Korsuva® (Difelikefalin)

Policy Number: 2026D0115F
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➲ Instructions for Use

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Related Policies
None

Application

UnitedHealthcare Commercial

This Medical Policy applies to UnitedHealthcare Commercial benefit plans.

UnitedHealthcare Individual Exchange

This Medical Policy applies to Individual Exchange benefit plans.

Coverage Rationale

➲ See Benefit Considerations

Korsuva (difelikefalin) is proven for the treatment of moderate-to-severe pruritus associated with chronic kidney disease in adults undergoing hemodialysis when the following criteria are met:

- For **initial therapy**, **all** of the following:
  - Diagnosis of moderate-to-severe pruritus associated with chronic kidney disease; **and**
  - Patient is on hemodialysis; **and**
  - Dosing is in accordance with the United States Food and Drug Administration approved labeling; **and**
  - Initial authorization will be for no longer than 12 months
- For **continuation of therapy**, **all** of the following:
  - Documentation of a positive clinical response (i.e., reduction in itch from baseline); **and**
  - Dosing is in accordance with the United States Food and Drug Administration approved labeling; **and**
  - Reauthorization will be for no longer than 12 months

Korsuva (difelikefalin) is medically necessary for the treatment of moderate-to-severe pruritus associated with chronic kidney disease in adults undergoing hemodialysis when the following criteria are met:

- For **initial therapy**, **all** of the following:
  - Diagnosis of moderate-to-severe pruritus associated with chronic kidney disease; **and**
  - Patient is on hemodialysis; **and**
  - Pruritus is not attributed to a cause other than end stage renal disease or its complications (e.g., pruritic dermatological disease, cholestatic liver disease); **and**
  - Pruritus is not limited to occurring only during the dialysis session; **and**
  - Pruritis is not localized to just the palms of the hands; **and**

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- History of failure, contraindication, or intolerance to other pruritis treatments (e.g., antihistamines, corticosteroids, gabapentin, pregabalin, capsaicin); **and**
- Prescribed by or in consultation with a nephrologist; **and**
- Dosing is in accordance with the United States Food and Drug Administration approved labeling; **and**
- Initial authorization will be for no longer than 12 months

- For **continuation of therapy**, **all** of the following:
  - Documentation of a positive clinical response (i.e., reduction in itch from baseline); **and**
  - Prescribed by or in consultation with a nephrologist; **and**
  - Dosing is in accordance with the United States Food and Drug Administration approved labeling; **and**
  - Reauthorization will be for no longer than 12 months

Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this policy does not imply that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other policies and guidelines may apply.

HCPCS Code	Description
J0879	Injection, difelikefalin, 0.1 microgram

Diagnosis Code	Description
L29.89	Other pruritus
L29.9	Pruritus, unspecified

Background

Chronic kidney disease–associated pruritus, also known as uremic pruritus, affects more than 60% of patients undergoing hemodialysis, with 20 to 40% of patients reporting moderate-to-severe pruritus. Intense and generalized systemic itching in these patients is associated with poor sleep quality, depression, reduced quality of life, increased risk of infection, and an increased risk of death. The pathogenesis of chronic kidney disease–associated pruritus is incompletely understood. Several hypotheses have been proposed, including metabolic disturbances, dysregulated immune response, and imbalances in the endogenous opioid system, with peripherally distributed kappa opioid receptors potentially playing a role.

Korsuva is a kappa opioid receptor (KOR) agonist. The relevance of KOR activation to therapeutic effectiveness is not known.

Benefit Considerations

Some Certificates of Coverage allow for coverage of experimental/investigational/unproven treatments for life-threatening illnesses when certain conditions are met. The member specific benefit plan document must be consulted to make coverage decisions for this service. Some states mandate benefit coverage for off-label use of medications for some diagnoses or under some circumstances when certain conditions are met. Where such mandates apply, they supersede language in the benefit document or in the medical or drug policy.

Clinical Evidence

The efficacy of Korsuva was evaluated in two randomized, multicenter, double-blind, placebo-controlled trials that enrolled a total of 851 subjects 18 years of age and older undergoing hemodialysis who had moderate-to-severe pruritus. In both trials, subjects received intravenous bolus injections of Korsuva 0.5 mcg per kilogram of dry body weight into the venous line of the hemodialysis circuit at the end of each hemodialysis session or placebo three times per week for 12 weeks. In both trials, a 7-day run-in period prior to randomization was used to confirm that each subject had moderate-to-severe pruritus and to establish a baseline itch intensity, as measured by the patient-reported daily 24-hour Worst Itching Intensity Numerical Rating Scale (WI-NRS) scores (0 “no itch” to 10 “worst itch imaginable”). The mean (SD) baseline WI-NRS score was 7.1 (1.5) in Trial 1 and 7.2 (1.4) in Trial 2. At baseline in Trial 1, 61% of subjects were male, 49% were White, 42% were Black or African American, the mean age was 57 years (range 22 to 88 years), and 40% of subjects

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were using prior anti-pruritic medications (including sedating antihistamines) and continued the use throughout the trial. At baseline in Trial 2, 58% of subjects were male, 70% were White, 19% were Black or African American, the mean age was 60 years (range 23 to 90 years), and 36% of subjects were using prior anti-pruritic medications (including sedating antihistamines) and continued the use throughout the trial.

In each trial, efficacy was assessed based on the proportion of subjects achieving a 4-point or greater improvement (reduction) from baseline in the weekly mean of the daily 24-hour WI-NRS score at Week 12. Korsuva resulted in significant improvements, as compared with placebo, in the primary outcome. At week 12, the estimated percentage of patients who had an improvement (decrease) of at least 3 points from baseline on the WI-NRS was significantly greater in the Korsuva group than in the placebo group (49.1% vs. 27.9%; relative risk, 1.65; 95% confidence interval, 1.26 to 2.14; $p < 0.001$). The treatment effect was evident at week 1. Similar results were reported when only data during receipt of Korsuva or placebo were used (51.0% vs. 27.6%). Sensitivity analyses of the primary outcome yielded results that were consistent with those of the primary analysis. All secondary outcomes in the prespecified testing hierarchy showed significant improvement with Korsuva as compared with placebo. The active agent significantly improved itch-related quality of life as compared with placebo as measured by the total scores on the 5-D itch scale ($p < 0.001$) and the Skindex-10 scale ($p < 0.001$).

U.S. Food and Drug Administration (FDA)

This section is to be used for informational purposes only. FDA approval alone is not a basis for coverage.

Korsuva is a kappa opioid receptor agonist indicated for the treatment of moderate-to-severe pruritus associated with chronic kidney disease (CKD-aP) in adults undergoing hemodialysis (HD).

Limitation of Use: Korsuva has not been studied in patients on peritoneal dialysis and is not recommended for use in this population.

References

1. Korsuva [prescribing information]. Stamford, CT; Cara Therapeutics, Inc.; April 2024.
2. Fishbane S, Jamal A, Munera C, Wen W, Menzaghi F; KALM-1 Trial Investigators. A Phase 3 Trial of Difelikefalin in Hemodialysis Patients with Pruritus. n Engl J Med. 2020;382(3):222-232.
3. Topf J, Wooldridge T, McCafferty K, et al. Efficacy of Difelikefalin for the Treatment of Moderate to Severe Pruritus in Hemodialysis Patients: Pooled Analysis of KALM-1 and KALM-2 Phase 3 Studies. Kidney Med. 2022;4(8):100512.

Policy History/Revision Information

Date	Summary of Changes

07/01/2026	**Template Update**
	• Transferred content to shared policy template that applies to both UnitedHealthcare Commercial and Individual Exchange benefit plans
	• Added *Application* section to indicate this policy applies to:
	  ○ UnitedHealthcare Commercial benefit plans
	  ○ Individual Exchange benefit plans
	Applicable Codes
	• Added list of applicable ICD-10 diagnosis codes: L29.89 and 29.9
	Supporting Information
	• Archived previous policy versions 2025D0115E and IEXD0115.06

Instructions for Use

This Medical Benefit Drug Policy provides assistance in interpreting UnitedHealthcare standard benefit plans. When deciding coverage, the member specific benefit plan document must be referenced as the terms of the member specific benefit plan may differ from the standard plan. In the event of a conflict, the member specific benefit plan document governs. Before using this policy, check the member specific benefit plan document and any applicable federal or state mandates. UnitedHealthcare reserves the right to modify its policies and guidelines as necessary. This Medical Benefit Drug Policy is provided for informational purposes. It does not constitute medical advice.

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This Medical Benefit Drug Policy may also be applied to Medicare Advantage plans in certain instances. In the absence of a Medicare National Coverage Determination (NCD), Local Coverage Determination (LCD), or other Medicare coverage guidance, CMS allows a Medicare Advantage Organization (MAO) to create its own coverage determinations, using objective evidence-based rationale relying on authoritative evidence (Medicare IOM Pub. No. 100-16, Ch. 4, §90.5).

UnitedHealthcare may also use tools developed by third parties, such as the InterQual® criteria, to assist us in administering health benefits. UnitedHealthcare Medical Benefit Drug Policies are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice.

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