Effective Date: 05/30/2026
Current Effective Date: 05/30/2026
Last P&T Approval/Version: 04/29/2026
Next Review Due By: 04/2027
Policy Number: C30610-A

Rhapsido (remibrutinib)

PRODUCTS AFFECTED

Rhapsido (remibrutinib)

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:
Chronic spontaneous urticaria

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. CHRONIC SPONTANEOUS URTICARIA:
   1. Documented diagnosis of Chronic Spontaneous Urticaria (CSU) as evidenced by the presence of urticaria (hives) that has been continuously or intermittently present for more than 6 weeks
      AND

2. Documented baseline score from an objective clinical evaluation tool [e.g., Urticaria Control Test (UCT), Urticaria Activity Score (UAS7), Angioedema Activity Score (AAS), Dermatology Life Quality Index (DLQI), Angioedema Quality of Life (AE-QoL), or Chronic Urticaria Quality of Life Questionnaire (CU-Q2oL) [DOCUMENTATION REQUIRED]
   AND
3. Documentation that member continues to experience hives associated with itching despite adequate, adherent trials (minimum 2 weeks) of ALL of the following treatments (See Appendix 2) (Reference: AAAAI/ACAAI guideline on diagnosis and management acute and chronic urticaria [J Allergy Clin Immunol 2014 May;133(5):1270] see BACKGROUND) [DOCUMENTATION REQUIRED of trial/failure with dates of therapy]:
   (a) Two different H1-antihistamines at the maximally tolerated doses (up to 4 times standard daily dose), unless medically contraindicated as monotherapy
   MOLINA REVIEWER NOTE: If denying for prior utilization at high doses, please enter override for antihistamine quantity limits
   AND
   (b) One H1-antihistamine IN COMBINATION with leukotriene receptor antagonist (LTRA) at the maximally tolerated doses (up to 4 times standard daily dose), unless medically contraindicated
   AND
   (c) One H1-antihistamine at the maximally tolerated doses (up to 4 times standard daily dose) in combination with ANY of the following: H2-Antihistamines OR an anti-inflammatory agent (e.g., dapsone, hydroxychloroquine, sulfasalazine) OR an immunosuppressant agent (e.g., cyclosporine, mycophenolate), unless medically contraindicated
   AND
4. Documentation that Rhapsido (remibrutinib) is not being used concurrently with anticoagulants (e.g., warfarin, edoxaban, rivaroxaban, apixaban)
   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 Rhapsido (remibrutinib) include: No labeled contraindications. Avoid concomitant use of Rhapsido with strong or moderate CYP3A4 modulators (inhibitors or inducers). Avoid use of live vaccines with Rhapsido.]
   AND
6. 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.

CONTINUATION OF THERAPY:

A. CHRONIC SPONTANEOUS URTICARIA:
   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 improvement from baseline using objective clinical evaluation tools [e.g., Urticaria Control Test (UCT), Urticaria Activity Score (UAS7), Angioedema Activity Score (AAS), Dermatology Life Quality Index (DLQI), Angioedema

Quality of Life (AE- QoL), or Chronic Urticaria Quality of Life Questionnaire (CU- Q2oL)]. [DOCUMENTATION REQUIRED]
AND

4. Prescriber attests a recent review of member's current medication has been completed and there is no concomitant use of anticoagulants (e.g., warfarin, edoxaban, rivaroxaban, apixaban)
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 Rhapsido (remibrutinib) include: No labeled contraindications. Avoid concomitant use of Rhapsido with strong or moderate CYP3A4 modulators (inhibitors or inducers). Avoid use of live vaccines with Rhapsido.]

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 allergist, immunologist, or dermatologist. [If prescribed in consultation, consultation notes must be submitted with initial request and reauthorization requests]

AGE RESTRICTIONS:
18 years of age and older

QUANTITY:
25 mg twice daily

PLACE OF ADMINISTRATION:
The recommendation is that oral medications in this policy will be for pharmacy benefit coverage and patient self-administered.

DRUG INFORMATION

ROUTE OF ADMINISTRATION:
Oral

DRUG CLASS:
Immunomodulators - BTK Inhibitors

FDA-APPROVED USES:
Indicated for the treatment of chronic spontaneous urticaria (CSU) in adult patients who remain symptomatic despite H1 antihistamine treatment.
Limitations of Use: Not indicated for other forms of urticaria.

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 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:
Dermatology Life Quality Index (DLQI): A self-administered 10-item questionnaire that rates the impact of skin disease on symptoms and feelings, daily activities, leisure, work and school, personal relationships, and treatment. The average completion time of 2 minutes. The DLQI may be used for routine clinical use by clinicians in order to assist the clinical consultation, member evaluation and monitoring and to help with clinical decision-making process.

Urticaria Activity Score (UAS): A member reported urticaria measure which captures intensity of pruritus and number of hives. Daily intensity of pruritus, or ISS – Itch Severity Score (range: 0 = none to 3 = severe) and number of hives rating, or HHS – Hive Severity Score (range: 0 = none to 3 = more than 12 hives) are summed over a week to create the UAS7 (range: 0 to 42) score.

APPENDIX 2:
First generation H1 antihistamine: hydroxyzine, cyproheptadine
Second generation H1 antihistamine: cetirizine, levocetirizine, fexofenadine, loratadine, desloratadine
Leukotriene receptor antagonist (LTRA): montelukast (Singulair), zafirlukast (Accolate), zileuton (Zyflo)
H2-Antihistamines: cimetidine (Tagamet), famotidine (Pepcid), nizatidine (Axid), ranitidine (Zantac)

BACKGROUND AND OTHER CONSIDERATIONS

BACKGROUND:
Chronic spontaneous urticaria (CSU) is characterized by recurrent pruritic wheals (hives), angioedema, or both, lasting for ≥6 consecutive weeks in the absence of an identifiable external trigger. CSU was previously known as chronic idiopathic urticaria (CIU).

Almost all patients with CSU will experience hives/urticaria (>90%), though over 10% of patients may only experience angioedema. CSU can come with daily or almost daily symptoms or an intermittent/recurrent course and may recur after full remission. CSU is typically self-limiting, lasting 3–5 years on average, but it can last for more than 5 years in over 10% of patients. Although CSU is not life-threatening in most cases,

the unpredictability and chronicity of symptoms substantially impair health-related quality of life (QOL).

The main drivers of CSU involve activation of skin mast cells and basophil degranulation with subsequent release of histamine and other inflammatory mediators, but its pathophysiology is heterogeneous.

CSU is primarily diagnosed clinically, based on a characteristic history of recurrent hives and/or angioedema for ≥6 weeks without a consistent, inducible trigger. Based on the patient's history and physical exam, further tests may be used to exclude diseases that mimic CSU (e.g. urticarial vasculitis, bradykinin-mediated angioedema) and identify any relevant nonspecific aggravating factors (e.g. non-steroidal anti-inflammatory drugs [NSAIDs], infections, stress).

The goal of treatment is to achieve complete disease control, improve QOL, and prevent recurrence. These goals may be more difficult in patients with higher disease burden, a longer disease course, or with comorbid CSU.

Second-generation (2G) H1-antihistamines (H1-AHs) are the cornerstone treatment in CSU; however, more than one-half of patients do not respond adequately to these agents. In 2014, Xolair (omalizumab), became the first targeted therapy FDA-approved for CSU. In April 2025, Dupixent (dupilumab), became the second targeted agent for CSU. Both Xolair and Dupixent are indicated for patients ≥12 years of age with CSU who remain symptomatic despite H1-AH treatment.

Current CSU guidelines developed by the Joint Task Force on Practice Parameters (JTFPP), representing the American Academy of Allergy, Asthma & Immunology (AAAAI); ACAAI; and Joint Council of Allergy, Asthma & Immunology (published in May 2014) predate Dupixent's approval for CSU. These guidelines recommend a stepwise approach with a 2G H1-AH at an FDA-approved ('standard') dose as first line therapy (e.g. cetirizine, levocetirizine, loratadine, desloratadine, fexofenadine). If the response is inadequate, then the dose can be increased up to four times the standard dose. After 2–4 weeks, if the response remains inadequate, the addition of Xolair is generally the next step recommended. Short courses of oral corticosteroids may be used for acute exacerbations but not as chronic therapy because of their safety profile.

The 2022 CU guideline recommends the UCT PROM to help guide treatment decisions. A UCT score of <12 indicates uncontrolled disease and the need for treatment escalation; 12–15 indicates well-controlled disease and continuing the current regimen is recommended with routine monitoring; 16 indicates complete control and eligibility for step-down therapy if the patient is symptom-free for 3–6 months (based on individual factors).

In September 2025, Rhapsido (remibrutinib) was approved for the treatment of adults with CSU who remain symptomatic despite H1-AH therapy. Rhapsido is the first oral targeted therapy and the first Bruton's tyrosine kinase inhibitor (BTKi) approved for CSU. Inhibition of the BTK pathway reduces histamine release and proinflammatory mediators from mast cells and basophils, targeting the underlying mechanism of CSU.

The efficacy of Rhapsido for CSU was evaluated in two identically designed Phase 3 clinical trials: REMIX-1 (NCT05030311) and REMIX-2 (NCT05032157). The trials enrolled a total of 925 adults with CSU (≥6 months duration) inadequately controlled despite treatment with 2G H1-AHs (either standard dose or up to four times the standard dose). Inadequate disease control was defined as the presence of itch and hives for ≥6 consecutive weeks prior to screening despite the use of 2G H1-AHs during this time, as well as UAS7 ≥16, ISS7 ≥6, and HSS7 ≥6 for 7 days prior to randomization.

Results from REMIX-1 and REMIX-2 demonstrated that Rhapsido outperformed placebo in efficacy across subgroups, categorized by baseline age, gender, body mass index, CSU duration, previous experience of angioedema at baseline, disease severity, prior use of 2G H1-AHs at a licensed dose and up to four times the standard dose, and prior use of Xolair for CSU.

Rhapsido is generally well tolerated and requires no laboratory monitoring. Rhapsido should be avoided in patients with hepatic impairment (Child-Pugh Class A, B, or C) due to a risk of increased systemic exposure.

The label for Rhapsido includes a bleeding risk warning, but no severe bleeding events have been reported in clinical trials to date.

Safety data from REMIX-1 and REMIX-2 evaluated bleeding-related adverse drug reactions (ADRs) through Week 24 in patients treated with Rhapsido versus placebo. The reported bleeding ADRs in Rhapsido-treated patients included petechiae (3.8%), contusion (2.1%), ecchymosis (1.5%), hematuria (1.0%), epistaxis (0.8%), purpura (0.8%), conjunctival bleeding/hemorrhage (0.3%), and 0.2% for each of the following: gingival bleeding, hematoma, hemorrhagic ovarian cyst, intermenstrual bleeding, and urinary occult blood positive. No severe bleeding reactions were observed, and bleeding events were not associated with decreased platelet counts. Discontinuation due to bleeding occurred in 0.5% of patients on Rhapsido and none on placebo. Safety findings were consistent through Week 52.

Chronic Spontaneous Urticaria:
In 2014, the Joint Task Force on Practice Parameters (JTFPP), representing the American Academy of Allergy, Asthma & Immunology (AAAAI); the American College of Allergy, Asthma & Immunology (ACAAI); and the Joint Council of Allergy, Asthma & Immunology updated the practice parameter for the diagnosis and management of acute and chronic urticaria (CU). The practice parameter established a step-care approach to the treatment of chronic urticaria and angioedema. The task force recommended the following step-care treatment approach:

- Monotherapy with second-generation antihistamines: H1-antagonists are effective in the majority of patients with CU but might not achieve complete control in all patients.

- Dose advancement of H1-antihistamine therapy, combining first- and second-generation agents and adding an H2-antihistamine and/or an antileukotriene agent: Higher doses of second-generation antihistamines can provide greater efficacy when control is not achieved with conventional doses of these agents.

- Therapeutic trial of potent antihistamine (e.g., hydroxyzine or doxepin): First-generation antihistamines should be prescribed cautiously in the elderly or patients with occupations (e.g., machine operators, airline pilots, or alpine skiers) for which alertness is essential.

- Add an immunosuppressant or biologic agent: Omalizumab and cyclosporine have the greatest published experience documenting efficacy in patients with CU compared with all other alternative agents. The EAACI/GA2LEN/EDF/AAAAI/WAO Guideline for the Management of Urticaria include Xolair in combination with H1-antihistamines as a third line treatment option in patients who have failed to respond to higher doses of H1-Antihistamines.

The Joint Task Force on Practice Parameters representing various American allergy organizations include biologics in combination with H1-antihistamines as a fourth line treatment option following a stepwise approach starting with a second-generation antihistamine. This is followed by one or more of the following: a dose increases of the second-generation antihistamine, or the addition of another second- generation antihistamine, H2-antagonist, LTRA, or first-generation antihistamine. Treatment with hydroxyzine or doxepin can be considered in patients whose symptoms remain poorly controlled. Dupixent was not yet FDA approved for urticaria at the time of this publication.

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:
All other uses of Rhapsido (remibrutinib) are considered experimental/investigational and therefore, will follow Molina's Off- Label policy. Contraindications to Rhapsido (remibrutinib) include: No labeled contraindications.

Avoid concomitant use of Rhapsido with strong or moderate CYP3A4 inhibitors. Avoid concomitant use of Rhapsido with strong or moderate CYP3A4 inducers. Avoid use of Rhapsido in patients with mild, moderate or severe hepatic impairment (Child-Pugh Class A, B, and C). Avoid live or live-attenuated vaccines in patients receiving Rhapsido.

Exclusions/Discontinuation:
Interrupt treatment with Rhapsido (remibrutinib) if bleeding is observed or pre- and post-surgery. Concomitant use of antithrombotic agents with Rhapsido may further increase risk of bleeding.

OTHER SPECIAL CONSIDERATIONS:
Swallow tablets whole. Do not split, crush, or chew Rhapsido (remibrutinib).

Bleeding can occur with the use of Rhapsido. Consider the risks and benefits of concomitant use of antithrombotic agents with Rhapsido. Interrupt treatment Rhapsido for 3 to 7 days pre- and post surgery depending upon the type of surgery and the risk of bleeding.

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:
Rhapsido TABS 25MG

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SUMMARY OF REVIEW/REVISIONS	DATE
NEW CRITERIA CREATION	Q1 2026