Clinical Policy: Iptacopan (Fabhalta)

Reference Number: PA.CP.PHAR.656
Effective Date: 08/2024
Last Review Date: 07/2025

Description
Iptacopan (Fabhalta®) is a complement inhibitor of factor B.

FDA Approved Indication(s)
Fabhalta is indicated for:

- 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

**This indication is approved under accelerated approval based on reduction of proteinuria. It has not been established whether Fabhalta slows kidney function decline in patients with IgAN. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory clinical trial.*

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of PA Health & Wellness® that Fabhalta is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Paroxysmal Nocturnal Hemoglobinuria (must meet all)**:**

1. Diagnosis of PNH;
2. Prescribed by or in consultation with an hematologist;
3. Age ≥ 18 years;
4. Flow cytometry shows detectable glycosylphosphatidylinositol (GPI)-deficient hematopoietic clones or ≥ 10% PNH cells;
5. Documentation of hemoglobin < 10 g/dL;
6. Fabhalta is not prescribed concurrently with another FDA-approved product for PNH (e.g., Soliris®, Ultomiris®, Empaveli®, Voydeya™, Bkemv™, Epysqli®, PiaSky®);
7. Dose does not exceed 400 mg (2 capsules) per day.

Approval duration: 6 months

B. Immunoglobulin A Nephropathy (must meet all)**:**

1. Diagnosis of IgAN confirmed via kidney biopsy;
2. Prescribed by or in consultation with a nephrologist;
3. Age ≥ 18 years;
4. Documentation of both of the following (a and b):
   a. Proteinuria of ≥ 1 g/day or UPCR ≥ 1.5 g/g;

b. Estimated glomerular filtration rate (eGFR) ≥ 20 mL/min/1.73 m^2;

5. Member meets both of the following, unless contraindicated or clinically significant adverse effects are experienced (a and b, *see Appendix D*):
   a. Failure of a renin-angiotensin-aldosterone system (RAAS) inhibitor (e.g., irbesartan, losartan, lisinopril, benazepril) for at least 12 weeks;
   b. RAAS inhibitor therapy dose was maximum tolerated dose;
6. Failure of Filspari® or Vanrafia™ at up to maximally indicated doses, unless clinically significant adverse effects are experienced or both are contraindicated;
7. Dose does not exceed 400 mg (2 capsules) per day.

Approval duration: 6 months

C. Complement 3 Glomerulopathy (must meet all)**:**

1. Diagnosis of C3G confirmed via kidney biopsy;
2. Prescribed by or in consultation with a nephrologist;
3. Age ≥ 18 years;
4. Documentation of both of the following (a and b):
   a. UPCR ≥ 1 g/g;
   b. eGFR ≥ 30 mL/min/1.73 m^2;
5. Failure of at least a 12-week trial of a RAAS inhibitor (e.g., irbesartan, losartan, lisinopril, benazepril) at up to maximally tolerated doses, unless contraindicated or clinically significant adverse effects are experienced (*see Appendix D*);
6. Dose does not exceed 400 mg (2 capsules) per day.

Approval duration: 6 months

D. Other diagnoses/indications

1. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

II. Continued Therapy

A. Paroxysmal Nocturnal Hemoglobinuria (must meet all)**:**

1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.PHARM.01) applies;
2. Member is responding positively to therapy as evidenced by, including but not limited to, improvement in <u>any</u> of the following parameters:
   a. Improved measures of intravascular hemolysis or extravascular hemolysis (e.g., normalization of lactate dehydrogenase, reduced absolute reticulocyte count, reduced bilirubin);
   b. Reduced need for red blood cell transfusions;
   c. Increased or stabilization of hemoglobin levels;
   d. Less fatigue;
   e. Improved health-related quality of life;
   f. Fewer thrombotic events;
3. Fabhalta is not prescribed concurrently with another FDA-approved product for PNH (e.g., Soliris, Ultomiris, Empaveli, Voydeya, Bkemv, Epysqli, PiaSky);

4. If request is for a dose increase, new dose does not exceed 400 mg (2 capsules) per day.

Approval duration: 12 months

B. All Other Indications in Section I (must meet all)**:**
1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.PHARM.01) applies;
2. Member is responding positively to therapy as evidenced by one of the following (a or b):
   a. Decrease in UPCR from baseline;
   b. Reduction of proteinuria as evidence by a lower total urine protein per day from baseline;
3. If request is for a dose increase, new dose does not exceed 400 mg (2 capsules) per day.

Approval duration: 12 months

C. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.PHARM.01) applies.
   Approval duration: Duration of request or 12 months (whichever is less); or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – PA.CP.PMN.53

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

ACEI: angiotensin-converting-enzyme inhibitor
ARB: angiotensin receptor blocker
eGFR: estimated glomerular filtration rate
C3G: complement 3 glomerulopathy
FDA: Food and Drug Administration
GPI: glycosylphosphatidylinositol
IgAN: immunoglobulin A nephropathy
PNH: paroxysmal nocturnal hemoglobinuria
RAAS: renin-angiotensin-aldosterone system
UPCR: urine protein-to-creatinine ratio

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent and may require prior authorization.

Drug Name	Dosing Regimen	Maximum Dose
ACEIs		
benazepril (Lotensin®)	Various	80 mg/day
captopril (Capoten®)	Various	450 mg/day
enalapril (Vasotec®, Epaned®)	Various	40 mg/day
fosinopril (Monopril®)	Various	80 mg/day
lisinopril (Prinivil®, Zestril®, Qbrelis®)	Various	80 mg/day
moexipril (Univasc®)	Various	30 mg/day
perindopril (Aceon®)	Various	16 mg/day
quinapril (Accupril®)	Various	80 mg/day
ramipril (Altace®)	Various	20 mg/day
trandolapril (Mavik®)	Various	8 mg/day
ARBs		
azilsartan (Edarbi®)	Various	80 mg/day
candesartan (Atacand®)	Various	32 mg/day
eprosartan (Teveten®)	Various	900 mg/day
irbesartan (Avapro®)	Various	300 mg/day
losartan (Cozaar®)	Various	100 mg/day
olmesartan (Benicar®)	Various	40 mg/day
telmisartan (Micardis®)	Various	80 mg/day
valsartan (Diovan®)	Various	320 mg/day
Endothelin receptor antagonists		
Filspari (sparsentan)	**IgAN** Initial treatment: 200 mg PO QD Maintenance: After 14 days, increase to recommended dose of 400 mg PO QD	400 mg/day
Vanrafia (atrasentan)	**IgAN** 0.75 mg PO QD with or without food	0.75 mg/day

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): serious hypersensitivity to iptacopan or any of the excipients; initiation in patients with unresolved serious infection caused by encapsulated bacteria, including Streptococcus pneumoniae, Neisseria meningitidis, or Haemophilus influenzae type B
- Boxed warning(s): serious infections caused by encapsulated bacteria

Appendix D: General Information

- The 2021 Kidney Disease Improving Global Outcomes (KDIGO) recommends initial therapy with a RAAS inhibitor (ACEI or ARB) for patients with proteinuria > 0.5 g per day, regardless of whether the patient has hypertension.
- Patients with IgAN who are considered high risk for progressive chronic kidney disease despite maximum supportive care (defined as blood pressure control, reduction of proteinuria, and lifestyle modifications) may consider treatment with corticosteroids or immunosuppressive drugs; however, there is current uncertainty over the safety and efficacy of existing immunosuppressive treatment choices. For all patients in whom immunosuppression is being considered, a detailed discussion of the risks and benefits of each drug should be undertaken with the patient recognizing that adverse treatment effects are more likely in patients with eGFR < 50 mL/min/1.73 m^2.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
PNH, IgAN, C3G	200 mg PO BID with or without food	400 mg/day

VI. Product Availability

Capsule: 200 mg

VII. References

1. Fabhalta Prescribing Information. East Hanover, NJ: Novartis Pharmaceuticals Corporation.; March 2025. Available at https://www.fabhalta-hcp.com/. Accessed April 21, 2025.
2. Parker C, Omine M, Richards S, et al. Diagnosis and management of paroxysmal nocturnal hemoglobinuria. Blood 2005; 106(12):3699-3709. Doi:10.1182/blood-2005-04-1717.
3. Borowitz MJ, Craig FE, DiGiuseppe JA, et al. Guidelines for the diagnosis and monitoring of paroxysmal nocturnal hemoglobinuria and related disorders by flow cytometry. Cytometry Part B (Clinical Cytometry). 2010; 78B: 211-230.
4. ClinicalTrials.gov. NCT04820530. Study of efficacy and safety of twice daily oral iptacopan (LNP023) in adult PNH patients who are naïve to complement inhibitor therapy (APPOINT-PNH). Available at www.clinicaltrials.gov. Accessed May 1, 2025.
5. ClinicalTrials.gov. NCT04558918. Study of efficacy and safety of twice daily oral LNP023 in adult PNH patients with residual anemia despite anti-C5 antibody treatment (APPLY-PNH). Available at www.clinicaltrials.gov. Accessed May 1, 2025.
6. Kidney Disease: Improving Global Outcomes (KDIGO) Glomerular Diseases Work Group. KDIGO 2021 clinical practice guideline for the management of glomerular diseases. Kidney Int. 2021 Oct;100(4S):S1-S276. doi: 10.1016/j.kint.2021.05.021.
7. ClinicalTrials.gov. NCT04578834. Study of efficacy and safety of LNP023 in primary IgA nephropathy patients (APPLAUSE-IgAN). Available at www.clinicaltrials.gov. Accessed May 1, 2025.
8. ClinicalTrials.gov. NCT04817618. Study of efficacy and safety of iptacopan in patients with C3 glomerulopathy (APPEAR-C3G). Available at www.clinicaltrials.gov. Accessed May 1, 2025.

Reviews, Revisions, and Approvals	Date
Policy created	07/2024
RT4: added newly approved FDA indication of IgAN and C3G.	04/2025
3Q 2025 annual review: for PNH, added Epysqli and PiaSky to the list of therapies that Fabhalta should not be prescribed concurrently with, and revised continued approval duration from 6 to 12 months as PNH is a chronic condition; references reviewed and updated. Per June SDC: for IgAN, added redirection to Filspari or Vanrafia in initial approval criteria.	07/2025