BlueCross BlueShield
Federal Employee Program

FABHALTA
(iptacopan)

RATIONALE FOR INCLUSION IN PA PROGRAM

Background

Fabhalta (iptacopan) binds to Factor B of the alternative complement pathway and regulates the cleavage of C3, generation of downstream effectors, and the amplification of the terminal pathway. In paroxysmal nocturnal hemoglobinuria (PNH), intravascular hemolysis (IVH) is mediated by the downstream membrane attack complex, while extravascular hemolysis (EVH) is facilitated by C3b opsonization. Fabhalta acts proximally in the alternative pathway of the complement cascade to control both Cb3-mediated EVH and terminal complement-mediated IVH. In primary immunoglobulin A nephropathy (IgAN), the deposition of galactose deficient IgA1 containing immune complexes in the kidney locally activates the alternative complement pathway which is thought to contribute to the pathogenesis of IgAN. In 3 glomerulopathy (C3G), overactivation of the alternative complement pathway leads to C3 cleavage within the glomeruli resulting in C3 deposition and inflammation, which are thought to contribute to the pathogenesis of C3G (1).

Regulatory Status

FDA-approved indications: Fabhalta is a complement factor B inhibitor, indicated for: (1)

- the treatment of adults with paroxysmal nocturnal hemoglobinuria (PNH).
- the reduction of proteinuria in adults with primary immunoglobulin A nephropathy (IgAN) at risk of rapid disease progression, generally a urine protein-to-creatinine ratio (UPCR) ≥1.5 g/g.
- the treatment of adults with complement 3 glomerulopathy (C3G), to reduce proteinuria.

Fabhalta has a boxed warning regarding serious infections caused by encapsulated bacteria. Fabhalta increases the risk of serious infections, especially those caused by encapsulated bacteria, such as *Streptococcus pneumoniae*, *Neisseria meningitidis*, and *Haemophilus influenzae* type B. These infections may become rapidly life-threatening or fatal if not recognized and treated early. Patients should be vaccinated against encapsulated bacteria at least 2 weeks prior to initiation of Fabhalta therapy according to current Advisory Committee on Immunization Practices (ACIP) guidelines. Patients should be monitored for early signs and symptoms of serious infections and evaluate immediately if infection is suspected. Because of the risk of serious infections caused by encapsulated bacteria, Fabhalta is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the Fabhalta REMS (1).

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Fabhalta also has warnings regarding hyperlipidemia and monitoring of PNH manifestations after Fabhalta discontinuation (1).

The safety and effectiveness of Fabhalta in pediatric patients less than 18 years of age have not been established (1).

Summary

Fabhalta is a complement factor B inhibitor indicated for the treatment of paroxysmal nocturnal hemoglobinuria (PNH), primary immunoglobin A nephropathy (IgAN), and complement 3 glomerulopathy (C3G). Fabhalta has a boxed warning citing the risk of serious infections caused by encapsulated bacteria and it is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS). The safety and effectiveness of Fabhalta in pediatric patients less than 18 years of age have not been established (1).

Prior authorization is required to ensure the safe, clinically appropriate, and cost-effective use of Fabhalta while maintaining optimal therapeutic outcomes.

References

1. Fabhalta [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; March 2025.