Original Effective Date: 10/26/2022
Current Effective Date: 11/29/2024
Last P&T Approval/Version: 10/30/2024
Next Review Due By: 04/2025
Policy Number: C24324-A

Zoryve (roflumilast) Cream

PRODUCTS AFFECTED

Zoryve (roflumilast) cream

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

REQUIRED MEDICAL INFORMATION:
This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. 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 along with state and federal requirements, benefit being administered and formulary preferencing. 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.

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

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2. Documentation member's affected BSA is NOT more than 20%
   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 of prescriber 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 (0.15% CREAM ONLY):

1. Documented diagnosis of mild to moderate atopic dermatitis (eczema)
   AND
2. Documentation that the member experienced an inadequate treatment response (minimum 2-week trial), serious side effects, or contraindication (e.g., areas involving the face, neck or intertriginous areas) to at least TWO preferred/formulary medium or high topical steroids (see Appendix)
   AND
3. Documentation that member experience an inadequate treatment response (minimum of 6-week consecutive trial), serious side effects or contraindication to ONE preferred/formulary topical calcineurin inhibitor (tacrolimus, pimecrolimus)
   AND
4. Documentation of prescriber baseline assessment of disease activity (e.g., affected BSA, severity of eczematous lesions, pruritis, etc.)
   AND
5. 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).
   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).]

CONTINUATION OF THERAPY:

A. PLAQUE PSORIASIS (0.3% 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. 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

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B. ATOPIC DERMATITIS (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 Texas Marketplace, please see Appendix.

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

AGE RESTRICTIONS:
6 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:
Topical

DRUG CLASS:
Antipsoriatics, Phosphodiesterase 4 (PDE4) Inhibitors - Topical

FDA-APPROVED USES:
0.3% cream: Indicated for 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

COMPENDIAL APPROVED OFF-LABELED USES:
None

APPENDIX

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

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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	Plaque thickening = none or possible thickening but difficult to ascertain if there is a
	Clear	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

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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.

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) cream include: Moderate to severe liver impairment (Child-Pugh B or C).

OTHER SPECIAL CONSIDERATIONS:

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None

CODING/BILLING INFORMATION

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HCPCS CODE	DESCRIPTION
NA	

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

REFERENCES

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SUMMARY OF REVIEW/REVISIONS	DATE

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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 DEVELOPMENT	Q4 2022

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