difelikefalin (Korsuva™)

Policy # 00807
Original Effective Date: 10/10/2022
Current Effective Date: 10/14/2024

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc.(collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on review of available data, the Company may consider the use of difelikefalin (Korsuva™)‡ for the treatment of moderate to severe pruritus associated with chronic kidney disease to be **eligible for coverage.****

Patient Selection Criteria

Coverage eligibility for difelikefalin (Korsuva) will be considered when the following criteria are met:

Initial (12 weeks)

- Patient has a diagnosis of moderate to severe pruritus associated with chronic kidney disease; AND
- Pruritus is not caused by a primary dermatologic condition (e.g., psoriasis, contact dermatitis, scabies); AND
- Patient is undergoing hemodialysis; AND
- Patient is NOT undergoing peritoneal dialysis; AND
- Patient is 18 years of age or older; AND
- Administration of difelikefalin (Korsuva) will occur at the end of hemodialysis session; AND
- Dose will not exceed 0.5 mcg/kg of body weight per hemodialysis session; AND

- Patient has tried and failed (e.g., intolerance or inadequate response) at least ONE oral antihistamine (e.g., diphenhydramine or hydroxyzine) unless there is clinical evidence or patient history that suggest the use of these products will be ineffective or cause an adverse reaction to the patient; AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary ** if not met)*
- Patient has tried and failed (e.g., intolerance or inadequate response) at least ONE generic gabapentinoid (e.g., gabapentin or pregabalin) unless there is clinical evidence or patient history that suggest the use of these products will be ineffective or cause an adverse reaction to the patient.
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary ** if not met)*

Continuation (1 year)

- Patient has received an initial authorization for difelikefalin (Korsuva); AND
- Patient has had a positive clinical response (e.g., reduction in severity of itching from baseline) to difelikefalin (Korsuva) as determined by the prescriber; AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary ** if not met)*
- Dose will not exceed 0.5 mcg/kg of body weight per hemodialysis session.

When Services Are Considered Not Medically Necessary

Based on review of available data, the Company considers the use of difelikefalin (Korsuva) when the patient has not tried and failed at least ONE oral antihistamine to be **not medically necessary.****

Based on review of available data, the Company considers the use of difelikefalin (Korsuva) when the patient has not tried and failed at least ONE generic gabapentinoid to be **not medically necessary.****

Based on review of available data, the Company considers the continued use of difelikefalin (Korsuva) when the patient has not had a clinical response to be **not medically necessary.****

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When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers the use of difelikefalin (Korsuva) when patient selection criteria are not met (except those denoted above as **not medically necessary.****) to be **investigational.***

Background/Overview

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). It is administered as an intravenous bolus injection into the venous line of the dialysis circuit at the end of each hemodialysis treatment. The recommended dose of Korsuva is 0.5 mcg/kg, and it is to be administered at the end of the HD session. Korsuva is not recommended in patients who are on peritoneal dialysis.

Chronic kidney disease-associated pruritus (CKD-aP), also known as uremic pruritus, is a condition that causes chronic itching at varying degrees of severity. The itching may be generalized or be specific to a certain area of the body such as the back, face, or arms. The exact cause of this condition is unknown, but there are several hypotheses that have been proposed. One mechanism by which CKD-aP occurs is thought to be immunologic, as patients with this condition have been observed to have increased inflammatory markers such as helper T cells, C-reactive protein, and interleukin-6 and decreased albumin levels. It is also thought that an imbalance between the mu and kappa opioid receptors plays a role in CKD-aP. In this hypothesis, there is increased mu-receptor activation and kappa-receptor blockade. Mast cell release of histamine is also considered to be a contributing factor to CKD-aP. Management of this condition has not been formally established in treatment guidelines as there is a lack of strong supportive evidence on the current therapies utilized. Optimal dialysis dosing and evaluation and treatment of hyperparathyroidism, hyperphosphatemia, and hypermagnesemia is encouraged prior to initiating therapies for CKD-aP. These therapies often include topical emollients, topical analgesics, phototherapy, oral antihistamines, montelukast, gabapentin, or pregabalin. Korsuva is the first drug to be approved for this condition.

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FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)
Korsuva was approved in August of 2021 for the treatment of moderate to severe pruritus associated with chronic kidney disease (CKD-aP) in adults undergoing hemodialysis (HD).

Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, technology evaluation centers, reference to federal regulations, other plan medical policies, and accredited national guidelines.

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”).

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. In trial 1, the percentage of subjects with greater than or equal to 4-point improvement from baseline in WI-NRS score was 40% in subjects who received Korsuva compared to 21% of subjects who received placebo. In trial 2, the percentages were 37% and 26%, respectively.

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References

1. Korsuva [package insert]. Cara Therapeutics. Stamford, Connecticut. Updated August 2021.
2. Treatment Update: Chronic Kidney Disease-Associated Pruritus. IPD Analytics. PDF file. Published November 2021.
3. Uremic pruritus. UpToDate. Accessed August 2022.
4. Nephrology: Uremic Pruritus. IPD Analytics. www.secure.ipdanalytics.com. Accessed August 2022.

Policy History

Original Effective Date: 10/10/2022
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09/01/2022	Medical Policy Committee review
09/14/2022	Medical Policy Implementation Committee approval. New policy.
09/07/2023	Medical Policy Committee review
09/13/2023	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
09/05/2024	Medical Policy Committee review
09/11/2024	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.

Next Scheduled Review Date: 09/2025

Coding

The five character codes included in the Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines are obtained from Current Procedural Terminology (CPT®)‡, copyright 2023 by the American Medical Association (AMA). CPT is developed by the AMA as a listing of descriptive terms and five character identifying codes and modifiers for reporting medical services and procedures performed by physician.

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CPT is a registered trademark of the American Medical Association.

Codes used to identify services associated with this policy may include (but may not be limited to) the following:

Code Type	Code
CPT	No code
HCPCS	J0879
ICD-10 Diagnosis	All related Diagnoses

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
    1. Consultation with technology evaluation center(s);

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2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
3. Reference to federal regulations.

**Medically Necessary (or "Medical Necessity") - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

A. In accordance with nationally accepted standards of medical practice;
B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, "nationally accepted standards of medical practice" means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

‡ Indicated trademarks are the registered trademarks of their respective owners.

NOTICE: If the Patient's health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.

NOTICE: Federal and State law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage.