Original Effective Date: 10/26/2022
Current Effective Date: 06/11/2026
Last P&T Approval/Version: 04/29/2026
Next Review Due By: 04/2027
Policy Number: C24324-A

Zoryve (roflumilast)

PRODUCTS AFFECTED

Zoryve (roflumilast) cream, Zoryve (roflumilast) foam

COVERAGE POLICY

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Coverage Guideline must be read in its entirety to determine coverage eligibility, if any. This Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide Molina Healthcare complete medical rationale when requesting any exceptions to these guidelines.

Documentation Requirements:
Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

DIAGNOSIS:
Plaque psoriasis, Atopic dermatitis, Seborrheic dermatitis

REQUIRED MEDICAL INFORMATION:
This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. This clinical policy will be reviewed along with state and federal requirements, the benefit being administered, and formulary preferencing. If a drug within this policy receives an updated FDA label within the last 180 days, medical necessity for the member will be reviewed using the updated FDA label information. Coverage will be determined on a case-by-case basis until the criteria can be updated through Molina Healthcare, Inc. clinical governance. Additional information may be required on a case-by-case basis to allow for adequate review. When the requested drug product for coverage is dosed by weight, body surface area or other member specific measurement, this data element is required as part of the medical necessity review. The Pharmacy and Therapeutics Committee has determined that the drug benefit shall be a mandatory generic and that generic drugs will be dispensed whenever available. The Pharmacy and Therapeutics Committee has determined that biosimilars may be preferred.

A. PLAQUE PSORIASIS (0.3% CREAM, FOAM ONLY):
   1. Documented diagnosis of plaque psoriasis

AND

2. Documentation treatment area is ≤ 20% body surface area (BSA)
   AND
3. Documentation of inadequate response, serious side effects, contraindication or clinical rationale of inappropriateness to topical corticosteroids OR plaque psoriasis involves sensitive areas of the body or areas that would significantly impact daily function (ex. face, neck, hands, feet, genitals)
   AND
4. Documentation of inadequate response, serious side effects, contraindication or clinical rationale of inappropriateness to ONE of the following: tacrolimus, pimecrolimus, calcipotriene, or tazarotene
   AND
5. Documentation by prescriber of baseline disease activity evaluation and goals for treatment to be used to evaluate efficacy of therapy at renewal
   AND
6. Prescriber attests to (or the clinical reviewer has found that) the member not having any FDA labeled contraindications that haven't been addressed by the prescriber within the documentation submitted for review [Contraindications to Zoryve (roflumilast) include: Moderate to severe liver impairment (Child-Pugh B or C)]

B. ATOPIC DERMATITIS (0.05%, 0.15% CREAM ONLY):

1. Documented diagnosis of mild to moderate atopic dermatitis (eczema)
   AND
2. Documentation of inadequate response, serious side effects, or contraindication to TWO of the following: topical corticosteroids or preferred/formulary topical calcineurin inhibitor (tacrolimus, pimecrolimus)
   AND
3. Documentation by prescriber of baseline assessment of disease activity (e.g., affected BSA, severity of eczematous lesions, pruritus, etc.)
   AND
4. IF THIS IS A NON-FORMULARY/NON-PREFERRED PRODUCT: Documentation of trial/failure of or serious side effects to a majority (not more than 3) of the preferred formulary/PDL alternatives for the given diagnosis. Submit documentation including medication(s) tried, dates of trial(s) and reason for treatment failure(s).
   MOLINA REVIEWER NOTE: For Illinois Marketplace, please see Appendix.
   AND
5. Prescriber attests to (or the clinical reviewer has found that) the member not having any FDA labeled contraindications that haven't been addressed by the prescriber within the documentation submitted for review [Contraindications to Zoryve (roflumilast) include: Moderate to severe liver impairment (Child-Pugh B or C).]

C. SEBORRHEIC DERMATITIS (FOAM ONLY):

1. Documented diagnosis of seborrheic dermatitis
   AND
2. Documentation by prescriber of baseline disease activity evaluation and goals for treatment to be used to evaluate efficacy of therapy at renewal
   AND
3. Documentation of trial/failure of or serious side effects to a majority (not more than 3) of the preferred formulary/PDL alternatives for the given diagnosis. Submit documentation including medication(s) tried, dates of trial(s) and reason for treatment failure(s).
   MOLINA REVIEWER NOTE: For Illinois Marketplace, please see Appendix.
   AND
4. Prescriber attests to (or the clinical reviewer has found that) the member not having any FDA labeled contraindications that haven't been addressed by the prescriber within the documentation submitted for review [Contraindications to Zoryve (roflumilast) include: Moderate to severe liver impairment (Child-Pugh B or C).]

CONTINUATION OF THERAPY:

A. PLAQUE PSORIASIS (0.3% CREAM, FOAM ONLY), SEBORRHEIC DERMATITIS (FOAM ONLY):

1. Adherence to therapy at least 85% of the time as verified by the prescriber or member medication fill history OR adherence less than 85% of the time due to the need for surgery or treatment of an infection, causing temporary discontinuation
   AND
2. Prescriber attests to or clinical reviewer has found no evidence of intolerable adverse effects or drug toxicity
   AND
3. Documentation of positive clinical response as demonstrated by low disease activity and/or improvements in the condition's signs and symptoms

B. ATOPIC DERMATITIS (0.05%, 0.15% CREAM ONLY):

1. Adherence to therapy at least 85% of the time as verified by the prescriber or member medication fill history OR adherence less than 85% of the time due to the need for surgery or treatment of an infection, causing temporary discontinuation
   AND
2. Documentation that member's condition has improved based upon the prescriber's assessment of disease control and clinical improvements while on therapy (e.g., reduction of affected BSA, improvements in severity of eczematous lesions, decrease in pruritus severity, etc.)
   AND
3. Prescriber attests to or clinical reviewer has found no evidence of intolerable adverse effects or drug toxicity

DURATION OF APPROVAL:

Initial authorization: 6 months, Continuation of Therapy: 12 months
MOLINA REVIEWER NOTE: For Illinois Marketplace and Texas Marketplace, please see Appendix.

PRESCRIBER REQUIREMENTS:

Prescribed by or in consultation with a board-certified dermatologist, allergist, or immunologist [If prescribed in consultation, consultation notes must be submitted with initial request and reauthorization requests]

AGE RESTRICTIONS:

Zoryve Cream:
0.05%: 2 to 5 years of age
0.15%, 0.3%: 6 years of age and older

Zoryve Foam:
Seborrheic dermatitis: 9 years of age and older
Plaque psoriasis: 12 years of age and older

QUANTITY:

Member's BSA affected <10%: maximum 60 grams/30 days
Member's BSA affected >10%: maximum of 180 grams/30 days

PLACE OF ADMINISTRATION:

The recommendation is that topical medications in this policy will be for pharmacy benefit coverage and patient self-administered.

DRUG INFORMATION

ROUTE OF ADMINISTRATION:

DRUG CLASS:
Phosphodiesterase 4 (PDE4) Inhibitors - Topical

FDA-APPROVED USES:
0.3% cream: Indicated for the topical treatment of plaque psoriasis, including intertriginous areas, in adult and pediatric patients 6 years of age and older
0.15% cream: Indicated for the treatment of mild to moderate atopic dermatitis in adult and pediatric patients 6 years of age and older
0.05% cream: Indicated for the topical treatment of mild to moderate atopic dermatitis in pediatric patients 2 to 5 years of age
0.3% foam: Indicated for the treatment of seborrheic dermatitis in adult and pediatric patients 9 years of age and older and plaque psoriasis of the scalp and body in adult and pediatric patients 12 years of age and older

COMPENDIAL APPROVED OFF-LABELED USES:
None

APPENDIX

Reserved for State specific information. *Information includes, but is not limited to, State contract language, Medicaid criteria and other mandated criteria.*

State Specific Information
State Marketplace
Illinois (Source: Illinois General Assembly)
"(215 ILCS 200/65) Sec. 65. Length of prior authorization approval for *treatment for chronic or long-term conditions*. If a health insurance issuer requires a prior authorization for a recurring health care service or maintenance medication for the treatment of a chronic or long-term condition, *the approval shall remain valid for the lesser of 12 months from the date the health care professional or health care provider receives the prior authorization approval or the length of the treatment as determined by the patient's health care professional*. This Section shall not apply to the prescription of benzodiazepines or Schedule II narcotic drugs, such as opioids. Except to the extent required by medical exceptions processes for prescription drugs set forth in Section 45.1 of the Managed Care Reform and Patient Rights Act, nothing in this Section shall require a policy to cover any care, treatment, or services for any health condition that the terms of coverage otherwise completely exclude from the policy's covered benefits without regard for whether the care, treatment, or services are medically necessary. (Source: P.A. 102-409, eff. 1-1-22.)"

Illinois (Source: Illinois General Assembly)
"(215 ILCS 134/45.1) Sec. 45.1. Medical exceptions procedures required. (c) An off-formulary exception request shall not be denied if: (1) the formulary prescription drug is contraindicated; (2) the patient has tried the formulary prescription drug while under the patient's current or previous health insurance or health benefit plan and the prescribing provider submits evidence of failure or intolerance; or (3) the patient is stable on a prescription drug selected by his or her health care provider for the medical condition under consideration while on a current or previous health insurance or health benefit plan. (d) Upon the granting of an exception request, the insurer, health plan, utilization review organization, or other entity shall authorize the coverage for the drug prescribed by the enrollee's treating health care provider, to the extent the prescribed drug is a covered drug under the policy or contract up to the quantity covered. (e) Any approval of a medical exception request made pursuant to this Section shall be honored for 12 months following the date of the approval or until renewal of the plan."

Texas (Source: Texas Statutes, Insurance Code)
"Sec. 1369.654. PROHIBITION ON MULTIPLE PRIOR AUTHORIZATIONS.
(a) A health benefit plan issuer that provides prescription drug benefits *may not require an enrollee to receive*

more than one prior authorization annually of the prescription drug benefit for *a prescription drug prescribed to treat an autoimmune disease, hemophilia, or Von Willebrand disease*.

(b) This section does not apply to:

(1) opioids, benzodiazepines, barbiturates, or carisoprodol;

(2) prescription drugs that have a typical treatment period of less than 12 months;

(3) drugs that:

(A) have a boxed warning assigned by the United States Food and Drug Administration for use; and

(B) must have specific provider assessment; or

(4) the use of a drug approved for use by the United States Food and Drug Administration in a manner other than the approved use."

APPENDIX 1:

Dosing

No universal standard exists for quantity of application, although suggested methods include use of the adult fingertip unit (the amount from the distal interphalangeal joint to the fingertip, or approximately 0.5 grams (gm), being applied over an area equal to 2 adult palms), following the rule of 9's that measures the percent affected area, and use of charts that propose amounts based on patient age and body site. In adults, the rule of nines is used as a rough indicator of % BSA. Palmar hand surface is approximately 1% BSA.

Anatomic Surface % of Body Surface

Head and neck 9%
Anterior trunk 18%
Posterior trunk 18%
Arms, including hands 9% each
Legs, including feet 18% each
Genitalia 1%
Quantity for 1% BSA, suggested AAD estimation Grams per application
• 0.5gm per application over 2 palms (1% BSA per palm) = 0.25gm per application over 1% BSA

Grams per month for 1% BSA
• At 0.25gm per application over 1%BSA x 40 applications per month = 0.25gm x 40 = 10gm per 1%BSA per month
• For example, Quantity sufficient based on above calculations for 9%BSA and 18%BSA

Grams per month for 9% BSA
• 9% BSA x 10gm = 90 grams / month

Grams per month for 18% BSA
• 18% BSA x 10gm = 180 grams / month
• For example, Quantity sufficient based on above calculations for select drugs with max dosing

APPENDIX 2:

Investigator Global Assessment of Disease (IGA)

Scale	Grade	Description
0	Clear	Plaque thickening = no elevation or thickening over normal skin Scaling = no evidence of scaling Erythema = none (no residual red coloration but post-inflammatory hyperpigmentation may be present)
1	Almost Clear	Plaque thickening = none or possible thickening but difficult to ascertain if there is a slight elevation above normal skin level Scaling = none or residual surface drying and scaling Erythema = light pink coloration

2	Mild	Plaque thickening = slight but definite elevation Scaling = fine scales partially or mostly covering the lesions Erythema = light red coloration
3	Moderate	Plaque thickening = moderate elevation with rounded or sloped edges Scaling = most lesions at least partially covered Erythema = definite red coloration
4	Severe	Plaque thickening = marked or very marked elevation typically with hard or sharp edges Scaling = non-tenacious or thick tenacious scale, covering most or all of lesions Erythema = very bright red coloration; extreme red coloration; deep red coloration

APPENDIX 3:
Guidelines of care for the management of psoriasis and psoriatic arthritis (AAD 2009)
Guidelines of care for the management and treatment of psoriasis with topical therapy and alternative medicine modalities for psoriasis severity measures (Joint AAD-NPF 2021)
Although not FDA approved for psoriasis, the topical calcineurin inhibitors tacrolimus and pimecrolimus are often used in the treatment of psoriasis. Both agents have demonstrated efficacy when used under occlusion, on facial and intertriginous psoriasis, and are used as steroid-sparing agents for prolonged (>4 weeks) use. The off-label combination of tacrolimus and 6% salicylic acid for 12 weeks may be used for the treatment of plaque psoriasis.

BACKGROUND AND OTHER CONSIDERATIONS

BACKGROUND:
Zoryve is the first topical phosphodiesterase-4 (PDE4) inhibitor approved for the treatment of plaque psoriasis. The approval was based two randomized, double-blind, vehicle-controlled, Phase 3 trials, DERMIS-1 and DERMIS-2, which enrolled a total of 881 patients with mild to severe plaque psoriasis and BSA of 2%–20%.
Patients were randomized to receive Zoryve or vehicle applied once daily for 8 weeks. Zoryve met its primary endpoint in both trials, which was the proportion of subjects who achieved IGA treatment success at Week 8. IGA treatment success was defined as a score of “clear” (0) or “almost clear” (1), plus a 2-grade improvement from baseline.
Results from DERMIS-1 and DERMIS-2 showed that 41.5% and 36.7% of patients treated with Zoryve achieved IGA treatment success at week 8, respectively, compared with 5.8% and 7.1% of patients who received vehicle (P <.0001 in both studies). Among patients with an intertriginous IGA (I-IGA) score of at least 2 at baseline, a greater percentage of patients in the Zorvye arm achieved I-IGA success at week 8 compared with those in the vehicle arm (DERMIS-1: 71.5% vs 13.8%; DERMIS-2: 67.5% vs 17.4%).

Additionally, among patients with a Worst Itch-Numerical Rating Score of 4 or higher at baseline, a greater percentage of patients in the Zoryve arm achieved at least a 4-point reduction in itch at week 8 vs the vehicle group (DERMIS-1: 67% vs 26%; DERMIS-2: 69% vs 33%; P <.0001). Statistically significant improvements in key secondary endpoints, including Psoriasis Area Severity Index-75 (PASI-75) and patient perceptions of signs and symptoms (eg, itching, pain, and scaling, as measured by the Psoriasis Symptoms Diary) were also observed with Zoryve.

Zoryve is contraindicated in patients with moderate to severe liver impairment (Child-Pugh B or C). The most common adverse reactions (reported in ≥1% of patients) are diarrhea (3.1%), headache (2.4%), insomnia (1.4%), nausea (1.2%), application site pain (1.0%), upper respiratory tract infections (1.0%), and urinary tract infections (1.0%). There are no warnings or precautions in Zoryve’s labeling. pediatric patients 6 to less than 18 years of age is supported by data from two 8-week, vehicle-controlled

Labeled age was expanded to 6 years of age and older in October 2023. Use of Zoryve cream in safety and efficacy trials which included 18 pediatric subjects 6 to 17 years of age, of whom 11 received Zoryve cream. Use of Zoryve cream in pediatric patients 6 to less than 12 years of age is also supported by data from one 4-week, open-label, safety and pharmacokinetic (PK) study which included 20 pediatric subjects 6 to less

than 12 years of age. The adverse reaction profile in subjects 6 to less than 18 years of age was consistent with that observed in adults.

Labeled age was expanded to 2 years of age and older in October 2025. Use of Zoryve cream was studied in a multicenter, randomized, double-blind, vehicle-controlled trial (INTEGUMENT-PED [NCT04845620]) which enrolled a total of 652 pediatric subjects 2 to 5 years of age with mild to moderate atopic dermatitis. At baseline, 22% of subjects had a validated Investigator Global Assessment for Atopic Dermatitis (vIGA-AD) score of 2 (mild), and 78% had a vIGA-AD score of 3 (moderate). The primary endpoint was the proportion of subjects who achieved vIGA-AD treatment success at Week 4 (Table 7). Success was defined as a score of "Clear" (0) or "Almost Clear" (1), plus a 2-grade improvement from baseline. The Zoryve group had a statistically significant improvement over vehicle cream.

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:
All other uses of Zoryve (roflumilast) are considered experimental/investigational and therefore, will follow Molina's Off- Label policy. Contraindications to Zoryve (roflumilast) include: Moderate to severe liver impairment (Child-Pugh B or C).

OTHER SPECIAL CONSIDERATIONS:
None

CODING/BILLING INFORMATION

CODING DISCLAIMER. *Codes listed in this policy are for reference purposes only and may not be all-inclusive or applicable for every state or line of business. Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement. Listing of a service or device code in this policy does not guarantee coverage. Coverage is determined by the benefit document. Molina adheres to Current Procedural Terminology (CPT®), a registered trademark of the American Medical Association (AMA). All CPT codes and descriptions are copyrighted by the AMA; this information is included for informational purposes only. Providers and facilities are expected to utilize industry-standard coding practices for all submissions. Molina has the right to reject/deny the claim and recover claim payment(s) if it is determined it is not billed appropriately or not a covered benefit. Molina reserves the right to revise this policy as needed.*

HCPCS CODE	DESCRIPTION
NA	

AVAILABLE DOSAGE FORMS:
Zoryve CREA 0.05% (60 gm)
Zoryve CREA 0.3% (60 gm)
Zoryve CREA 0.15% (60 gm)
Zoryve FOAM 0.3% (60 gm)

REFERENCES

1. Zoryve (roflumilast) cream 0.3%, 0.15%, 0.05%, for topical use [prescribing information]. Westlake Village, CA: Arcutis Biotherapeutics Inc; October 2025.
2. Zoryve (roflumilast) topical foam, 0.3% [prescribing information]. Westlake Village, CA: Arcutis Biotherapeutics Inc; May 2025.
3. Armstrong AW, Siegel MP, Bagel J, et al. From the Medical Board of the National Psoriasis Foundation: Treatment targets for plaque psoriasis. J Am Acad Dermatol 2017; 76:290.
4. American Academy of Dermatology Work Group, Menter A, Korman NJ, et al. Guidelines of care for

the management of psoriasis and psoriatic arthritis: section 6. Guidelines of care for the treatment of psoriasis and psoriatic arthritis: case-based presentations and evidence-based conclusions. J Am Acad Dermatol 2011; 65:137.
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7. Twin Trial of PDE4 Inhibition With Roflumilast for the Management of Plaque Psoriasis (DERMIS-2). https://clinicaltrials.gov/ct2/show/NCT04211389
8. Trial of PDE4 Inhibition With Roflumilast for the Management of Plaque Psoriasis (DERMIS-1). https://clinicaltrials.gov/ct2/show/NCT04211363
9. Sidbury R, Alikhan A, Bercovitch L, Cohen DE, Darr JM, Drucker AM, Eichenfield LF, Frazer-Green L, Paller AS, Schwarzenberger K, Silverberg JI, Singh AM, Wu PA, Davis DMR, Guidelines of care for the management of atopic dermatitis in adults with topical therapies, Journal of the American Academy of Dermatology (2023), doi: https://doi.org/10.1016/j.jaad.2022.12.029.

SUMMARY OF REVIEW/REVISIONS	DATE
REVISION- Notable revisions: Required Medical Information Duration of Approval Appendix	Q2 2026
REVISION- Notable revisions: Diagnosis Required Medical Information Continuation of Therapy Age Restrictions FDA-Approved Uses Background Available Dosage Forms References	Q1 2026
REVISION- Notable revisions: Required Medical Information References	Q2 2025
REVISION- Notable revisions: Diagnosis Required Medical Information Continuation of Therapy Drug Class FDA-Approved Uses Available Dosage Forms References	Q4 2024
REVISION- Notable revisions: Required Medical Information Duration of Approval References	Q2 2024
REVISION- Notable revisions: Age Restrictions FDA-Approved Uses Background References	Q1 2024
REVISION- Notable revisions: Quantity Appendix	Q2 2023

NEW CRITERIA CREATION	Q4 2022