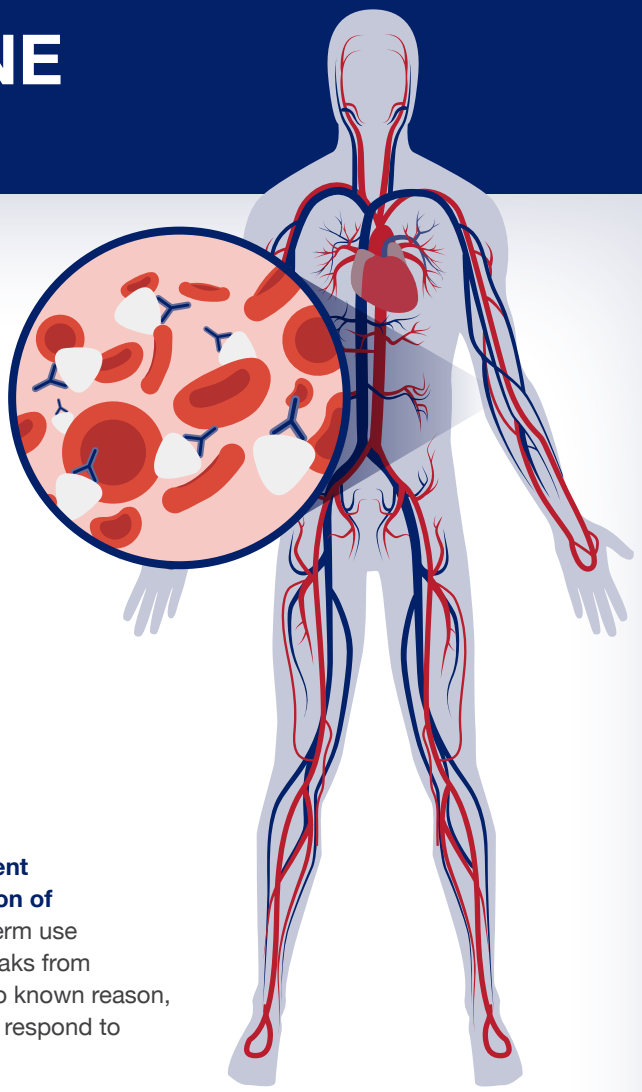
WHAT IS CHRONIC IMMUNE THROMBOCYTOPENIA?



Immune thrombocytopenia (ITP) is a rare, autoimmune, bleeding disorder[1] and is considered chronic when it has lasted more than 12 months[2]. In healthy individuals, platelets stick together (clot) to seal small cuts or breaks in blood vessel walls to stop the bleeding. In ITP, the blood doesn't clot as it should due to a low number of platelets (also known as thrombocytes).[3]

ITP is an immune mediated disease in which the primary mechanism is platelet destruction. Antibodies are produced by the immune system and attach themself to the platelets, marking them for destruction.[4] Common symptoms may include bruising, bleeding, and fatigue.[4,5] People suffering with chronic ITP live with an increased risk of bleeding events that may result in serious medical complications or even death. People living with chronic ITP do not know when their platelet counts may drop. The unpredictable nature of the condition, and the sequela of the ITP, can affect patients and their lifestyle.

Treatment Challenges in ITP

Patients need to be treated to maintain platelet counts in a range that reduces their risk of bleeding. Due to the heterogeneity of the disease, **chronic ITP can be challenging to treat because it is impossible to predict how an individual patient will respond to available treatments, and some patients may need a succession of treatments over time**. Certain treatments (such as costicosteroids) are for short term use and other treatments may be used for longer periods of time, but patients take breaks from treatment due to potential issues such as side effects and treatment fatigue. For no known reason, platelet counts can drop during or following a treatment course,[6] and patients who respond to treatment may stop responding at any time.

There can be challenges with selecting the appropriate therapy for patients when steroids fail. There are several treatment options commonly used, however ITP guidelines do not provide a recommendation regarding the sequencing of therapy for patients with persistent or chronic ITP who have progressed beyond initial treatment.

STANDARD INITIAL TREATMENT	OTHER TREATMENT OPTIONS
Corticosteroids	**TAVALISSE™** (fostamatinib disodium hexahydrate), anti-CD20, splenectomy, thrombopeietin receptor agonists (TPO-RAs), or immunosuppressants

TAVALISSE™ (fostamatinib disodium hexahydrate) Tablets

TAVALISSE™ is an oral spleen tyrosine kinase (SYK) inhibitor approved by the U.S. Food and Drug Administration (FDA) for the treatment of thrombocytopenia in adult patients with chronic ITP who have had an insufficient response to a previous treatment. The FDA approval of TAVALISSE was supported by data from the FIT clinical program, which included two randomized placebo-controlled Phase 3 trials (FIT-1 and FIT-2) and an open-label extension (FIT-3), as well as an initial proof of concept study.

TAVALISSE **inhibits spleen tyrosine kinase (SYK)**, a key component in the body's immune process that leads to platelet destruction in ITP. TAVALISSE may address the underlying autoimmune cause of ITP by preventing platelet destruction, providing an important new treatment option for those patients who do not derive a benefit from existing therapies.[6-13]

TAVALISSE offers **twice daily oral dosing** that can be taken with or without food and does not require weekly office visits.

Please see page 2 for Important Safety Information. Please see full Prescribing Information at www.tavalisse.com

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TAVALISSE™ (fostamatinib disodium hexahydrate) Tablets
Indication and Important Safety Information

Indication

TAVALISSE™ (fostamatinib disodium hexahydrate) tablets is indicated for the treatment of thrombocytopenia in adult patients with chronic immune thrombocytopenia (ITP) who have had an insufficient response to a previous treatment.

Important Safety Information

Warnings and Precautions

- Hypertension can occur with TAVALISSE treatment. Patients with pre-existing hypertension may be more susceptible to the hypertensive effects. Monitor blood pressure every 2 weeks until stable, then monthly, and adjust or initiate antihypertensive therapy for blood pressure control maintenance during therapy. If increased blood pressure persists, TAVALISSE interruption, reduction, or discontinuation may be required.
- Elevated liver function tests (LFTs), mainly ALT and AST, can occur with TAVALISSE. Monitor LFTs monthly during treatment. If ALT or AST increase to >3 x upper limit of normal, manage hepatotoxicity using TAVALISSE interruption, reduction, or discontinuation.
- Diarrhea occurred in 31% of patients and severe diarrhea occurred in 1% of patients treated with TAVALISSE. Monitor patients for the development of diarrhea and manage using supportive care measures early after the onset of symptoms. If diarrhea becomes severe (≥ Grade 3), interrupt, reduce dose or discontinue TAVALISSE.
- Neutropenia occurred in 6% of patients treated with TAVALISSE; febrile neutropenia occurred in 1% of patients. Monitor the ANC monthly and for infection during treatment. Manage toxicity with TAVALISSE interruption, reduction, or discontinuation.
- TAVALISSE can cause fetal harm when administered to pregnant women. Advise pregnant women the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment and for at least 1 month after the last dose. Verify pregnancy status prior to initiating TAVALISSE. It is unknown if TAVALISSE or its metabolite is present in human milk. Because of the potential for serious adverse reactions in a breastfed child, advise a lactating woman not to breastfeed during TAVALISSE treatment and for at least 1 month after the last dose.

Drug Interactions

- Concomitant use of TAVALISSE with strong CYP3A4 inhibitors increases exposure to the major active metabolite of TAVALISSE (R406), which may increase the risk of adverse reactions. Monitor for toxicities that may require a reduction in TAVALISSE dose.
- It is not recommended to use TAVALISSE with strong CYP3A4 inducers, as concomitant use reduces exposure to R406.
- Concomitant use of TAVALISSE may increase concentrations of some CYP3A4 substrate drugs and may require a dose reduction of the CYP3A4 substrate drug.
- Concomitant use of TAVALISSE may increase concentrations of BCRP substrate drugs (eg, rosuvastatin) and P-Glycoprotein (P-gp) substrate drugs (eg, digoxin), which may require a dose reduction of the BCRP and P-gp substrate drug.

Adverse Reactions

- Serious adverse drug reactions in the ITP double-blind studies were febrile neutropenia, diarrhea, pneumonia, and hypertensive crisis, which occurred in 1% of TAVALISSE patients. In addition, severe adverse reactions occurred including dyspnea and hypertension (both 2%), neutropenia, arthralgia, chest pain, diarrhea, dizziness, nephrolithiasis, pain in extremity, toothache, syncope, and hypoxia (all 1%).
- Common adverse reactions (≥5% and more common than placebo) from FIT-1 and FIT-2 included: diarrhea, hypertension, nausea, dizziness, ALT and AST increased, respiratory infection, rash, abdominal pain, fatigue, chest pain, and neutropenia.

Please see www.TAVALISSE.com for full Prescribing Information.

To report side effects of prescription drugs to the FDA, visit www.fda.gov/medwatch or call 1-800-FDA-1088 (1-800-332-1088).

ABOUT RIGEL

Rigel Pharmaceuticals, Inc., is a biotechnology company dedicated to discovering, developing and providing novel small molecule drugs that significantly improve the lives of patients with immune and hematologic disorders, cancer and rare diseases.

References

1. http://www.itpfoundation.org/itpdefined.htm
2. Rodeghiero F, et al. Blood. 2009;113(11):2386-2393
3. https://www.nhlbi.nih.gov/health/health-topics/topics/itp
4. http://www.mayoclinic.org/diseases-conditions/idiopathic-thrombocytopenic-purpura/home/ovc-20201208
5. Hill QA, Newland AC, British Journal of Haematology, 2015, 170, 141–149, 30 March 2015 doi: 10.1111/bjh.13385 http://onlinelibrary.wiley.com/doi/10.1111/bjh.13385/pdf
6. Cleve Clin J Med. 2011 Jun; 78(6): 358–373
7. Feudjo-tepie, M. A., Robinson, N. J. And Bennett, D. Thromb Haemost 2006; Journal of Thrombosis and Hemostasis, 6: 711–712
8. Provan D, et al. Blood. 2010;115:168-186.
9. Kuter DJ, et al. Lancet. 2008;371:395-403.
10. Cheng G, et al. Lancet. 2011;377:393-402.
11. Braselmann S, et al. J Pharmacology and Exp Ther.2006;319:998-1008.
12. Podolanczuk A, et al. Blood. 2009;113:3154-3160.
13. https://clinicaltrials.gov/ct2/show/NCT02076399?term=fostamatinib+and+ITP&rank=1&submit_fld_opt=