New Drug Overview

Wayrilz (rilzabrutinib)

PDL Category: Anti-Thrombocytopenics

Introduction

Disease Background:

- Immune thrombocytopenia (ITP) is an acquired autoimmune bleeding condition depicted as immune-mediated damage of normal platelets, with lack of compensatory platelet production (*McCrae et al 2026*).
  - ITP is defined as a platelet count <100 X 10^9/L because of platelet destruction, with the lack of other reasons for thrombocytopenia.
  - The estimated prevalence is about 10-23 per 100,000 people and the estimated incidence is about 2 to 4 per 100,000 of the population globally (*Kuter et al 2025*).
  - ITP is termed as primary, secondary, or drug-induced immune thrombocytopenia (DITP) (*Arnold and Cuker 2025*).
    - Primary ITP is due to autoimmune reasons, which leads to destruction of platelets and limited platelet production not due to an associated disorder.
    - Secondary ITP is associated with a separate condition
    - DITP is because of drug-dependent platelet antibodies that results in destruction of platelets.
- While many patients with ITP may be asymptomatic, life-threatening bleed is possible (*McCrea et al 2025*).
  - The most frequent display of bleeding is mucocutaneous bleeding, including petechiae or more rarely purpura, ecchymosis, epistaxis, oral cavity/gum bleeding, menorrhagia, gastrointestinal bleeding, or hematuria.
  - Factors related to bleeding at diagnosis includes being female, exposure to NSAIDs or anticoagulants, and platelet count <20 X 10^9/L.
- Management includes treatment to increase platelet count in order to obtain adequate hemostasis, in other words to stop active bleeding and risk reduction of bleeding again (*McCrae et al 2025*).
  - Corticosteroids are generally the first-line treatment, while IV immunoglobulin (IVIG) may also be used as first-line.
  - Currently, second-line and subsequent agents may include thrombopoietin receptor agonists (TPO-RAs), rituximab, fostamatinib, and splenectomy.
- Wayrilz was FDA approved in 2025.

Pharmacology/Usage

- Wayrilz (rilzabrutinib) is a kinase inhibitor. It is a small-molecule, covalent, reversible kinase inhibitor targeting Bruton's tyrosine kinase (BTK). Rilzabrutinib mediates its therapeutic effect in immune thrombocytopenia through immune modulation including inhibition of B cell activation and interruption of antibody-coated cell phagocytosis by Fcy receptor (FcyR) in spleen and liver. In vitro, rilzabrutinib reduced autoantibody signaling mediated through the FcyR pathway, blocked B cell signaling, and decreased autoantibody generation through effects on B cell activation.

Indications

Table 1. Food and Drug Administration Approved Indications

Indication	Wayrilz (rilzabrutinib)
• For the treatment of adult patients with persistent or chronic immune thrombocytopenia (ITP) who have had an insufficient response to a previous treatment.	✔

(Prescribing information: Wayrilz 2025)

- Information on indications, mechanism of action, pharmacokinetics, dosing, safety, and clinical efficacy summary has been obtained from the prescribing information for the individual products, except where noted otherwise.

Dosing and administration

Table 2. Dosing and Administration

Drug	Available Formulations	Route	Usual Recommended Frequency	Comments
Wayrilz (rilzabrutinib)	Film-Coated Tablets	Oral	Twice daily	• Verify pregnancy status of females of reproductive potential prior to starting treatment. • Take with or without food. If experience GI symptoms, taking with food may improve tolerability. • If a dose is missed, take the missed dose as soon as possible on the same day and at least 2 hours apart from the next regular scheduled dose. • Assess bilirubin and transaminases at baseline and as clinically indicated during treatment. If develop abnormal liver tests after Wayrilz, monitor more frequently for liver test abnormalities and clinical signs/ symptoms of hepatic toxicity. If drug-induced liver injury (DILI) is suspected, withhold Wayrilz. With confirmation of DILI, discontinue Wayrilz. • Avoid use in moderate or severe hepatic impairment.

Drug	Available Formulations	Route	Usual Recommended Frequency	Comments
				• Avoid use in severe renal impairment.

See the current prescribing information for full details.

Clinical Efficacy Summary

- The safety and efficacy of Wayrilz were assessed in a randomized, double-blind (DB), placebo-controlled, parallel-group study that consisted of 24 weeks of blinded treatment followed by an open-label (OL) period (LUNA-3 Study). In this study, 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.
- Patients enrolled 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 or placebo and randomization was stratified based on prior splenectomy (yes/no) and severity of thrombocytopenia (platelet count $<15 \times 10^9$/L or $\geq 15 \times 10^9$/L). Concomitant ITP medicines (oral CS and/or TPO-RA) were allowed at stable doses at least 2 weeks before the start of the study and throughout the DB period.
- At baseline, the median age of included patients was 47 years (range 18 to 80), while 63% were female and 62% were Caucasian. In addition, at baseline 93% of patients had chronic ITP (ie, for 1 year or longer), with a median time since ITP diagnosis of 7.69 years. Furthermore, 28% had undergone splenectomy, the median platelet count was 15.3×10^9/L (with 48% less than 15×10^9/L), and the median number of prior therapies, including splenectomy, was 4. Prior ITP treatments varied, with the most common prior therapies being CS (96%), TPO-RAs (69%), IVIG or anti-D immunoglobulins (55%), and anti-CD20 monoclonal antibody/rituximab (35%). In addition, at baseline 66% of patients received both CS and TPO-RAs.
  - Baseline disease characteristics and demographics were generally similar across groups with the exception of sex which was 59% female in the Wayrilz group and 71% in the placebo group.
- During the DB period, the median duration of exposure was 98 days and 84 days for the Wayrilz and placebo groups, respectively. The cumulative duration of treatment exposure was 44 participant-years and 18 participant-years for the Wayrilz and placebo groups, respectively. Concomitant use of CS and/or TPO-RA with study drug occurred in 60% of the Wayrilz group and 67% of the placebo group.
- During the first 12 weeks of the DB period, 85 patients (63.9%) in the Wayrilz group and 22 patients (31.9%) in the placebo group achieved platelet count response ($\geq 50 \times 10^9$/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 $\geq 50 \times 10^9$/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 $\geq 50 \times 10^9$/L during the last 6 weeks of the DB period.
  - Efficacy results are presented in the table below, which was adapted from the prescribing information.

Table 3. Efficacy results

Study Outcomes	Statistic	Wayrilz 400mg BID (N=133)	Placebo (N=69)
Durable Platelet Response	n (%)	31 (23.3%)	0 (0%)
	95% CI	16.12, 30.49	0.00, 0.00
	Risk difference	23.1	

Study Outcomes	Statistic	Wayrilz 400mg BID (N=133)	Placebo (N=69)
	p-value	<0.0001	
Number of weeks with platelet response:			
≥50 X 10^9/L or between 30 X 10^9/L and <50 X 10^9/L and doubled from baseline	Least Square (LS) mean	7.18	0.72
	LS mean difference	6.46	
	95% CI	4.92, 7.99	
	p-value	<0.0001	
≥30 X 10^9/L and doubled from baseline	LS Mean	6.95	0.64
	LS mean difference	6.31	
	95% CI	4.79, 7.83	
	p-value	<0.0001	
Time to first Platelet Response	Median # of days to first platelet count	36	Not reached
	Hazard Ratio (HR)	3.10	
	p-value	<0.0001	

- Rescue medication was required by 33% and 58% of patients receiving Wayrilz and placebo, respectively.
  - The median time to first use of rescue therapy was not reached in the Wayrilz group and 56 days in the placebo group.
- During the OL period, 7 out of 73 patients (10%) who received Wayrilz during the DB period achieved a durable response for the first time.

Clinical guidelines

- Wayrilz has yet to be included in any guidelines as the guidelines were published prior to its approval.
- **American Society of Hematology 2019 guidelines for immune thrombocytopenia** (*Neunert et al 2019*).
  - Recommendations include:
    - When newly diagnosed with ITP, it is suggested that asymptomatic adults or with minor mucocutaneous bleeding and who have a platelet count <30 X 10^9/L use corticosteroids instead of observation.
    - Monotherapy with corticosteroids is suggested instead of rituximab plus corticosteroids as initial therapy in adults newly diagnosed with ITP.
    - If corticosteroid-dependent or not responsive to corticosteroids in adults diagnosed with ITP for ≥3 months, it is suggested to use either eltrombopag or romiplostim if it is decided to treat with a thrombopoietin receptor agonist (TPO-RA).
    - If corticosteroid-dependent or not responsive to corticosteroids in adults diagnosed with ITP for ≥3 months, it is suggested to have a splenectomy or to use a TPO-RA.
    - If corticosteroid-dependent or not responsive to corticosteroids in adults diagnosed with ITP for ≥3 months, it is suggested to use rituximab instead of splenectomy.
    - If corticosteroid-dependent or not responsive to corticosteroids in adults diagnosed with ITP for ≥3 months, it is suggested to use TPO-RA instead of rituximab.

- In newly diagnosed ITP with no or minor bleeding, it is suggested to observe instead of corticosteroid use in children, and it is recommended to observe rather than use IVIG in children.
- With non-life-threatening mucosal bleeding and/or reduced health-related quality of life in children newly diagnosed with ITP, it is recommended against corticosteroid use for more than 7 days, and it is suggested to use corticosteroids rather than IVIG.
- With non-life-threatening mucosal bleeding and/or reduced health-related quality of life in children who are not responsive to first-line treatment, it is suggested to use TPO-RAs instead of rituximab and instead of splenectomy.
- With non-life-threatening mucosal bleeding and/or reduced health-related quality of life in children who are not responsive to first-line treatment, it is suggested to use rituximab instead of splenectomy.

Safety summary

- **Contraindications:** None.

- **Box Warning:** None.

- **Warnings and precautions:**
  - An increased risk of serious infections can occur in patients treated with BTK inhibitors, including Wayrilz. Monitor patients for signs and symptoms of infection and treat appropriately.
  - Hepatotoxicity, including severe, life-threatening, and potentially fatal cases of drug-induced liver injury (DILI), can occur in patients treated with BTK inhibitors. Evaluate bilirubin and transaminases at baseline and as clinically indicated during treatment with Wayrilz. For patients who develop abnormal liver tests after Wayrilz, monitor more frequently for liver test abnormalities and clinical signs and symptoms of hepatic toxicity. If DILI is suspected, withhold Wayrilz. Upon conformation of DILI, discontinue Wayrilz.

- **Common adverse drug reactions:** Listed % incidence for adverse drug reactions= reported % incidence for drug (Wayrilz) for all grades minus reported % incidence for placebo for all grades. Please note that an incidence of 0% means the incidence was the same as or less than placebo.
  - The most frequently reported adverse events included diarrhea (22%), nausea (14%), headache (11%), abdominal pain (13%), COVID-19 (10%), arthralgia (5%), dizziness (7%), nasopharyngitis (4%), vomiting (6%), dyspepsia (5%), and cough (5%).

- **Drug interactions:**
  - Rilzabrutinib is a CYP3A substrate.
    - Avoid concomitant use of Wayrilz with strong or moderate CYP3A inhibitors. If a strong or moderate CYP3A inhibitor cannot be avoided, and these inhibitors will be used short term (such as anti-infectives for seven days or less), interrupt treatment with Wayrilz.
    - Avoid concomitant use of grapefruit, starfruit and products containing these fruits, and Seville oranges with Wayrilz, as these are moderate and strong inhibitors of CYP3A.
    - Avoid concomitant use of Wayrilz with strong or moderate CYP3A inducers.
  - Rilzabrutinib exhibits pH-dependent solubility. Acid reducing agents decrease rilzabrutinib exposure, which may reduce Wayrilz efficacy.
    - Administer the dose of Wayrilz at least 2 hours before administration of an antacid or histamine H2 receptor antagonist.
    - Avoid concomitant use of proton pump inhibitors with Wayrilz.
  - Rilzabrutinib is a moderate inhibitor of CYP3A.

    - Monitor for adverse reactions of the concurrently administered CYP3A substrate more frequently and consider dosage adjustment per the prescribing information of the CYP3A substrate.
  - Rilzabrutinib is an inhibitor of P-gp, breast cancer resistance protein (BCRP), and OATP1B in *vitro*. The effect of concomitant use of Wayrilz with OATP1B and BCRP substrates has not been established in clinical trials. However, based on *in vitro* inhibitory potential, concomitant use of Wayrilz may increase the risk of adverse reactions related to these substrates.
    - Monitor for adverse reactions of the concurrently administered P-gp, BCRP, or OATP1B substrate more frequently, unless otherwise recommended in the substrate prescribing information, when Wayrilz is used concomitantly with P-gp, BCRP, or OATP1B substrates where minimal substrate concentration changes may lead to serious adverse reactions.

- **Special populations:**
  - There is no pregnancy category for this medication; however, the risk summary indicates that based on animal data, Wayrilz may cause fetal harm when administered to a pregnant woman. There are no available clinical data on use during pregnancy to assess for a drug-associated risk of major birth defects, miscarriage, or other adverse maternal or fetal outcomes. Advise pregnant women of the potential risk to a fetus.
    - Verify the pregnancy status of females of reproductive potential prior to starting treatment.
      - Advise females of reproductive potential to use effective contraception during Wayrilz treatment and for 1 week after stopping treatment.
  - The safety and efficacy of use in the pediatric population have not been established.

Conclusion

- Immune thrombocytopenia (ITP) is an acquired autoimmune bleeding condition depicted as immune-mediated damage of normal platelets, with lack of compensatory platelet production (*McCrae et al 2026*).
- Wayrilz is a kinase inhibitor indicated for the treatment of adult patients with persistent or chronic immune thrombocytopenia (ITP) who have had an insufficient response to a previous treatment.
- Its efficacy was assessed in a randomized, double-blind, placebo-controlled, parallel-group study followed by an open-label period.
  - During the first 12 weeks of the double-blind period, 85 patients (63.9%) in the Wayrilz group and 22 patients (31.9%) in the placebo group, achieved platelet count response (≥50 X 10^9/L or between 30 X 10^9/L and <50 X 10^9/L and doubled from baseline). Those who achieved platelet count response were eligible to continue the double-blind period.
  - The efficacy of Wayrilz was based on durable platelet response. A durable platelet response was defined as a weekly platelet count ≥50 X 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 X 10^9/L during the last 6 weeks of the DB period.
    - Statistically more achieved a durable platelet response in the Wayrilz group as compared with placebo ($p<0.0001$).
- Guidelines have yet to be updated to include Wayrilz. While its place in therapy it not yet known, this treatment has a new mechanism of action and is not indicated as first-line treatment.

- There is no evidence to suggest that Wayrilz is safer or more effective than other currently preferred, more cost-effective medications. It is therefore recommended that Wayrilz remain non-preferred and require prior authorization and be available to those who are unable to tolerate or who have failed on preferred medications.

- **PDL Placement:**
  - ☐ Preferred
  - ☒ Non-Preferred with Conditions

References

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- McCrae KR, Berry J, Aird W, et al. Immune thrombocytopenia (ITP) in adults. Dynamed Web site. Updated January 9, 2026. Accessed January 22, 2026. www.dynamed.com.
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