Clinical Policy: Rilzabrutinib (Wayrilz)

Reference Number: CP.PHAR.751
Effective Date: 12.01.25
Last Review Date: 11.26
Line of Business: Commercial, HIM/ICHRA, Medicaid Revision Log

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

Description

Rilzabrutinib (Wayrilz™) is Bruton's tyrosine kinase (BTK) inhibitor.

FDA Approved Indication(s)

Wayrilz is indicated for the treatment of adult patients with persistent or chronic immune thrombocytopenia (ITP) who have had an insufficient response to a previous treatment.

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 Wayrilz is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Immune Thrombocytopenia (must meet all)**:**

1. Diagnosis of persistent or chronic ITP (*see Appendix D*);
2. Prescribed by or in consultation with a hematologist;
3. Age ≥ 18 years;
4. One of the following (a or b):
   a. Current (within 30 days) platelet count < 30,000/µL;
   b. Member has an active bleed;
5. Failure of a systemic corticosteroid, unless contraindicated or clinically significant adverse effects are experienced (*see Appendix B*);
6. Failure of eltrombopag (generic Promacta®), unless contraindicated or clinically significant adverse effects are experienced;*
   **For Illinois HIM requests, the step therapy requirements above do not apply as of 1/1/2026 per IL HB 5395*
7. Wayrilz is not prescribed concurrently with rituximab, a thrombopoietin receptor agonist (e.g., Doptelet®, Promacta, Mulpleta®, Nplate®), or spleen tyrosine kinase inhibitor (e.g., Tavalisse™);
8. Dose does not exceed 800 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/ICHRA) 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/ICHRA, and CP.PMN.255 for Medicaid; or
b. For drugs NOT on the formulary (commercial, health insurance marketplace/ICHRA) 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/ICHRA, 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/ICHRA, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Immune Thrombocytopenia (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 (e.g., increase in platelet count from baseline, reduction in bleeding events);
3. Wayrilz is not prescribed concurrently with rituximab, a thrombopoietin receptor agonist (e.g., Doptelet, Promacta, Mulpleta, Nplate), or spleen tyrosine kinase inhibitor (e.g., Tavalisse);
4. If request is for a dose increase, new dose does not exceed 800 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/ICHRA) 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/ICHRA, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace/ICHRA) 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/ICHRA, 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/ICHRA, 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/ICHRA, and CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

ASH: American Society of Hematology
BTK: Bruton's tyrosine kinase
FDA: Food and Drug Administration
ITP: immune thrombocytopenia

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
Immune Thrombocytopenia		
eltrombopag (Promacta)	50 mg PO QD Adjust to maintain platelet count ≥ 50,000/µL.	75 mg/day
Corticosteroids*		
dexamethasone	Varies	Highly variable depending on the nature and severity of the disease, route of treatment, and on patient response
methylprednisolone		
prednisone		

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.
**Examples of corticosteroids/immunosuppressive agents provided are not all inclusive*

Appendix C: Contraindications/Boxed Warnings

None reported

Appendix D: General Information

- Definitions of ITP (newly diagnosed, persistent, and chronic):
  - Per an International Working Group consensus panel of ITP experts, ITP is defined as newly diagnosed (diagnosis to 3 months), persistent (3 to 12 months from diagnosis), or chronic (lasting for more than 12 months). These definitions are supported and used by the American Society of Hematology (ASH).

- Per the 2019 ASH guidelines, response to treatment was defined by the following:
  - A response is defined as a platelet count ≥ 30,000/µL and a greater than 2-fold increase in platelet count from baseline measured on 2 occasions > 7 days apart and the absence of bleeding.
  - A failure is defined as a platelet count < 30,000/µL or a less than 2-fold increase in platelet count from baseline or the presence of bleeding. Platelet count must be measured on 2 occasions more than a day apart.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
ITP	400 mg PO BID	800 mg/day

VI. Product Availability

Tablet: 400 mg

VII. References

1. Wayrilz Prescribing Information. Cambridge, MA: Genzyme; August 2025. Available at: https://www.wayrilz.com/us. Accessed July 8, 2026.
2. Kuter DJ, Ghanima W, Cooper N, et al. Safety and efficacy of rilzabrutinib vs placebo in adults with immune thrombocytopenia: the phase 3 LUNA3 study. Blood. 2025;145(24):2914-2926.
3. Neunert CE, Arnold DM, Grace RF, et al. The 2022 review of the 2019 American Society of Hematology guidelines on immune thrombocytopenia. Blood Adv. 2024;8(13):3578-3582.
4. Neunert C, Terrell DR, Arnold DM, et al. American Society of Hematology 2019 guidelines for immune thrombocytopenia. Blood Adv. 2019; (3)23:3829-3866.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	09.09.25	11.25
Per December SDC, added redirection to generic Promacta for ITP, removed redirection to immune globulin if intolerant or contraindicated to systemic corticosteroid.	12.04.25	02.26
4Q 2026 annual review: no significant changes; added ICHRA line of business; references reviewed and updated.	07.08.26	11.26

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.

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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.

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