Clinical Policy: Iptacopan (Fabhalta)

Reference Number: CP.PHAR.656
Effective Date: 12.05.23
Last Review Date: 08.25
Line of Business: Commercial, HIM, Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

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 health plans affiliated with Centene Corporation® 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 a 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*):*
   **For Illinois HIM requests, the step therapy requirements below do not apply as of 1/1/2026 per IL HB 5395*
   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 at least 50% of maximum labeled dose;
6. Failure of Filspari® or Vanrafia™ at up to maximally indicated doses, unless clinically significant adverse effects are experienced or both are contraindicated;*
   **For Illinois HIM requests, the step therapy requirements above do not apply as of 1/1/2026 per IL HB 5395*
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 indicated doses, unless contraindicated or clinically significant adverse effects are experienced (*see Appendix D*);*
   **For Illinois HIM requests, the step therapy requirements above do not apply as of 1/1/2026 per IL HB 5395*
6. Dose does not exceed 400 mg (2 capsules) per day.

Approval duration: 6 months

D. Other diagnoses/indications (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND

criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

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

1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B)*;
2. Member is responding positively to therapy as evidenced by, including but not limited to, improvement in any 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. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B)*;
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. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

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 – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid or evidence of coverage documents.

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 for all relevant lines of business 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

Drug Name	Dosing Regimen	Maximum Dose
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	P&T Approval Date
Policy created pre-emptively	09.27.23	11.23
Drug is now FDA-approved – criteria updated per FDA labeling; revised formulation from tablet to capsule; in continued therapy criteria, added improvement of extravascular hemolysis as an example of positive response to therapy; references reviewed and updated.	12.19.23	

Reviews, Revisions, and Approvals	Date	P&T Approval Date
3Q 2024 annual review: no significant changes; added Voydeya and Bkemv to the list of therapies that Fabhalta should not be prescribed concurrently with; references reviewed and updated.	05.15.24	08.24
RT4: added newly approved FDA indication of IgAN.	08.14.24	
RT4: added newly approved FDA indication of C3G.	04.04.25	05.25
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. Added step therapy bypass for IL HIM per IL HB 5395.	06.24.25	08.25

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions, and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members, and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.