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Policy Number: C30341-A

Wayrilz (rilzabrutinib)

PRODUCTS AFFECTED

Wayrilz (rilzabrutinib)

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 immune thrombocytopenia (ITP)

REQUIRED MEDICAL INFORMATION:
This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. 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 along with state and federal requirements, benefit being administered and formulary preferencing. 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.

A. CHRONIC IMMUNE THROMBOCYTOPENIA (ITP):

Drug and Biologic Coverage Criteria

1. Documented diagnosis of chronic immune thrombocytopenia (ITP)
   AND
2. Documentation of ONE of the following [DOCUMENTATION REQUIRED]:
   a) Platelet count less than 30 $\times 10^9$/L (30,000/mm³)
      OR
   b) Platelet count between 30 x 10^9/L to 50 x 10^9/L with symptomatic bleeding or whose degree of thrombocytopenia and clinical condition(s) increase the risk of bleeding (e.g., peptic ulcer disease, hypertension, renal insufficiency, concomitant antiplatelet agents or anticoagulant medications, liver disease, infections, undergoing a medical or dental procedure with blood loss anticipation, recent surgery, head trauma)
   AND
3. Documented failure, serious side effects, or contraindication to at least ONE of the following ITP treatments:
   a) Corticosteroids (i.e., prednisone, methylprednisolone, dexamethasone) at immunosuppressive doses (See Appendix)
      OR
   b) Intravenous immune globulin (IVIG)
      OR
   c) Immunosuppressive therapy (i.e., cyclosporine, mycophenolate mofetil, sirolimus)
      OR
   d) Has had splenectomy or is not a surgery candidate
   AND
4. Documentation of ONE of the following:
   a) Wayrilz (rilzabrutinib) is not being used concurrently with a thrombopoietic agent [e.g., Doptelet (avatrombopag), eltrombopag, Nplate (romiplostim)] or spleen tyrosine kinase inhibitor [e.g., Tavalisse (fostamatinib)]
      OR
   b) Inadequate treatment response to thrombopoietin receptor agonist
   AND
5. 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 IMMUNE THROMBOCYTOPENIA (ITP):

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 (e.g., hepatotoxicity, etc.)
   AND
3. Documentation of positive clinical response as demonstrated by increase in platelet count between 30 x 10^9/L and less than 50 $\times$ 10^9/L and doubled from baseline OR increase of platelet count to greater than or equal to 50 x 10^9/L

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 hematologist or physician specializing in the treatment of thrombocytopenia in patients with chronic ITP [If prescribed in consultation, consultation notes must be submitted with initial request and reauthorization requests]

AGE RESTRICTIONS:
18 years of age and older

QUANTITY:
400 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 CLAS:
Bruton's Tyrosine Kinase (BTK) Inhibitors

FDA-APPROVED USES:
Indicated for the treatment of adult patients with persistent or chronic immune thrombocytopenia (ITP) who have had an insufficient response to a previous treatment

COMPENDIAL APPROVED OFF-LABELED USES:
None

APPENDIX

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)
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:
Systemic corticosteroid immunosuppressive doses include:
≥ 14 days therapy with doses ≥ 80 mg per day of prednisone.
Equivalent doses include:
- ≥ 400mg/day cortisone
- 320mg/day hydrocortisone
- 80mg/day prednisolone
- 64mg/day methylprednisolone
- 12mg/day dexamethasone

BACKGROUND AND OTHER CONSIDERATIONS

BACKGROUND:
Immune thrombocytopenia (ITP) is a hematological disease in which the body's immune system produces antibodies that destroy its functioning platelets. Primary ITP is when the etiology of disease is unknown. Secondary causes of ITP include H. pylori infection, certain drugs, bone marrow transplantation, vaccinations, HIV, Hepatitis C, cytomegalovirus, and more. Persistent ITP is defined as symptoms present for 3 to 12 months, while chronic ITP is defined as symptoms present for ≥12 months. Normal platelet counts typically range from 150 × 10^9/L to 400 × 10^9/L, but clinically significant bleeding does not usually occur unless the count drops below 50 × 10^9/L.

Treatment of ITP can be initiated in the event of severe bleeding. Patients receive intravenous immune globulin (IVIG)/anti-D and/or corticosteroids with the goal of raising the platelet count. Patients with minor or no bleeding may not require treatment, but are more likely to receive treatment in cases where platelet counts are very low in combination with other risk factors (i.e. older age, nonsteroidal anti-inflammatory drug [NSAID] use, prior bleeding events).

For patients who are unresponsive to or dependent on corticosteroids, second-line therapies include splenectomy and thrombopoietin receptor agonists (TPO-RAs), including eltrombopag, Doptelet (avatrombopag), and Nplate (romiplostim). Splenectomy offers a one-time treatment option, but

includes risks of infection and blood clots. Robust data support the use of TPO-RAs, but they are required to be taken continuously. Rituximab and its biosimilars are occasionally used off-label despite immunosuppressive effects, offering an option where patients are dosed once weekly for 4 weeks and do not require continuous treatment if a durable response is achieved.

Tavalisse (fostamatinib) is a twice-daily oral prodrug of a tyrosine kinase inhibitor that inhibits spleen tyrosine kinase (SYK) and is indicated for treatment of adults with chronic ITP who have had an insufficient response to a previous treatment. Tavalisse can be used as a primary second-line therapy or in a later line of therapy after a TPO-RA or rituximab. In some cases, immunosuppressants (e.g. azathioprine, mycophenolate mofetil, and cyclosporine) may be used, sometimes in combination with ITP therapies such as TPO-RAs, for patients who are unresponsive to multiple lines of therapy.

The safety and efficacy of Wayrilz (rilzabrutinib) in adult patients with primary persistent or chronic ITP was evaluated in a randomized, double-blind (DB), placebo-controlled, parallel-group study consisting of 24 weeks of blinded treatment followed by an open-label (OL) period [LUNA-3 Study (NCT04562766)]. Patients received an initial 12 weeks of DB period treatment. Those who achieved platelet count response at 12 weeks were eligible to continue the full 24-week DB period. The patients enrolled in this study had an unsustained response to either intravenous immunoglobulin (IVIg/anti-D) or corticosteroid (CS) or had a documented intolerance or insufficient response to any appropriate course of standard-of-care ITP therapy.

Patients were randomized to receive Wayrilz 400 mg or placebo. Concomitant ITP medicines [oral CS and/or thrombopoietin receptor agonist (TPO-RA)] were allowed at stable doses at least 2 weeks before the start of the study and throughout the DB period.

During the first 12 weeks of the DB period, 85 (63.9%) patients and 22 (31.9%) patients in the Wayrilz group and placebo group, respectively, achieved platelet count response (50×10^9/L or between 30×10^9/L and $<50 \times 10^9$/L and doubled from baseline). Those who achieved platelet count response were eligible to continue the DB period.

The efficacy of Wayrilz was based on durable platelet response. A durable platelet response was defined as a weekly platelet count 50×10^9/L for two-thirds of at least 8 non-missing weekly scheduled platelet measurements during the last 12 weeks of the 24-week DB period in the absence of rescue therapy, provided that at least 2 non-missing weekly scheduled platelet measurements were 50×10^9/L during the last 6 weeks of the DB period.

Wayrilz met the primary endpoint of the trial, with 23.3% of patients who received Wayrilz achieving a durable platelet response at Week 24 compared to 0% of patients who received placebo ($P < 0.0001$). In addition, patients who received Wayrilz experienced a faster time to first platelet response and longer duration of platelet response than those who received placebo.

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

Avoid administration of rilzabrutinib in patients with moderate or severe hepatic impairment (Child-Pugh class B-C) because of potential for increased rilzabrutinib exposures.

Avoid concomitant use of rilzabrutinib with strong or moderate CYP3A inhibitors. Avoid concomitant use of rilzabrutinib with strong or moderate CYP3A inducers.

Exclusions/Discontinuation:
If Drug-Induced Liver Injury (DILI) is suspected, withhold Wayrilz (rilzabrutinib). Upon confirmation of DILI, discontinue rilzabrutinib.

Based on data from animal reproduction studies, exposure to Wayrilz (rilzabrutinib) may cause fetal harm when administered to a pregnant woman. For female patients of reproductive potential, verify pregnancy status prior to initiating rilzabrutinib, and advise using effective contraception during treatment and for 1 week after stopping treatment.

OTHER SPECIAL CONSIDERATIONS:
Hepatotoxicity, including severe, life-threatening, and potentially fatal cases of drug-induced liver injury, may occur in patients treated with Bruton tyrosine kinase (BTK) inhibitors, including Wayrilz (rilzabrutinib). Evaluate bilirubin and transaminases at baseline and as clinically indicated during treatment.

Patients treated with BTK inhibitors, including Wayrilz (rilzabrutinib), may experience an increased risk of serious infections (including bacterial, viral, or fungal); a fatal case of pneumonia occurred in a patient treated with rilzabrutinib in clinical trials. Other serious infections occurred rarely, including COVID-19 infection, wound infection, urinary tract infection, and kidney abscess. Monitor patients for signs and symptoms of infection, evaluate promptly, and treat.

Concomitant use of grapefruit, starfruit and products containing these fruits, and Seville oranges with Wayrilz (rilzabrutinib) is not recommended, as these are moderate and strong inhibitors of CYP3A.

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:
Wayrilz TABS 400MG

REFERENCES

1. Wayrilz (rilzabrutinib) tablets, for oral use [prescribing information]. Cambridge, MA: Genzyme

Corporation; August 2025.
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3. Kuter, D. J., Arnold, D. M., Bussel, J. B., Cuker, A., Mayer, J., Chong, B. H., ... & Newland, A. C. (2025). Safety and efficacy of rilzabrutinib vs placebo in adults with immune thrombocytopenia: The Phase 3 LUNA3 study. Blood, 145(24), 2914–2926. https://doi.org/10.1182/blood.2024027336
4. Liu, X., Zhao, Y., Wang, Y., Zhang, Y., & Hou, M. (2023). How we treat primary immune thrombocytopenia in adults. Journal of Hematology & Oncology, 16(4). https://doi.org/10.1186/s13045-023-01401-z
5. National Organization for Rare Disorders. (2022, July 12). Immune thrombocytopenia. https://rarediseases.org/rare-diseases/immune-thrombocytopenia/
6. Neunert, C., Terrell, D. R., Arnold, D. M., Buchanan, G., Cines, D. B., Cooper, N., ... & Vesely, S. K. (2019). American Society of Hematology 2019 guidelines for immune thrombocytopenia. Blood Advances, 3(23), 3829–3866. https://doi.org/10.1182/bloodadvances.2019000966; https://doi.org/10.1182/bloodadvances.2019001380

SUMMARY OF REVIEW/REVISIONS	DATE
NEW CRITERIA CREATION	Q4 2025