



Positive Quality Intervention: Fostamatinib (Tavalisse®) Use in Chronic Immune Thrombocytopenia

Description: Fostamatinib is an oral spleen tyrosine kinase (Syk) inhibitor indicated for the treatment of thrombocytopenia in adult patients with chronic immune thrombocytopenia (ITP) who have had an insufficient response to a previous treatment. ITP is mediated by platelet antibodies that accelerate platelet destruction and inhibit their production. Common treatments for ITP include corticosteroids, rituximab, IVIG, splenectomy and/or thrombopoietin receptor agonists (TPO-RA). This PQI will review appropriate use of fostamatinib in this setting.

Background: SyK signaling is central to phagocytosis based, antibody mediated platelet destruction in adults with ITP. Fostamatinib is a tyrosine kinase inhibitor with demonstrated activity against SyK. The major metabolite of fostamatinib, R406, inhibits signal transduction of Fc-activating receptors and B cell receptors, leading to decreased destruction of platelets.¹ In two parallel, phase 3, multicenter, randomized, double blind, placebo-controlled trials (FIT1 and FIT2), adult patients with chronic ITP were randomized 2:1 to fostamatinib or placebo. Fostamatinib was dosed at 100mg BID for 24 weeks with a dose increase to 150mg BID in non-responders after 4 weeks. Primary endpoint was stable response, which was defined as platelet $\geq 50,000 \times 10^9/L$ at ≥ 4 of 6 biweekly visits, weeks 14 through 24, without rescue therapy. Stable responses occurred in 18% of patients in the fostamatinib group compared to 0% in the placebo group. Post hoc endpoints also showed an overall response rate of 43% and long term extension show 54% response by line of therapy. The most common adverse events were diarrhea, hypertension, nausea, dizziness, and ALT increase.

PQI process: Upon receipt of fostamatinib:

- Confirm appropriate dosing: Typical starting dose is 100mg twice daily²
- May increase to 150mg twice daily if 100mg twice daily does not increase platelet count to $>50,000 \times 10^9/L$ after 1 month
- Use the lowest possible dose to achieve and maintain a platelet count of at least $50,000 \times 10^9/L$
- Fostamatinib may be taken with or without food. In the case of a missed dose, instruct patients to take their next dose at its regularly scheduled time
- Obtain baseline LFTs and repeat monthly throughout therapy
- Obtain baseline CBC and repeat monthly while on therapy. If ANC drops below $1.0 \times 10^9/L$ for more than 72 hours temporarily interrupt until resolved
- Monitor blood pressure (BP) every 2 weeks after starting therapy until patient is established on a stable dose, then obtain BP monthly
- Screen for drug interactions with CYP3A4 inhibitors and inducers
 - Fostamatinib is a prodrug that is metabolized into its active metabolite, R406. Co-administration of ketoconazole caused a 2-fold increase in R406 exposure, verapamil increased R406 exposure by 39% and rifampicin co-administration decreased exposure by 75%³
- Discontinue fostamatinib after 12 weeks of therapy if the platelet count does not increase to a level sufficient to avoid clinically important bleeding

Important notice: NCODA has developed this Positive Quality Intervention platform. This platform represents a brief summary of medication uses and therapy options derived from information provided by the drug manufacturer and other resources. This platform is intended as an educational aid and does not provide individual medical advice and does not substitute for the advice of a qualified healthcare professional. This platform does not cover all existing information related to the possible uses, directions, doses, precautions, warning, interactions, adverse effects, or risks associated with the medication discussed in the platform and is not intended as a substitute for the advice of a qualified healthcare professional. The materials contained in this platform are for informational purposes only and do not constitute or imply endorsement, recommendation, or favoring of this medication by NCODA, which assumes no liability for and does not ensure the accuracy of the information presented. NCODA does not make any representations with respect to the medications whatsoever, and any and all decisions, with respect to such medications, are at the sole risk of the individual consuming the medication. All decisions related to taking this medication should be made with the guidance and under the direction of a qualified healthcare professional.



Patient Centered Activities:

- Provide thorough verbal and written medication education; including, but not limited to, the [Oral Chemotherapy Education \(OCE\)](#) sheet
- Ensure the patient understands the lab schedule for follow up CBC, LFTs, and BP monitoring
- Avoid eating or drinking grapefruit and grapefruit juice while taking this medication
- If patient is of child-bearing age, review pregnancy and contraception information with them

Supplemental Information

Dose adjustments for toxicity:²

Usual maximum dose	150mg twice daily
First dose reduction	100mg twice daily
Second dose reduction	150mg once in the morning
Third dose reduction	100mg once in the morning

References:

1. Clemons Bankston P, Al-Horani RA. New small molecule drugs for thrombocytopenia: Chemical, Pharmacological, and Therapeutic Use Considerations. *Int J Mol Sci.* 2019;20(12):3013.
2. Tavalisse® (fostamatinib) [prescribing information]. South San Francisco, CA: Rigel Pharmaceuticals, Inc; April 2018.
3. Martin P, Gillen M, Millson D, et al. Effects of CYP3A4 Inhibitors Ketoconazole and Verapamil and the CYP3A4 Inducer Rifampicin on the Pharmacokinetic Parameters of Fostamatinib: Results from In Vitro and Phase I Clinical Studies. *Drugs R D.* 2016;16(1):81-92. doi:10.1007/s40268-015-0118-4.

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