remibrutinib (Rhapsido®)

EOCCO POLICY

Policy Type: PA/SP Pharmacy Coverage Policy: EOCCO338

Description

Remibrutinib (Rhapsido) is an orally administered Bruton tyrosine kinase (BTK) inhibitor.

Length of Authorization

- Initial: Six months
- Renewal: 12 months

Quantity Limits

Product Name	Indication	Dosage Form	Quantity Limit
remibrutinib (Rhapsido)	Chronic spontaneous urticaria (CSU)	25 mg tablets	60 tablets/30 days

Initial Evaluation

I. **Remibrutinib (Rhapsido)** may be considered medically necessary when the following criteria are met:
   A. Member is 18 years of age or older; **AND**
   B. Medication is prescribed by, or in consultation with, an allergist/immunologist or a dermatologist; **AND**
   C. Medication is not used in combination with another monoclonal antibody (e.g., omalizumab [Xolair], dupilimab [Dupixent]); **AND**
   D. A diagnosis of **chronic idiopathic urticaria/chronic spontaneous urticaria (CIU/CSU); AND**
   E. Underlying cause of the member's condition is not considered to be any other allergic condition(s) or other form(s) of urticaria; **AND**
   F. Member is avoiding triggers (e.g., NSAIDs, etc.); **AND**
   G. Member had an inadequate response to a minimum 2-week trial of a second-generation H1-antihistamine product (e.g., cetirizine, loratadine); **AND**
      1. Member had an inadequate response to a minimum 2-week trial on at least one of the following:
         i. Updosing/dose advancement (up to 4-fold) of a second generation H1-antihistamine (e.g., cetirizine, loratadine)
         ii. A different second generation H1-antihistamine (e.g., fexofenadine, desloratadine); **OR**
      2. Member had an inadequate response to a minimum one month on at least one of the following:
         i. Add-on therapy with a leukotriene antagonist (e.g., montelukast, zafirlukast, etc.)
         ii. Add-on therapy with a H2-antagonist (e.g. ranitidine, etc.)
         iii. Add-on therapy with cyclosporine; **AND**

H. Treatment with omalizumab (Xolair)* or dupilumab (Dupixent)* has been ineffective, not tolerated, or contraindicated.

*Please note: medications notated with an asterisk may require additional review.

II. Remibrutinib (Rhapsido) is considered investigational when used for all other conditions, including but not limited to:
   A. Chronic inducible urticaria
   B. Relapsing multiple sclerosis
   C. Generalized myasthenia gravis
   D. Sjorgen's Syndrome
   E. Hidradenitis Suppurative
   F. Allery to peanuts

Renewal Evaluation

I. Member has received a previous prior authorization approval for this agent through this health plan or has been established on therapy from a previous health plan; **AND**
II. Member is not continuing therapy based off being established on therapy through samples, manufacturer coupons, or otherwise. If they have, initial policy criteria must be met for the member to qualify for renewal evaluation through this health plan; **AND**
III. Member has exhibited improvement or stability of disease symptoms (e.g., decreased itch severity, decreased number of hives or decreased size of hives, etc.) **AND**
IV. Medication is not used in combination with another monoclonal antibody (e.g., omalizumab (Xolair), dupilimab (Dupixent)).

Supporting Evidence

I. The safety and efficacy of remibrutinib (Rhapsido) has not been established in patients aged <18 years at this time.
II. Assessment and management of chronic spontaneous urticaria (CSU) requires expert guidance to differentiate from other forms of urticaria. Remibrutinib (Rhapsido) should be prescribed by, or in consultation with, a specialist such as an allergist/immunologist or a dermatologist.
III. There is a lack of evidence supporting treatment with dual biologic therapies and a potential for increased risk of side effects.
IV. Chronic idiopathic urticaria and chronic spontaneous urticaria (CIU/CSU) are used interchangeably and refer to the same condition. Chronic spontaneous urticaria is the preferred term and has relapsed chronic idiopathic urticaria as it acknowledges that the condition occurs without a consistent external trigger and often has an autoimmune or mast-cell driven mechanism.
V. Per the EAACI/GA²LEN/EDF/WAO guidelines for the definition, classification, diagnosis, and management of urticaria, first line treatment for CSU is a 2nd generation H1-antihistamine. If there is inadequate control or response, then it is recommended to increase the 2nd generation

H1-antihistamine dose up to 4x the standard dose. If there is no adequate response to the high dose 2nd generation H1-antihistamine after 2-4 weeks, then adding omalizumab (Xolair) 300 mg every 4 weeks is recommended. If needed, guidelines endorse increasing omalizumab (Xolair) dose or shortening interval up to 600mg every 2 weeks. If symptoms persist, cyclosporine is recommended to be added. The guidelines also state that H2-antihistamines (e.g. ranitidine) and leukotriene receptor antagonist (e.g. montelukast) may be alternative treatment options for certain clinical scenarios. Given different pharmacokinetic/pharmacodynamic parameters associated with different 2nd generation antihistamines (e.g., differences in half-life, different tissue penetration), a trial of a second different 2nd generation antihistamine is also a reasonable approach to treatment.

VI. Treatment with omalizumab (Xolair) or dupilumab (Dupixent) represent cost-effective alternatives to remibrutinib (Rhapsido) and are required to be tried and failed first, unless contraindicated. REMIX-1 and REMIX-2 studies demonstrated efficacy for remibrutinib (Rhapsido) in anti-IgE refractory patients, which comprised roughly 30% of the treatment population. Additionally, studies evaluating superiority of one agent vs another are not available at this time and are currently underway (NCT06042478, NCT06868212).

VII. The efficacy and safety of remibrutinib (Rhapsido) in the treatment of chronic spontaneous urticaria (CSU) is supported by REMIX-1 and REMIX-2 Phase 3, double-blind, randomized, clinical trials in 925 adults diagnosed with CSU inadequately controlled despite treatment with H1 antihistamines. All patients enrolled had moderate to severe urticaria, defined by a weekly Urticaria Activity Score (UAS7) of ≥16. The majority were female (65%) and White (52%), followed by Asian (40%). The mean weekly hives severity score (HSS7) was 16, and the itch severity score (ISS7) was 15, both indicating severe disease. Approximately half of the patients had angioedema, and 30% had prior exposure to anti-IgE biologics. The co-primary endpoints were the change from baseline in ISS7 and HSS7 at Week 12. Both co-primary endpoints demonstrated statistically significant results. The remibrutinib (Rhapsido) arm improved ISS7 by -9.5 points vs placebo -6.9 points, $p<0.0001$ in REMIX-1. Similar results were attained in REMIX-2. The two co-primary endpoints were validated to assess improvements in itch severity and hive count among patients with chronic spontaneous urticaria (CSU). The results are considered clinically meaningful, as both ISS7 and HSS7 scores met the minimal clinically important difference (MCID) threshold of approximately 5 points. Remibrutinib (Rhapsido) demonstrates a generally well-tolerated safety profile, with adverse effects that are milder compared to currently available BTK inhibitors (e.g., ibrutinib [Imbruvica]). The most common adverse events (AEs) were nasopharyngitis, bleeding (petechiae, contusion, ecchymosis), headache, nausea, and abdominal pain. Serious adverse events were rare, with comparable rates between treatment groups (3% for remibrutinib [Rhapsido] vs 2% for placebo).

Investigational or Not Medically Necessary Uses

I. Remibrutinib (Rhapsido) has not been FDA-approved, or sufficiently studied for safety and efficacy for the conditions or settings listed below:
   A. Chronic inducible urticaria

i. A Phase 3 placebo-controlled study in patients with CINDU is underway with primary completion in 2026. Results have not been disclosed at this time (NCT05976243).

B. Relapsing multiple sclerosis
   i. A Phase trial 3 study evaluating remibrutinib (Rhapsido) vs teriflunomide is currently underway with an estimated completion in 2030 (NCT05156281).

C. Generalized myasthenia gravis
   i. A Phase 3 study evaluating remibrutinib (Rhapsido) vs placebo in adults who are stable on standard of care is currently underway with an estimated completion in 2028 (NCT06744920).

D. Sjorgen's Syndrome
   i. A Phase 2 clinical trial has been completed, showing lack of benefit in patient reporter outcomes. A confirmatory Phase 3 trial is required to validate benefit.

E. Hidradenitis Suppurative
   i. A Phase 3 trial is currently underway which aims to establish efficacy of remibrutinib (Rhapsido) in this patient population. The estimated completion is 2028 (NCT06840392).

F. Allery to peanuts
   i. A Phase 2 trial (NCT05432388) has been completed at this time. A phase 3 trial with additional participants and longer assessment time is required.

References

1. Rhapsido product dossier. Novartis Pharmaceuticals; October 2025.
2. Rhapsido. Package Insert. Novartis Pharmaceuticals; September 2025.
3. 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;77(3):734-766. doi:10.1111/all.15090
4. 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. doi:10.1016/j.jaci.2014.02.036
5. 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

Related Policies

Policies listed below may be related to the current policy. Related policies are identified based on similar indications, similar mechanisms of action, and/or if a drug in this policy is also referenced in the related policy.

Policy Name	Disease state
omalizumab (Xolair)	Chronic spontaneous urticaria, allergic asthma, chronic rhinosinusitis with nasal polyposis, IgE-mediated Food Allergy, Systemic mastocytosis
dupilumab (Dupixent)	Chronic spontaneous urticaria, asthma, atopic dermatitis, chronic rhinosinusitis with nasal polyposis, prurigo nodularis, eosinophilic esophagitis, chronic obstructive pulmonary disease, bullous pemphigoid.

Policy Implementation/Update:

Action and Summary of Changes	Date
Policy created	02/2026