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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, platelet infusion, and/or thrombopoietin receptor agonists. 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 100 mg BID for 24 weeks with a dose increase to 150 mg BID in non-responders after 4 weeks. Primary endpoint was stable response, which was defined as platelet ≥ 50,000 $x10^9$/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 100 mg twice daily[2]
- May increase to 150 mg twice daily if 100 mg twice daily does not increase platelet count to ≥50 $x10^9$/L after 1 month
- Use the lowest possible dose to achieve and maintain a platelet count of at least 50 $x10^9$/L
- In the case of a missed dose, instruct patients to take their next dose at its regularly scheduled time
- Obtain baseline LFTs and CBC and repeat monthly while on therapy
    - If ANC drops below 1.0 x 10^9/L for more than 72 hours temporarily interrupt until resolved
- Monitor blood pressure every 2 weeks until established on a stable dose, then 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]
- Dose adjustments for toxicity[2]

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

- Discontinue fostamatinib after 12 weeks of therapy if the platelet count does not increase to a level sufficient to avoid clinically important bleeding (at least 50 ×10^9/L)

Patient-Centered Activities:

- Provide Oral Chemotherapy Education (OCE) Sheet
- Fostamatinib may be taken with or without food
- 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
- Patient Assistance: NCODA Financial Assistance Tool

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].
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.