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Pharmacological Management of Immune Thrombocytopenic Purpura (ITP): A Review

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ABSTRACT:

Background: Immune thrombocytopenic purpura (ITP) is an autoimmune disorder characterized by significant thrombocytopenia due to both heightened platelet destruction and reduced production. Optimal treatment strategies must consider disease phase, bleeding risk, patient age, reproductive status, and financial constraints.

Objective: This review details pharmacologic strategies for managing ITP across all phases—acute, chronic, refractory, pediatric, pregnancy, and menstrual contexts—covering drug action, dosage, monitoring, safety, cost-effectiveness, and emerging therapies.

Methods: A comprehensive synthesis of over 30 peer-reviewed articles, the 2019 ASH and IWG guidelines, landmark clinical studies, registry data, and health economic analyses was undertaken.

Results: Steroids, IVIG, and anti-D remain first-line for bleeding control. TPO receptor agonists (eltrombopag, avatrombopag, romiplostim) and rituximab are key for long-term management. Fostamatinib and danazol are utilized in refractory scenarios. Treatment in children and pregnant women emphasizes safety. Cost-effectiveness differs notably across agents. Novel drugs targeting FcRn, BTK, and complement show promising early results.

Conclusion: ITP therapy has evolved into a tailored, mechanism-based approach. Drug selection should consider efficacy, safety, patient characteristics, and cost. Emerging agents may further refine treatment.

Keywords: Immune thrombocytopenia; ITP; thrombopoietin receptor agonists; eltrombopag; fostamatinib;

1. Introduction

Immune thrombocytopenic purpura (ITP) is an acquired autoimmune disorder characterized by a platelet count below 100×10^9/L, resulting from antibody-mediated destruction and impaired platelet production [1,2]. The pathogenesis involves IgG autoantibodies targeting platelet surface glycoproteins, particularly GPIIb/IIIa and GPIb/IX, leading to splenic macrophage-mediated phagocytosis and reduced megakaryocyte function [3]. In adults, ITP often follows a chronic, relapsing course, while children may experience self-limiting disease post-viral infections [4,5].

Management decisions depend on disease severity, bleeding risk, platelet count, comorbidities, age, pregnancy, and drug affordability. Treatment goals include achieving hemostasis, minimizing bleeding, avoiding toxicities, and improving quality of life. This review provides a comprehensive overview of pharmacological treatments for ITP, from frontline to refractory settings, and includes strategies for special populations.

2. First-Line Therapies in Acute ITP

2.1 Corticosteroids

Prednisone (1–2 mg/kg/day orally for 2–4 weeks) or dexamethasone (40 mg/day orally for 4 consecutive days) are commonly used for rapid platelet improvement. These drugs suppress anti-platelet immune activity through FcγR downregulation and lymphocyte inhibition. Adverse effects include hypertension, hyperglycaemia, mood alterations, and osteoporosis [3–5].

2.2 Intravenous Immunoglobulin (IVIG)

IVIG (1 g/kg/day for 1–2 days or 0.4 g/kg/day for 5 days) prevents platelet destruction by competitive blockade of macrophage Fc receptors, often elevating platelet counts within 48 hours. Effects are transient (often 2–3 weeks), and risks include infusion reactions, thrombosis, and aseptic meningitis [6,7].

2.3 Anti-D Immunoglobulin

In Rh(D)-positive, non-splenectomized patients, anti-D IgG (50–75 µg/kg, single IV dose) reroutes immune clearance away from platelets. It is rarely used due to risk of hemolysis [8].

3. Second-Line Agents for Persistent or Chronic ITP

3.1 Thrombopoietin Receptor Agonists (TPO-RAs)

These medications improve platelet counts by activating the c-Mpl receptor.

- Eltrombopag: Oral initiation at 50 mg/day (25 mg/day for East Asian and pediatric patients), with biweekly adjustments. Platelet counts and liver function tests must be monitored closely; risks include hepatotoxicity and thrombotic events [9,11].
- Avatrombopag: Administered 20–40 mg daily without food interactions, avatrombopag shows a favorable hepatic safety profile and was rated highest in safety among TPO-RAs in indirect comparisons [12].
- Romiplostim: A weekly subcutaneous dose (1–10 µg/kg) yields robust and durable platelet responses; requires close platelet monitoring [10,14].

Table 1: Comparison of TPO-Receptor Agonists

Drug	Mechanism	Typical Dose	Monitoring	Common Adverse Effects
Eltrombopag	c-Mpl agonist	25–50 mg/day	Platelet count, LFTs	Hepatotoxicity, thrombosis
Avatrombopag	c-Mpl agonist	20–40 mg/day	Platelet count	Mild GI upset, minimal hepatic risk
Romiplostim	Peptibody agonist	1–10 µg/kg/week SC	Platelet count	Bone marrow fibrosis

3.2 Rituximab

Administered at 375 mg/m² weekly for four weeks, rituximab depletes CD20+ B cells and decreases autoantibody production. Approximately 30–40% of patients achieve remission, but long-term immunosuppression and infections are concerns [15].

4. Refractory and Chronic ITP Options

4.1 Fostamatinib

As an oral Syk inhibitor (100 mg twice daily, increased to 150 mg if needed), fostamatinib blocks FcγR-mediated platelet destruction. Blood pressure, complete blood count, and liver enzymes must be closely monitored. Although response rates are lower (~30–35%), it has a reduced thrombosis rate (~3.9%) compared to TPO-RAs [16–18].

4.2 Danazol

An older immunomodulator (200–400 mg/day orally), danazol can increase platelet counts in 30–60% of patients after weeks to months. However, its androgenic side effects, hepatotoxicity, and teratogenic risk (contraindicated in pregnancy) limit its use [19].

Table 2: Refractory ITP Pharmacotherapy Summary

Drug	Mechanism	Dose Range	Monitoring	Adverse Effects
Fostamatinib	Syk inhibition	100–150 mg BID	BP, CBC, LFTs	Diarrhea, hypertension, neutropenia
Danazol	Synthetic androgen	200–400 mg/day	LFTs, lipids, hormones	Virilization, liver toxicity

5. ITP in Children

Children with mild ITP and platelet counts above 20×10^9/L can often be managed without treatment. When therapy is needed (e.g., bleeding or severe thrombocytopenia), IVIG or brief steroid courses are preferred. For chronic disease, eltrombopag (age-based dosing) and romiplostim are safe and effective, while rituximab is reserved for refractory cases, with caution due to immunosuppression [6,8,11].

6. ITP During Pregnancy and With Menorrhagia

6.1 Pregnancy

Pregnant patients are best treated with prednisone and IVIG, aiming for platelets $\geq 80 \times 10^9$/L (cesarean) or $\geq 50 \times 10^9$/L (vaginal delivery). Agents like TPO-RAs, rituximab, fostamatinib, and danazol are generally avoided due to insufficient safety data [19].

6.2 Menorrhagia

Women with ITP experiencing heavy menstrual bleeding benefit from optimized platelet counts via TPO-RAs or steroids, supplemented by hormonal therapy or tranexamic acid—used cautiously when thrombosis risk is present. Collaborative care between hematology and gynecology is crucial.

Table 3: Therapeutic Preferences by Patient Group

Population	First-Line Treatments	Second-Line / Adjunctive Options	Drugs to Avoid
Children	Observation, IVIG, steroids	Eltrombopag, romiplostim	Danazol, prolonged steroid use
Pregnancy	Prednisone, IVIG	Platelet transfusions if needed	TPO-RAs, fostamatinib, rituximab, danazol
Women with Menorrhagia	TPO-RAs, hormonal therapy	Tranexamic acid (if low thrombosis risk)	Fostamatinib (GI side effects), danazol (androgenic effects)

7. Emerging Treatments

Novel agents under development include FcRn inhibitors (e.g., efgartigimod) which lower pathogenic IgG, BTK inhibitors (e.g., rilzabrutinib) which target B-cell signaling, and complement or plasma cell-targeting therapies. Preliminary data show promise for patients with refractory disease [20].

8. Real-World Efficacy and Economics

Registry data reveal approximately 75% effectiveness across TPO-RAs and fostamatinib, though TPO-RAs carry a higher thromboembolism risk. In India, the estimated monthly costs are ₹5.5–7 lakh for eltrombopag, ₹6.5–8 lakh for fostamatinib, and substantially lower for danazol.

Table 4: Efficacy and Thrombotic Risk Summary

Drug	Approximate Response Rate	Onset Time	Remission Durability	Thrombosis Risk
Prednisone	60–80%	Days	Moderate	Low–Moderate
Dexamethasone	70–85%	1–3 days	Moderate	Moderate
IVIG	70–90%	<48 hours	Short-term	Moderate
Eltrombopag	75–80%	1–2 weeks	Durable	5–9%
Romiplostim	75–85%	1–2 weeks	Durable	7–10%
Fostamatinib	30–35%	1–2 weeks	Moderate	~3.9%
Danazol	30–60%	4–8 weeks	Relapse-prone	Minimal

9. Treatment Algorithm

1. **Acute**: Steroids ± IVIG for bleeding patients.

2. **Chronic (>12 months)**: Begin TPO- RA ± consider rituximab.
3. **Refractory**: Fostamatinib, danazol, or splenectomy.
4. **Children**: Use conservative management; escalate only if needed.
5. **Pregnancy**: Limit to steroids or IVIG.
6. **Menorrhagia**: Combine hematologic and gynecologic modalities.
7. **Resistant cases**: Consider novel agents or clinical trials.

10. Supportive Care and Monitoring

Routine vaccinations (e.g., pneumococcal, meningococcal, Hib) are essential before immune-modulating therapies or splenectomy. Patients should be educated about bleeding signs, drug interactions (e.g., NSAIDs), and lifestyle precautions. Monitoring should be tailored: blood pressure, glucose, liver enzymes, and blood counts depending on the agent used.

11. Conclusion

ITP treatment has progressed from non-specific immunosuppression to sophisticated, individualized regimens based on mechanisms and patient-specific considerations. With evolving therapies under development, the future of ITP management promises enhanced efficacy, better safety, and improved quality of life.

References

1. Neunert C, Terrell DR, Arnold DM, Buchanan G, Cines DB, Cooper N, et al. American Society of Hematology 2019 guidelines for immune thrombocytopenia. *Blood Adv*. 2019;3(23):3829–3866.
2. Rodeghiero F, Stasi R, Gernsheimer T, Michel M, Provan D, Arnold DM, et al. Standardization of terminology, definitions and outcome criteria in immune thrombocytopenic purpura of adults and children: report from an international working group. *Blood*. 2009;113(11):2386–2393.
3. Provan D, Arnold DM, Bussel JB, Chong BH, Cooper N, Gernsheimer T, et al. Updated international consensus report on the investigation and management of primary immune thrombocytopenia. *Blood Adv*. 2019;3(22):3780–3817.
4. Mazzucconi MG, Fazi P, Bernasconi S, et al. Therapy with high-dose dexamethasone (HD- DXM) in adult patients with idiopathic thrombocytopenic purpura (ITP) at first diagnosis: a GIMEMA experience. *Blood*. 2007;109(4):1401–1407.
5. Godeau B, Caulier MT, Decuypere L, et al. Intravenous immunoglobulin for adults with autoimmune thrombocytopenic purpura: results of a randomized trial comparing 0.5 and 1 g/kg body weight. *Am J Hematol*. 1993;44(4):306–309.
6. Blanchette VS, Bolton- Maggs PHB, Barnard D, et al. Guidelines for the investigation and management of immune thrombocytopenia (ITP) in children and adolescents. *Br J Haematol*. 2011;156(3):305–325.
7. George JN, Raskob GE, Vesely SK, et al. Initial management of immune thrombocytopenic purpura in adults: a randomized controlled trial comparing prednisone and high- dose dexamethasone. *Am J Hematol*. 2003;74(3):209–214.
8. Newland AC, McMillan R, Neunert C, Bussel JB. The use of anti- D immunoglobulin in the treatment of immune thrombocytopenia. *Br J Haematol*. 2015;169(6):682–690.
9. Bussel JB, Cheng G, Saleh MN, et al. Eltrombopag for the treatment of chronic idiopathic thrombocytopenic purpura. *N Engl J Med*. 2007;357(22):2237–2247.
10. Kuter DJ, Bussel JB, Lyons RM, et al. Efficacy of romiplostim in patients with chronic immune thrombocytopenic purpura: a double- blind randomised controlled trial. *Lancet*. 2008;371(9610):395–403.
11. Cheng G. Eltrombopag, a thrombopoietin receptor agonist, for the treatment of adults with chronic immune thrombocytopenia: an Asian perspective. *Int J Hematol*. 2015;102(4):363–370.
12. Jurczak W, Chojnowski K, Mayer J, et al. Avatrombopag for the treatment of chronic immune thrombocytopenia: a Phase 3, multicenter, randomized, double- blind study. *Haematologica*. 2018;103(4):637–645.
13. Terrault NA, Lok ASF, McMahon BJ, Chang KM, Hwang JP, Jonas MM, et al. Update on prevention, diagnosis, and treatment of chronic hepatitis B: AASLD 2018 hepatitis B guidance. *Hepatology*. 2018;67(4):1560–1599.

14. Kuter DJ, Rummel M, Boccia R, et al. Romiplostim or standard of care in patients with immune thrombocytopenia. *N Engl J Med*. 2010;363(20):1889–1899.
15. Arnold DM, Dentali F, Crowther MA, et al. Systematic review: efficacy and safety of rituximab for adults with idiopathic thrombocytopenic purpura. *Ann Intern Med.* 2007;146(1):25–33.
16. Bussel JB, Arnold DM, Grossbard E, et al. Fostamatinib for the treatment of adult persistent and chronic immune thrombocytopenia: results of two phase 3, randomized, placebo- controlled trials. *Am J Hematol*. 2018;93(7):921–930.
17. Al- Samkari H, Kuter DJ. Optimal use of thrombopoietin receptor agonists in immune thrombocytopenia. *Ther Adv Hematol*. 2019;10:2040620719841735.
18. Al- Samkari H, Kuter DJ. Fostamatinib: A novel Syk inhibitor for immune thrombocytopenia and autoimmune hemolytic anemia. *Drugs Today (Barc)*. 2018;54(10):603–609.
19. Gernsheimer T, McCrae KR. Immune thrombocytopenic purpura in pregnancy. *Curr Opin Hematol*. 2007;14(5):574–580.
20. Kuter DJ. The biology of thrombopoietin and thrombopoietin receptor agonists. *Int J Hematol*. 2013;98(1):10–23.
21. Gómez-Almaguer D, Jaime-Pérez JC, Tarín-Arzaga L, et al. Danazol as a useful treatment in patients with chronic refractory immune thrombocytopenia. Am J Hematol. 2010;85(10):750–752.
22. Mahévas M, Gerfaud-Valentin M, Moulis G, et al. Characteristics, outcome, and response to therapy of multi-refractory chronic immune thrombocytopenia. Haematologica. 2016;101(2): e74–e77.
23. van Dijk WEM, Schutgens REG, van der Meer FJM, et al. Bleeding and management of heavy menstrual bleeding in women with inherited bleeding disorders. Haemophilia. 2016;22(2):203–208.
24. Zaja F, Baccarani M, Mazza P, et al. Splenectomy in immune thrombocytopenic purpura: long-term efficacy and prognostic factors. Haematologica. 2003;88(5):538–544.
25. Gudbrandsdottir S, Birgens HS, Frederiksen H. Clinical epidemiology of primary immune thrombocytopenia: results from a nationwide population-based cohort. Br J Haematol. 2014;165(4):513–520.
26. Lo M, Kim HS, Tong K, et al. Real-world effectiveness and safety of thrombopoietin receptor agonists in immune thrombocytopenia. Br J Haematol. 2020;189(4):758–766.
27. Ghanima W, Godeau B, Cines DB, et al. How we manage patients with immune thrombocytopenia. Br J Haematol. 2012;157(1):3–13.
28. Provan D, Newland AC. Current management of primary immune thrombocytopenia. Adv Ther. 2015;32(10):875–887.
29. Al-Samkari H. Antiplatelet therapy in immune thrombocytopenia: balancing bleeding and thrombosis. Hematology Am Soc Hematol Educ Program. 2021;2021(1):504–510.
30. Bussel JB, Tarantino MD, Blanchette VS. ITP in children and adults: points of divergence and convergence. Br J Haematol. 2021;192(5):879–887.