# PRIOR AUTHORIZATION POLICY

**POLICY:** Complement Inhibitors – Fabhalta Prior Authorization Policy
- Fabhalta® (iptacopan capsules – Novartis)

**REVIEW DATE:** 12/20/2023; selected revision 01/17/2024, 02/28/2024, 08/14/2024

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## OVERVIEW

Fabhalta, a Factor B inhibitor, is indicated for the following uses:[1]
- **Paroxysmal nocturnal hemoglobinuria** (PNH), treatment in adults.
- **Primary immunoglobulin A nephropathy** (IgAN), for the reduction of proteinuria in adults at risk of rapid disease progression, generally a urine protein-to-creatinine ratio (UPCR) ≥1.5 g/g.

Fabhalta has a Boxed Warning about serious meningococcal infections.[1] Fabhalta is only available through a restricted access program, Fabhalta Risk Evaluation and Mitigation Strategy (REMS).

## Disease Overview

### PNH

PNH is a rare, genetic disorder of hematopoietic stem cells.[2,3] The mutation in the X-linked gene phosphatidylinositol glycan class A (PIGA) results in a deficiency in the glycosylphosphatidylinositol (GPI) protein, which is responsible for anchoring other protein moieties to the surface of the erythrocytes. Loss of anchoring of these proteins causes cells to hemolyze and leads to complications such as hemolytic anemia, thrombosis, and peripheral blood cytopenias. PNH is a clinical diagnosis that should be confirmed with peripheral blood flow cytometry to detect the absence or severe deficiency of GPI-anchored proteins on at least two lineages.[2,5] Prior to the availability of complement inhibitors, only supportive management, in terms of managing the cytopenias and controlling thrombotic risk were available. Supportive measures include platelet transfusion, immunosuppressive therapy for patients with bone marrow failure, use of erythropoietin for anemias, and aggressive anticoagulation.

### IgAN

IgAN is the most common primary glomerular disease in the world and it is the leading cause of CKD and kidney failure.[5] The disease is slowly progressive; approximately 25% to 30% of patients develop kidney failure within 20 to 25 years of presentation. The management of IgAN is focused on supportive care to slow the rate of disease progression. IgAN is characterized by a single histopathologic criterion of predominant or co-dominant IgA deposits on kidney biopsy, however, it is well recognized that the disease exhibits heterogeneity in clinical and pathological features. Hypertension and proteinuria are major risk factors for the progression of CKD. Guidelines from Kidney Diseases: Improving Global Outcomes (KDIGO) note that proteinuria reduction to < 1 g/day is a surrogate marker of improved kidney outcomes in IgAN, and is a reasonable target.

## POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of Fabhalta. All approvals are provided for the duration noted below. In cases where the approval is authorized in months, 1 month is equal to 30 days. Because of the specialized skills required for evaluation and diagnosis of patients treated with Fabhalt as well as the monitoring required for adverse events and long-term efficacy, approval requires Fabhalt to be prescribed by or in consultation with a physician who specializes in the condition being treated.

**Automation:** None.

## RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Fabhalta is recommended in those who meet the following criteria:

### FDA-Approved Indication

1. **Paroxysmal Nocturnal Hemoglobinuria.** Approve for the duration noted if the patient meets ONE of the following (A or B):
   - **A)** Initial therapy. Approve for 6 months if the patient meets ALL of the following (i, ii, and iii):
     - **i.** Patient is ≥ 18 years of age; AND
     - **ii.** Paroxysmal nocturnal hemoglobinuria diagnosis was confirmed by peripheral blood flow cytometry results showing the absence or deficiency of glycosylphosphatidylinositol-anchored proteins on at least two cell lineages; AND
     - **iii.** The medication is prescribed by or in consultation with a hematologist.
   - **B)** Patient is Currently Receiving Fabhalta. Approve for 1 year if the patient meets ALL of the following (i, ii, and iii):
     - **i.** Patient is ≥ 18 years of age; AND
     - **ii.** Patient is continuing to derive benefit from Fabhalta according to the prescriber; AND
       Note: Examples of benefit include increase in or stabilization of hemoglobin levels, decreased transfusion requirements or transfusion independence, reductions in hemolysis.
     - **iii.** The medication is prescribed by or in consultation with a hematologist.

2. **Primary Immunoglobulin A Nephropathy.** Approve for the duration noted if the patient meets ONE of the following (A or B):
   - **A)** Initial Therapy. Approve for 9 months if the patient meets ALL of the following (i, ii, iii, iv, v, and vi):
     - **i.** Patient is ≥ 18 years of age; AND
     - **ii.** The diagnosis has been confirmed by biopsy; AND
     - **iii.** Patient is at high risk of disease progression, defined by meeting BOTH of the following (a and b):
       - **a)** Patient meets ONE of the following [(1) or (2)]:
         - **(1)** Proteinuria > 1.0 g/day; OR
         - **(2)** Urine protein-to-creatinine ratio ≥ 1.5 g/g; AND
       - **b)** Patient has received the maximum or maximally tolerated dose of ONE of the following for ≥ 12 weeks prior to starting Fabhalta [(1) or (2)]:
         - **(1)** Angiotensin converting enzyme inhibitor; OR
         - **(2)** Angiotensin receptor blocker; AND
     - **iv.** Patient has received ≥ 3 months of optimized supportive care, including blood pressure management, lifestyle modification, and cardiovascular risk modification, according to the prescriber; AND
     - **v.** Patient has an estimated glomerular filtration rate ≥ 30 mL/min/1.73 $m^2$; AND
     - **vi.** The medication is prescribed by or on consultation with a nephrologist.
   - **B)** Patient is Currently Receiving Fabhalta. Approve for 1 year if the patient meets ALL of the following (i, ii, iii, iv, and v):
     - **i.** Patient is ≥ 18 years of age; AND
     - **ii.** The diagnosis has been confirmed by biopsy; AND
     - **iii.** Patient has had a response to Fabhalta, according to the prescriber; AND

Note: Examples of a response are a reduction in urine protein-to-creatinine ratio from baseline, reduction in proteinuria from baseline.

**iv.** Patient has an estimated glomerular filtration rate ≥ 30 mL/min/1.73 $m^2$; AND

**v.** The medication is prescribed by or on consultation with a nephrologist.

## CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Fabhalta is not recommended in the following situations:

1. **Concomitant Use with Another Complement Inhibitor**. There is no evidence to support concomitant use of Fabhalta with another another complement inhibitor.
   Note: Examples of complement inhibitors are Empaveli (pegcetacoplan subcutaneous injection), Soliris (eculizumab intravenous infusion), and Ultomiris (ravulizumab-cwzy intravenous infusion or subcutaneous injection).

2. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

## REFERENCES

1. Fabhalta® capsules [prescribing information]. East Hanover, NJ: Novartis; August 2024.
2. Cançado RD, da Silva Araújo A, Sandes AF, et al. Consensus statement for diagnosis and treatment of paroxysmal nocturnal haemoglobinuria. *Hematol Transfus Cell Ther*. 2021;43:341-348.
3. Shah N, Bhatt H. Paroxysmal Nocturnal Hemoglobinuria. [Updated 2023 Jul 31]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan. Available from: https://www.ncbi.nlm.nih.gov/books/NBK562292/. Accessed December 18, 2023.
4. Roth A, Maciejewski J, Nishinura JI, et al. Screening and diagnostic clinical algorithm for paroxysmal nocturnal hemoglobinuria: Expert consensus. *Eur J Haematol*. 2018;101(1):3-11.
5. Kidney Diseases: Improving Global Outcomes (KDIGO) 2021 clinical practice guidelines for the management of glomerular diseases. *Kidney Int.* 2021;100:S1-S276. Available at: https://www.kidney-international.org/action/showPdf?pii=S0085-2538%2821%2900562-7. Accessed on August 12, 2024.