Clinical Policy: Remibrutinib (Rhapsido)

Reference Number: CP.PHAR.756
Effective Date: 12.01.25
Last Review Date: 11.25
Line of Business: Commercial, HIM, Medicaid Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Remibrutinib (Rhapsido®) is a Bruton's tyrosine kinase inhibitor.

FDA Approved Indication(s)

Rhapsido is indicated for the treatment of chronic spontaneous urticaria (CSU) in adult patients who remain symptomatic despite H1 antihistamine treatment.

Limitation(s) of use: Not indicated for other forms of urticaria.

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results, or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Rhapsido is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Chronic Spontaneous Urticaria (must meet all)**:**

1. Diagnosis of CSU;
2. Prescribed by or in consultation with a dermatologist, immunologist, or allergist;
3. Age ≥ 18 years;
4. One of the following (a or b):
   a. For Illinois HIM requests only: Failure of one antihistamine at maximum indicated doses used for ≥ 2 weeks, unless clinically significant adverse effects are experienced or all are contraindicated;
   b. For all other requests: Failure of both of the following, unless clinically significant adverse effects are experienced or all are contraindicated (i and ii):
      i. Two antihistamines (including one second generation antihistamine – e.g., cetirizine, levocetirizine, fexofenadine, loratadine, desloratadine) at maximum indicated doses, each used for ≥ 2 weeks;
      ii. A leukotriene modifier (LTRA) in combination with an antihistamine at maximum indicated doses for ≥ 2 weeks;
5. Rhapsido is not prescribed concurrently with Dupixent® or Xolair®;
6. Dose does not exceed 50 mg (2 tablets) per day.

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Chronic Spontaneous Urticaria (must meet all)
1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B)*;
2. Member is responding positively to therapy;
3. Rhapsido is not prescribed concurrently with Dupixent or Xolair;
4. If request is for a dose increase, new dose does not exceed 50 mg (2 tablets) per day.

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line

of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

CSU: chronic spontaneous urticaria
FDA: Food and Drug Administration
LTRA: leukotriene modifier

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Antihistamines		
hydroxyzine (Vistaril®)	Adult: 25 mg PO TID to QID Age ≥ 6 years: 50 mg-100 mg/day in divided doses	Adult: Will vary according to condition Age ≥ 6 years: 50 mg-100 mg/day in divided doses
diphenhydramine (Benadryl®)	Adult: 25 mg to 50 mg PO TID to QID Pediatric: 12.5 mg to 25 mg PO TID to QID or 5 mg/kg/day or 150 mg/m²/day	Adult: Will vary according to condition Children: 300 mg/day
chlorpheniramine (Aller-Chlor®)	IR: 4 mg PO every 4 to 6 hours ER: 12 mg PO every 12 hours	Do not exceed 24 mg/day
cetirizine (Zyrtec®)	5 mg to 10 mg PO QD	10 mg/day
levocertirizine (Xyzal®)	2.5 mg to 5 mg PO QD	5 mg/day
loratadine (Claritin®)	10 mg PO QD	10 mg/day
desloratadine (Clarinex®)	5 mg PO QD	Will vary according to condition
fexofenadine (Allegra®)	60 mg PO BID or 180 mg QD	180 mg/day
LTRAs		
montelukast (Singulair®)	4 to 10 mg PO QD	10 mg per day
zafirlukast (Accolate®)	10 to 20 mg PO BID	40 mg per day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
zileuton ER (Zyflo® CR)	1,200 mg PO BID	2,400 mg per day
Zyflo® (zileuton)	600 mg PO QID	2,400 mg per day

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings
None reported

Appendix D: General Information
- CSU is classified as spontaneous onset of wheals, angioedema, or both, for more than 6 weeks due to an unknown cause.
- Clinical studies have shown that remibrutinib significantly improved the signs and symptoms of CSU compared to placebo in patients who had remained symptomatic despite the use of approved dose of H1-antihistamine. Approximately 30% of patients in these studies had previous anti-IgE biologic exposure.
- Remibrutinib for CSU is not currently included in clinical guideline treatment algorithms.
  - The 2014 Joint Task Force on Practice Parameters representing various American allergy organizations include omalizumab 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 increase 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.
  - The EAACI/GA2LEN/EDF/AAAAI/WAO Guideline for the Management of Urticaria include omalizumab 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 use of over-the-counter H1-antihistamines may not be a benefit to the treatment of CSU. Credit will be given for their use, but will not be covered under plan.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
CSU	25 mg PO BID	50 mg/day

VI. Product Availability
Tablet: 25 mg

VII. References
1. Rhapsido Prescribing Information. East Hanover, NJ: Novartis Pharmaceutical Corporation; September 2025. Available at: www.rhapsido.com. Accessed October 7, 2025.
2. Metz M, Giménez-Arnau A, Hide M, et al. Remibrutinib in chronic spontaneous urticaria. N Engl J Med. 2025; 392(10): 984-994. doi:10.1056/NEJMoa2408792.

3. Fine LM, Bernstein JA. Guideline of chronic urticaria beyond. Allergy Asthma Immunol Res. 2016 September; 8(5): 396-403.
4. Zuberbier T, Aberer W, Asero R, et al. The EAACI/GA(2) LEN/EDF/WAO guideline for the definition, classification, diagnosis, and management of urticaria (2018 revision). Allergy. 2018; 73: 1393-1414.
5. Zuberbier T, Abdul Latiff AH, Abuzakouk M, et al. The international EAACI/GA²LEN/EuroGuiDerm/APAAACI guideline for the definition, classification, diagnosis, and management of urticaria. Allergy. 2022 Mar; 77(3): 734-766.
6. Bernstein JA, Lang DM, Khan DA, et al. The diagnosis and management of acute and chronic urticaria: 2014 update. J Allergy Clin Immunol. 2014; 133(5); 1270-1277.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	10.07.25	11.25

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions, and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members, and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.