

remibrutinib (Rhapsido®)**Policy # 00959**

Original Effective Date: 04/01/2026

Current Effective Date: 04/01/2026

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.

Investigational or experimental services are not covered. This includes any drug, device, procedure, or service provided under the investigational arm of a clinical trial or clinical study. These services are excluded from coverage under benefits.

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 remibrutinib (Rhapsido®)[†] for the treatment of chronic spontaneous urticaria to be **eligible for coverage**.^{**}

Patient Selection Criteria

Coverage eligibility for remibrutinib (Rhapsido) for the treatment of chronic spontaneous urticaria will be considered when the patient selection criteria are met:

Initial

- Patient has a diagnosis of chronic spontaneous urticaria (defined by the presence of itchy hives that last for at least 6 weeks, with or without angioedema, and have no apparent external trigger); AND
- Patient is 18 years of age or older; AND
- Patient remains symptomatic despite at least 6 weeks of treatment with standard therapeutic doses of a second-generation H1 antihistamine (e.g., cetirizine 10 mg, levocetirizine 5 mg, fexofenadine 180 mg); AND
- Patient has tried and failed (e.g., intolerance or inadequate response) one of the following step-up measures unless there is clinical evidence or patient history that suggests these measures will be ineffective or cause an adverse reaction to the patient:
 - Addition of a different second-generation H1 antihistamine
 - Addition of an H2 antagonist
 - Addition of a first-generation H1 antihistamine at bedtime
 - Addition of a leukotriene receptor antagonist; 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.)*

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- Patient has tried and failed (e.g., intolerance or inadequate response) at least 3 to 6 months of therapy with omalizumab (Xolair®)[‡] or dupilumab (Dupixent®)[‡], unless there is clinical evidence or patient history that suggests 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.)*
- The requested medication will NOT be used in combination with omalizumab (Xolair) or dupilumab (Dupixent).

Continuation

- Patient has received an initial authorization for the requested medication; AND
- The requested medication will NOT be used in combination with omalizumab (Xolair) or dupilumab (Dupixent); AND
- Patient has responded to Rhapsido therapy as determined by the prescribing physician (e.g., reduction in exacerbations, itch severity, hives).
*(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.)*

When Services Are Considered Not Medically Necessary

Based on review of available data, the Company considers the use of remibrutinib (Rhapsido) when the patient has not tried and failed one of the following step-up measures to be **not medically necessary**.**

- Addition of a different second-generation H1 antihistamine
- Addition of an H2 antagonist
- Addition of a first-generation H1 antihistamine at bedtime
- Addition of a leukotriene receptor antagonist

Based on review of available data, the Company considers the use of remibrutinib (Rhapsido) when the patient has not tried and failed at least 3 to 6 months of therapy with omalizumab (Xolair) or dupilumab (Dupixent) to be **not medically necessary**.**

Based on review of available data, the Company considers the use of remibrutinib (Rhapsido) when the patient has not responded to Rhapsido therapy as determined by the prescribing physician (e.g., reduction in exacerbations, itch severity, hives) to be **not medically necessary**.**

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 remibrutinib (Rhapsido) when the patient selection criteria are not met (EXCEPT those denoted as **not medically necessary****) to be **investigational**.*

Based on review of available data, the Company considers the use of remibrutinib (Rhapsido) for any non-FDA approved indication to be **investigational**.*

Background/Overview

Rhapsido is an oral, small-molecule Bruton's tyrosine kinase (BTK) inhibitor approved for the treatment of chronic spontaneous urticaria (CSU) in adults who remain symptomatic despite H1 antihistamine therapy. BTK is a key intracellular signaling protein expressed in mast cells and basophils, among other immune cells, and plays an important role in Fc-receptor-mediated activation and degranulation. By inhibiting BTK, Rhapsido reduces mast cell and basophil degranulation and the downstream release of histamine and other proinflammatory mediators that contribute to urticaria symptoms. Rhapsido is administered orally at a recommended dose of 25 mg twice daily and is supplied as 25 mg tablets. Treatment interruption is recommended in the perioperative setting due to bleeding risk, and use of live or live-attenuated vaccines should be avoided during therapy.

Chronic spontaneous urticaria is a mast cell-driven inflammatory skin disorder characterized by the recurrent appearance of hives, angioedema, or both for more than six weeks without an identifiable trigger. Diagnosis is primarily clinical and based on patient history and physical examination, with assessment of symptom severity, disease activity, and impact on quality of life; routine extensive diagnostic testing is not generally required. CSU may persist for years with periods of remission and relapse and is associated with substantial impairment due to chronic pruritus, sleep disturbance, and functional limitations. International guidelines recommend a stepwise approach beginning with second-generation H1 antihistamines at standard doses, followed by dose escalation up to four times the standard dose if symptoms persist, and subsequent add-on therapy with biologic agents such as omalizumab (Xolair), an anti-immunoglobulin E monoclonal antibody that is FDA approved for CSU. In contrast, although U.S. guidelines from the American Academy of Allergy, Asthma & Immunology and the American College of Allergy, Asthma & Immunology have not been updated since 2014, they allow for greater flexibility earlier in treatment, including the addition of other antihistamines, leukotriene receptor antagonists, or sedating antihistamines before biologic therapy. dupilumab (Dupixent), an interleukin-4 receptor alpha antagonist, is also FDA approved for CSU and represents an additional add-on option for patients with inadequate response to antihistamines. Across guidelines, the overarching goals of CSU management are complete symptom control (urticaria activity score over 7 days of 0), prevention of angioedema, improvement in quality of life, and minimization of treatment-related adverse effects.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

Rhapsido was approved in September 2025 for the treatment of chronic spontaneous urticaria in adult patients who remain symptomatic despite H1 antihistamine treatment.

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 regulations, other plan medical policies, and accredited national guidelines.

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Rhapsido demonstrated clinically meaningful efficacy in adults with chronic spontaneous urticaria (CSU) inadequately controlled on second-generation H1 antihistamines based on two identical Phase III, randomized, double-blind, placebo-controlled trials, REMIX-1 and REMIX-2. The studies enrolled adults 18 years of age or older with a CSU diagnosis for at least 6 months who had persistent symptoms despite antihistamine therapy, defined as itch and hives for ≥ 6 consecutive weeks prior to screening and moderate-to-severe disease at baseline (urticaria activity score over 7 days [UAS7] ≥ 16 , itch-severity score over 7 days [ISS7] ≥ 6 , and hives-severity score over 7 days [HSS7] ≥ 6); patients with other forms of chronic urticaria or other chronic pruritic skin diseases were excluded. Patients were randomized 2:1 to Rhapsido 25 mg twice daily or placebo for 24 weeks in addition to a stable background second-generation H1 antihistamine. The primary endpoint was change in UAS7 from baseline to Week 12. In REMIX-1 (n = 462), the least-squares mean change in UAS7 at Week 12 was -20.0 with Rhapsido versus -13.8 with placebo (P < 0.001), with 31.1% of Rhapsido-treated patients achieving complete response (UAS7 = 0) compared with 10.5% on placebo. In REMIX-2 (n = 450), the least-squares mean change in UAS7 at Week 12 was -19.4 with Rhapsido versus -11.7 with placebo (P < 0.001), and complete response was achieved in 27.9% versus 6.5% of patients, respectively. Across both studies, Rhapsido also produced significantly greater improvements in itch (ISS7) and hives (HSS7) scores, a higher proportion of patients achieved well-controlled disease (UAS7 ≤ 6), symptom improvement was observed as early as Week 1, and efficacy was sustained through the 24-week treatment period and in 52-week extension data, including in patients with prior anti-immunoglobulin E therapy and those with baseline angioedema.

References

1. Rhapsido [package insert]. Novartis Pharmaceuticals Corporation. East Hanover, New Jersey. Updated September 2025.
2. Rhapsido Drug Evaluation. Express Scripts. Updated October 2015.
3. Chronic spontaneous urticaria: Standard management and patient education. UpToDate. Accessed February 2026.

Policy History

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03/05/2026 Medical Policy Committee review

03/11/2026 Medical Policy Implementation Committee approval. New policy.

Next Scheduled Review Date: 03/2027

*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

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- 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);
 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.

NOTICE: If an authorization for an ongoing course of treatment has been provided to a member and the member changes from one health plan to another health plan (e.g., a member moves from carrier A to Louisiana Blue), Louisiana Blue may honor the previous health plan’s authorization for the same service under the same type of in-network benefit for a 90-day transition period.

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Documentation of the authorization for the ongoing course of treatment from the previous health plan must be provided to us by the member or their provider and the services provided for the course of treatment must otherwise be a covered service under the Louisiana Blue health plan. This provision does not apply to medications covered under the plan's pharmacy benefit.