteroids, vitamin D analogs (calcipotriene and calcitriol), or tazarotene (Tazorac)
	  ○ Candidate for continuous therapy: calcineurin inhibitors (tacrolimus and pimecrolimus)
	• Severe (5% or more of BSA or involving the genitals, hands, feet, and face):
	  ○ Less than 20% of BSA affected: vitamin D analogs (calcipotriene and calcitriol) with or without phototherapy. These agents have a slower onset of action but a longer disease-free interval than topical corticosteroids

	○ 20% or more of BSA affected: systemic therapy with MTX, cyclosporine, acitretin, or biologics. Biologics are recommended for those with concomitant PsA • Less commonly used topical therapies include non-medicated moisturizers, salicylic acid, coal tar, and anthralin The American Academy of Dermatology (AAD) and National Psoriasis Foundation (NPF) categorize psoriasis severity as limited or mild (less than 3% of BSA), moderate (3% to 10% of BSA), or severe (greater than 10% of BSA). The AAD/NPF guidelines also note that psoriasis can be considered severe irrespective of BSA when it occurs in select locations (e.g., hands, feet, scalp, face, or genital area) or when it causes intractable pruritus.(4) The AAD psoriasis treatment guidelines recommend the following:(3,6) • Limited disease (less than 5% of BSA): ○ Topical corticosteroids are first line as either monotherapy or in conjunction with non-steroidal topical agents ○ Vitamin D analogs, calcipotriene, calcipotriol, and calcitriol, are other first line agents and are often used in combination with topical corticosteroids ○ Tazarotene is a corticosteroid sparing agent and can be used in combination with topical corticosteroids to produce a synergistic effect and longer durations of treatment benefit and remission ○ Phototherapy is another first line option for limited disease, and allows for selective targeting of localized lesions and resistant areas such as the scalp and skin folds, leaving surrounding, non-lesional skin unaffected ○ Calcineurin inhibitors (tacrolimus and pimecrolimus) may also be considered first line for intertriginous, inverse, face, and genital psoriasis ○ Systemic agents are considered second line and only for short term use • Moderate to severe disease without PsA (more than 5% of BSA or psoriasis in vulnerable areas [e.g., face, genitals, hands, and feet] that adversely affects quality of life): ○ UV-therapy is considered first line as monotherapy or in combination with acitretin or MTX ○ If UV-therapy is unavailable, first line therapies include MTX, cyclosporine, acitretin, and biologics ○ Second line systemic agents include leflunomide, sulfasalazine, and tacrolimus • Biologics are routinely used when one or more traditional systemic agents fail to produce adequate response, but are considered first line in patients with moderate to severe psoriasis with concomitant severe PsA The National Psoriasis Foundation (NPF) medical board recommend a treat-to-target approach to therapy for psoriasis that include the following:(5) • The preferred assessment instrument for determining disease severity is BSA • Target response after treatment initiation should be BSA less than or equal to 1% after 3 months • Acceptable response is either a BSA less than or equal to 3% or a BSA improvement greater than or equal to 75% from baseline at 3 months after treatment initiation
Seborrheic dermatitis (SD)	Seborrheic dermatitis (SD) is a common skin condition in infants, adolescents, and adults. The characteristic symptoms of scaling, erythema, and itching occur most often on the scalp, face, chest, back, axilla, and groin. SD is a clinical diagnosis based on the location and appearance of the lesions. Although some environmental triggers

	(e.g., low temperature and humidity in winter) are likely to promote its development, several other factors including fungal colonization by *Malassezia* spp, sebaceous gland activity, as well as immunosuppression, endocrine, neurologic and iatrogenic factors have been postulated.(8,9)
	
	Treatment of SD is aimed at modulating sebum production, reducing skin colonization by *Malassezia* spp and controlling inflammation. In mild-to moderate SD forms, topical antifungals and/or topical corticosteroids are first-line therapy. Topical calcineurin inhibitors are effective, well tolerated second-line treatments. In Severe and/or resistant cases the off-label use of some topical and systemic drugs, as well as physical treatment with ultraviolet blue (UVB) phototherapy may be considered. Topical treatments include:(8,9)
	
	• SD on scalp
	  ○ Topical antifungal agents
	  ▪ Ciclopirox shampoo
	  ▪ Ketoconazole shampoo
	  ○ Topical corticosteroids
	  ▪ Betamethasone valerate foam
	  ▪ Clobetasol shampoo
	  ▪ Fluocinolone shampoo
	  ▪ Fluocinolone solution
	  ○ Over the counter preparations
	  ▪ Coal tar shampoo
	  ▪ Selenium sulfide shampoo
	  ▪ Tea tree oil shampoo
	  ▪ Zinc pyrithione shampoo
	• SD on face and body
	  ○ Topical antifungals
	  ▪ Ciclopirox gel or cream
	  ▪ Clotrimazole cream
	  ▪ Ketoconazole cream, foam
	  ▪ Sertaconazole cream
	  ○ Calcineurin inhibitors
	  ▪ Pimecrolimus cream
	  ▪ Tacrolimus ointment
	  ○ Topical corticosteroids
	  ▪ Betamethasone valerate cream or lotion
	  ▪ Desonide cream, foam, gel, or ointment
	  ▪ Fluocinolone cream, oil, or solution
	  ▪ Hydrocortisone cream or ointment
	
	Systemic antifungals (terbinafine, itraconazole) are mainly indicated in acute and/or severe and/or resistant SD forms.(8)

Efficacy	**Plaque psoriasis** Two multicenter, randomized, double-blind, vehicle-controlled trials (DERMIS-1 [NCT04211363] and DERMIS-2 [NCT04211389]) enrolled a total of 881 subjects with mild to severe plaque psoriasis and an affected BSA of 2% to 20%. At baseline, 16% of subjects had an Investigator's Global Assessment (IGA) score of 2 (mild), 76% had an IGA score of 3 (moderate), and 8% had an IGA score of 4 (severe). One hundred seventy-nine (20%) subjects had an intertriginous IGA (I-IGA) score of 2 or higher (mild) at baseline, and 678 (77%) subjects had a baseline Worst Itch-Numeric Rating Score (WI-NRS) score of 4 or higher on a scale of 0 to 10.(1) Subjects were randomized 2:1 to receive Zoryve or vehicle applied once daily for 8 weeks. The primary endpoint was the proportion of subjects who achieved IGA treatment success at week 8. Success was defined as a score of "Clear" (0) or "Almost Clear" (1), plus a 2-grade improvement from baseline. Secondary endpoints included

	the proportion of subjects that achieved I-IGA success at week 8 and WI-NRS success sequentially at weeks 8, 4, and 2. WI-NRS success was defined as a reduction of at least 4 points from baseline in subjects with a baseline WI-NRS score of at least 4.(1) Patients treated with Zoryve achieved greater IGA success at week 8 compared to patients treated with vehicle (41.5% vs 5.8% [difference of 39.7% for DERMIS-1], 36.7% vs 7.1% [difference of 29.5% for DERMIS-2]. Among subjects with an I-IGA score of at least 2 (mild) at baseline (approximately 22% of subjects in DERMIS-1 and 19% in DERMIS-2), there was a higher percentage of subjects who achieved I-IGA success at week 8 in the group who received Zoryve compared to the group who received vehicle (DERMIS-1: 71.5% vs. 13.8%; DERMIS-2: 67.5% vs. 17.4%). Secondary endpoints were not statistically significant.(1) **Seborrheic dermatitis** Two randomized double-blind, vehicle-controlled trials (STRATUM [NCT04973228]) and Trial 203 [NCT04091646] enrolled patients with seborrheic dermatitis involving the scalp, face, and/or body with an Investigator Global Assessment (IGA) of moderate or severe (IGA of 4 or 3 on a 5 point scale from 0 to 4). The primary endpoint in both studies was the proportion of patients who achieved IGA treatment success at Week 8. Success was defined as a score of "Clear" (0) or "Almost Clear" (1), plus a 2-grade improvement from baseline. IGA was achieved in 79.5% and 71.1% of patients in STRATUM and Trial 203 respectively, with a 95% confidence interval in both trials.(7)
Safety	Zoryve is contraindicated in patients with moderate to severe liver impairment (Child-Pugh B or C).(1,7)

REFERENCES

Number	Reference
1	Zoryve cream prescribing information. Arcutis Biotherapeutics, Inc. October 2023.
2	Weigle, Nancy, M.D., et al. Psoriasis. American Academy of Family Physicians. May 2013. 87 (9): 626-633.
3	Menter A, Korman NJ, Elmets CA, et al. Guidelines of care for the management of psoriasis and psoriatic arthritis. J Am Acad Dermatol. 2011;65(1):137–174.
4	Menter, Alan et al. (2019). Joint AAD-NPF guidelines of care for the management and treatment of psoriasis with biologics. Journal of the American Academy of Dermatology. doi: https://doi.org/10.1016/j.jaad.2018.11.057.
5	Armstrong AW, Siegel MP, Bagel J, et al. From the medical board of the National Psoriasis Foundation: treatment targets for plaque psoriasis. Journal of the American Academy of Dermatology. 2017;76(2):290-298. doi: 10.1016/j.jaad.2016.10.017.
6	Menter A, et al. Guidelines of care for the management of psoriasis and psoriatic arthritis: Section 1. Overview of psoriasis and guidelines of care for the treatment of psoriasis with biologics. Journal of the American Academy of Dermatology. 2008; 58:826–850. doi: 10.1016/j.jaad.2008.02.039.
7	Zoryve foam prescribing information. Arcutis Biotherapeutics, Inc. December 2023.
8	Dall'Oglio F, Nasca MR, Gerbino C, Micali G. An Overview of the Diagnosis and Management of Seborrheic Dermatitis. Clin Cosmet Investig Dermatol. 2022 Aug 6;15:1537-1548. doi: 10.2147/CCID.S284671. PMID: 35967915; PMCID: PMC9365318.
9	Clark GW, Pope SM, Jaboori K. Diagnosis and Treatment of Seborrheic Dermatitis. Am Fam Physician. 2015;91(3):185-190.

POLICY AGENT SUMMARY PRIOR AUTHORIZATION

Target Brand Agent(s)	Target Generic Agent(s)	Strength	Targeted MSC	Available MSC	Final Age Limit	Preferred Status
Zoryve	roflumilast cream	0.3 %	M ; N ; O ; Y	N		
Zoryve	roflumilast foam	0.3 %	M ; N ; O ; Y	N		

CLIENT SUMMARY – PRIOR AUTHORIZATION

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Zoryve	roflumilast cream	0.3 %	FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx
Zoryve	roflumilast foam	0.3 %	FlexRx Closed ; FlexRx Open ; FocusRx ; GenRx Closed ; GenRx Open ; Health Insurance Marketplace/BasicRx ; KeyRx

PRIOR AUTHORIZATION CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
	Initial Evaluation **Target Agent(s)** will be approved when ALL of the following are met: 1. ONE of the following: A. The requested agent is Zoryve cream AND ALL of the following: 1. The patient has a diagnosis of plaque psoriasis **AND**: 2. The patient's affected body surface area (BSA) is less than or equal to 20% **AND** 3. ONE of the following: A. The patient has tried and had an inadequate response to a topical corticosteroid **OR** B. The patient has an intolerance or hypersensitivity to therapy with topical corticosteroids **OR** C. The patient has an FDA labeled contraindication to ALL topical corticosteroids **OR** D. The patient is currently being treated with the requested agent as indicated by ALL of the following: 1. A statement by the prescriber that the patient is currently taking the requested agent **AND** 2. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on the requested agent **AND** 3. The prescriber states that a change in therapy is expected to be ineffective or cause harm **OR** E. The prescriber has provided documentation that topical corticosteroids cannot be used due to a documented medical condition or comorbid condition that is likely to cause an adverse reaction, decrease ability of the patient to achieve or maintain reasonable functional ability in performing daily activities or cause physical or mental harm **AND** 4. ONE of the following:

Module	Clinical Criteria for Approval
	A. The patient has tried and had an inadequate response to another topical psoriasis agent with a different mechanism of action (e.g., vitamin D analogs, calcineurin inhibitors, tazarotene) **OR** B. The patient has an intolerance or hypersensitivity to another topical psoriasis agent with a different mechanism of action **OR** C. The patient has an FDA labeled contraindication to ALL other topical psoriasis agents with a different mechanism of action **OR** D. The patient is currently being treated with the requested agent as indicated by ALL of the following: 1. A statement by the prescriber that the patient is currently taking the requested agent **AND** 2. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on the requested agent **AND** 3. The prescriber states that a change in therapy is expected to be ineffective or cause harm **OR** E. The prescriber has provided documentation that ALL other topical psoriasis agents with a different mechanism of action cannot be used due to a documented medical condition or comorbid condition that is likely to cause an adverse reaction, decrease ability of the patient to achieve or maintain reasonable functional ability in performing daily activities or cause physical or mental harm **OR** B. The requested agent is Zoryve foam AND ALL of the following: 1. The patient has a diagnosis of seborrheic dermatitis **AND** 2. ONE of the following: A. The patient has tried and had an inadequate response to ONE topical antifungal OR ONE topical corticosteroid **OR** B. The patient has an intolerance or hypersensitivity to ONE topical antifungal OR ONE topical corticosteroid **OR** C. The patient has an FDA labeled contraindication to ALL topical antifungals AND topical corticosteroids **OR** D. The patient is currently being treated with the requested agent as indicated by ALL of the following: 1. A statement by the prescriber that the patient is currently taking the requested agent **AND** 2. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on the requested agent **AND** 3. The prescriber states that a change in therapy is expected to be ineffective or cause harm **OR** E. The prescriber has provided documentation that topical antifungals AND topical corticosteroids cannot be used due to a documented medical condition or comorbid condition that is likely to cause an adverse reaction, decrease ability of the patient to achieve or maintain reasonable functional ability in performing daily activities or cause physical or mental harm **AND** 3. ONE of the following: A. The patient has seborrheic dermatitis of the scalp **OR** B. The patient has tried and had an inadequate response to ONE topical calcineurin inhibitor (e.g., pimecrolimus, tacrolimus) **OR** C. The patient has an intolerance or hypersensitivity to ONE topical calcineurin inhibitor (e.g., pimecrolimus, tacrolimus) **OR** D. The patient has an FDA labeled contraindication to ALL topical calcineurin inhibitors (e.g., pimecrolimus, tacrolimus) **OR** E. The patient is currently being treated with the requested agent as indicated by ALL of the following: 1. A statement by the prescriber that the patient is currently taking the requested agent **AND**

Module	Clinical Criteria for Approval
	2. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on the requested agent **AND** 3. The prescriber states that a change in therapy is expected to be ineffective or cause harm **OR** F. The prescriber has provided documentation that topical calcineurin inhibitors (e.g., pimecrolimus, tacrolimus) cannot be used due to a documented medical condition or comorbid condition that is likely to cause an adverse reaction, decrease ability of the patient to achieve or maintain reasonable functional ability in performing daily activities or cause physical or mental harm **OR** C. The patient has another FDA labeled indication for the requested agent and route of administration **AND** 2. If the patient has an FDA labeled indication, then ONE of the following: A. The patient's age is within FDA labeling for the requested indication for the requested agent **OR** B. There is support for using the requested agent for the patient's age for the requested indication **AND** 3. The prescriber is a specialist in the area of the patient's diagnosis (e.g., dermatologist) or the prescriber has consulted with a specialist in the area of the patient's diagnosis **AND** 4. The patient does NOT have any FDA labeled contraindications to the requested agent **Length of Approval:** diagnosis of plaque psoriasis 12 months, diagnosis of seborrheic dermatitis 8 weeks, All other FDA approved indications 12 months **Renewal Evaluation** **Target Agent(s)** will be approved when ALL of the following are met: 1. The patient has been previously approved for the requested agent through the plan's Prior Authorization process [Note: patients not previously approved for the requested agent will require initial evaluation review] **AND** 2. The patient has had clinical benefit with the requested agent **AND** 3. The prescriber is a specialist in the area of the patient's diagnosis (e.g., dermatologist) or the prescriber has consulted with a specialist in the area of the patient's diagnosis **AND** 4. The patient does NOT have any FDA labeled contraindications to the requested agent **Length of Approval:** 12 months

