



PRIOR AUTHORIZATION POLICY

POLICY: Complement Inhibitors – Fabhalta Prior Authorization Policy

- Fabhalta® (iptacopan capsules – Novartis)

REVIEW DATE: 03/25/2026

INSTRUCTIONS FOR USE

THE FOLLOWING COVERAGE POLICY APPLIES TO HEALTH BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. CERTAIN CIGNA COMPANIES AND/OR LINES OF BUSINESS ONLY PROVIDE UTILIZATION REVIEW SERVICES TO CLIENTS AND DO NOT MAKE COVERAGE DETERMINATIONS. REFERENCES TO STANDARD BENEFIT PLAN LANGUAGE AND COVERAGE DETERMINATIONS DO NOT APPLY TO THOSE CLIENTS. COVERAGE POLICIES ARE INTENDED TO PROVIDE GUIDANCE IN INTERPRETING CERTAIN STANDARD BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. PLEASE NOTE, THE TERMS OF A CUSTOMER'S PARTICULAR BENEFIT PLAN DOCUMENT [GROUP SERVICE AGREEMENT, EVIDENCE OF COVERAGE, CERTIFICATE OF COVERAGE, SUMMARY PLAN DESCRIPTION (SPD) OR SIMILAR PLAN DOCUMENT] MAY DIFFER SIGNIFICANTLY FROM THE STANDARD BENEFIT PLANS UPON WHICH THESE COVERAGE POLICIES ARE BASED. FOR EXAMPLE, A CUSTOMER'S BENEFIT PLAN DOCUMENT MAY CONTAIN A SPECIFIC EXCLUSION RELATED TO A TOPIC ADDRESSED IN A COVERAGE POLICY. IN THE EVENT OF A CONFLICT, A CUSTOMER'S BENEFIT PLAN DOCUMENT ALWAYS SUPERSEDES THE INFORMATION IN THE COVERAGE POLICIES. IN THE ABSENCE OF A CONTROLLING FEDERAL OR STATE COVERAGE MANDATE, BENEFITS ARE ULTIMATELY DETERMINED BY THE TERMS OF THE APPLICABLE BENEFIT PLAN DOCUMENT. COVERAGE DETERMINATIONS IN EACH SPECIFIC INSTANCE REQUIRE CONSIDERATION OF 1) THE TERMS OF THE APPLICABLE BENEFIT PLAN DOCUMENT IN EFFECT ON THE DATE OF SERVICE; 2) ANY APPLICABLE LAWS/REGULATIONS; 3) ANY RELEVANT COLLATERAL SOURCE MATERIALS INCLUDING COVERAGE POLICIES AND; 4) THE SPECIFIC FACTS OF THE PARTICULAR SITUATION. EACH COVERAGE REQUEST SHOULD BE REVIEWED ON ITS OWN MERITS. MEDICAL DIRECTORS ARE EXPECTED TO EXERCISE CLINICAL JUDGMENT WHERE APPROPRIATE AND HAVE DISCRETION IN MAKING INDIVIDUAL COVERAGE DETERMINATIONS. WHERE COVERAGE FOR CARE OR SERVICES DOES NOT DEPEND ON SPECIFIC CIRCUMSTANCES, REIMBURSEMENT WILL ONLY BE PROVIDED IF A REQUESTED SERVICE(S) IS SUBMITTED IN ACCORDANCE WITH THE RELEVANT CRITERIA OUTLINED IN THE APPLICABLE COVERAGE POLICY, INCLUDING COVERED DIAGNOSIS AND/OR PROCEDURE CODE(S). REIMBURSEMENT IS NOT ALLOWED FOR SERVICES WHEN BILLED FOR CONDITIONS OR DIAGNOSES THAT ARE NOT COVERED UNDER THIS COVERAGE POLICY (SEE "CODING INFORMATION" BELOW). WHEN BILLING, PROVIDERS MUST USE THE MOST APPROPRIATE CODES AS OF THE EFFECTIVE DATE OF THE SUBMISSION. CLAIMS SUBMITTED FOR SERVICES THAT ARE NOT ACCOMPANIED BY COVERED CODE(S) UNDER THE APPLICABLE COVERAGE POLICY WILL BE DENIED AS NOT COVERED. COVERAGE POLICIES RELATE EXCLUSIVELY TO THE ADMINISTRATION OF HEALTH BENEFIT PLANS. COVERAGE POLICIES ARE NOT RECOMMENDATIONS FOR TREATMENT AND SHOULD NEVER BE USED AS TREATMENT GUIDELINES. IN CERTAIN MARKETS, DELEGATED VENDOR GUIDELINES MAY BE USED TO SUPPORT MEDICAL NECESSITY AND OTHER COVERAGE DETERMINATIONS.

CIGNA NATIONAL FORMULARY COVERAGE:

OVERVIEW

Fabhalta, a Factor B inhibitor, is indicated for the following uses:¹

- **Complement 3 glomerulopathy (C3G)**, to reduce proteinuria in adults.
- **Paroxysmal nocturnal hemoglobinuria (PNH)**, 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.

For the IgAN indication, Fabhalta was approved under accelerated approval based on reduction of proteinuria.¹ 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.

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

C3G

C3G, an ultra-rare complement-mediated kidney disease, is chronic and slowly progressive.^{2,3} The prevalence of C3G is challenging to estimate accurately; registry data suggest that incidence and prevalence are approximately 1 to 3 cases per million and 5 cases per million, respectively in the US.² C3G results from deregulation and consequently overactivation of the alternative pathway of the complement system, which allows the complement cascade to progress and activate all effector levels.^{2,3} In addition, deregulated complement results in deposition of C3b on target surfaces of the glomerulus. Urine analysis is typically the first step in diagnosis and typically shows proteinuria and hematuria. Renal biopsy is essential for diagnosis; histopathologic features of C3G are characterized by C3 deposits, absent or minimal immunoglobulin deposits within the glomeruli, evidence of glomerular inflammation, and mesangial cell proliferation. There are no approved disease-specific therapies for C3G. Standard of care includes supportive care, which includes blood pressure control with angiotensin-converting enzyme (ACE) inhibitors or angiotensin receptor blockers (ARBs) to reduce proteinuria and slow down kidney damage. Immunosuppressants such as corticosteroids, mycophenolate mofetil, cyclophosphamide, and rituximab are typically used to treat moderate to severe disease. Immunosuppressives may be used to reduce the production of autoantibodies and to reduce the inflammatory response. Some patients may be treated with plasma exchange or plasmapheresis, which are used to replace the defective complement proteins and to remove autoantibodies and other forms of debris.

PNH

PNH is a rare, genetic disorder of hematopoietic stem cells.^{4,5} 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.^{4,6} Prior to the availability of complement inhibitors, only supportive care to manage the cytopenias and control thrombotic risk was 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 chronic kidney disease (CKD) and kidney failure.⁷ 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 < 0.5 g/day, a surrogate marker of improved kidney outcomes in IgAN, is a reasonable target.

Clinical Efficacy

C3G

The efficacy of Fabhalta for the treatment of C3G was studied in a Phase III, randomized, double-blind, placebo-controlled study (APPEAR-C3G).^{1,8} All of the patients were between 18 and 60 years of age with biopsy-confirmed C3G within 12 months of enrollment. Inclusion criteria included reduced serum C3 concentration (< 77 mg/dL [defined as < 0.85 x lower limit of the central laboratory normal range) at screening; a urine protein-creatinine ratio (UPCR) of ≥ 1.0 g/g; and an estimated glomerular filtration rate (eGFR) ≥ 30 mL/min/1.73 m². In addition, all patients received maximally tolerated doses of an ACE inhibitor or ARB for ≥ 90 days before randomization. Other therapies (e.g., corticosteroids, mycophenolic acid, sodium-glucose cotransporter-2 [SGLT-2] inhibitors, mineralocorticoid receptor antagonists) were allowed if patients were stable on the therapies for ≥ 90 days before randomization. Patients who had previously received a cell or solid organ transplantation were excluded. Patients were randomized to receive Fabhalta 200 mg twice daily (BID) or placebo, in addition to supportive care (e.g., ARB/ACE) and immunosuppression, for 6 months, followed by open-label Fabhalta 200 mg BID for an additional 6 months.

The primary endpoint was relative reduction in proteinuria (measured by log-transformed ratio to baseline in UPCR sampled from a 24-hour urine collection) at 6 months. At 6 months, Fabhalta demonstrated superiority over placebo in reducing proteinuria. For the Fabhalta group, the 24-hour UPCR was 3.33 g/g at baseline and 2.17 g/g at 6 months, which was a percentage change relative to baseline of -30.2%. For the placebo group, the 24-hour UPCR was 2.58 g/g at baseline and 2.80 g/g at 6 months, which was a percentage change relative to baseline of 7.6%. The relative reduction in 24-hour UPCR was 35.1% (P = 0.0014) following 6 months of treatment with Fabhalta compared with placebo.

At 6 months, compared with patients in the placebo group, patients treated with Fabhalta had a 7-fold higher odds (P = 0.0166) of achieving a composite renal endpoint, defined as a $\geq 50\%$ reduction in 24-hour UPCR compared to baseline and stable or improved eGFR compared to baseline ($\leq 15\%$ reduction in eGFR). There was no difference between the groups in the proportion of patients with stable or improved eGFR compared to baseline at 6 months; 90% in the Fabhalta group vs. 89% in the placebo group; however, a greater proportion of patients in the Fabhalta group achieved a $\geq 50\%$ reduction in 24-hour UPCR compared to baseline (30% vs. 6%, respectively).

IgAN

The efficacy of Fabhalta was evaluated in one Phase III, pivotal, 24-month trial in patients ≥ 18 years of age with IgAN.^{1,9} Eligible patients had biopsy-proven IgAN, eGFR ≥ 30 mL/min/1.73 m², and a UPCR ≥ 1.0 g/g on a stable dose of maximally-tolerated renin-angiotensin system inhibitor for 3 months with or without a stable dose of an SGLT-2 inhibitor. Patients were randomized to Fabhalta 200 mg BID or placebo for 24 months while remaining on supportive care. Fabhalta resulted in a statistically and clinically meaningful reduction in proteinuria compared to placebo. Interim efficacy is reported at Month 9.

The primary efficacy endpoint was the change from baseline in the 24-hour UPCR (based on 24-hour urine sample) at Month 9.^{1,9} The primary analysis was based on an interim data cutoff of August 15, 2023. At Month 9, the primary endpoint was significantly greater with Fabhalta vs. placebo in the interim analysis set (comprised of the first 250 patients randomized in the study); the geometric least squares mean percent change in UPCR from baseline was -44% vs. -9%, respectively. This resulted in a statistically significant relative reduction from baseline in UPCR for the Fabhalta vs. placebo group (geometric mean ratio 0.617; 95% CI: 0.514, 0.740; P < 0.001), corresponding to a 38% relative reduction with Fabhalta. For Fabhalta, the UPCR changed from 1.9 g/g at baseline to 1.0 g/g at Month 9; for placebo, the change was from 2.0 g/g at baseline to 1.7 g/g at Month 9.

SAFETY

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).

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 Fabhalta as well as the monitoring required for adverse events and long-term efficacy, approval requires Fabhalta to be prescribed by or in consultation with a physician who specializes in the condition being treated.

• **Fabhalta® (iptacopan capsules – Novartis)**
is(are) covered as medically necessary when the following criteria is(are) met for FDA-approved indication(s) or other uses with supportive evidence (if applicable):

FDA-Approved Indications

1. Complement 3 Glomerulopathy. 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, iii, iv, v, and vi):

i. Patient is ≥ 18 years of age; AND

- ii. The diagnosis has been confirmed by biopsy; AND
 - iii. Patient has a urine protein-to-creatinine ratio ≥ 1.0 g/g; AND
 - iv. Patient has an estimated glomerular filtration rate ≥ 30 mL/min/1.73 m²; AND
 - v. Patient has received the maximum or maximally tolerated dose of at least ONE of the following for ≥ 12 weeks prior to starting Fabhalta (a or b):
 - a) Angiotensin converting enzyme inhibitor; OR
 - b) Angiotensin receptor blocker; AND
 - vi. The medication is prescribed by or in consultation with a nephrologist; OR
- 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. According to the prescriber, patient has had a response to Fabhalta; 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 m²; AND
 - v. The medication is prescribed by or in consultation with a nephrologist.

2. 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. The 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; OR
- 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. According to the prescriber, patient is continuing to derive benefit from Fabhalta; AND
Note: Examples of benefit include increase in or stabilization of hemoglobin levels, decreased transfusion requirements or transfusion independence, reductions in hemolysis, improvement in Functional Assessment of Chronic Illness Therapy (FACIT)-Fatigue score.
 - iii. The medication is prescribed by or in consultation with a hematologist.

3. Primary Immunoglobulin A Nephropathy. Approve for 1 year if the patient meets ONE of the following (A or B):

- A) Initial Therapy.** Approve 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 \geq 0.5 g/day; OR
 - (2) Urine protein-to-creatinine ratio \geq 1.5 g/g; AND
- b) Patient has received the maximum or maximally tolerated dose of ONE of the following for \geq 12 weeks prior to starting Fabhalta [(1) or (2)]:
 - (1) Angiotensin converting enzyme inhibitor; OR
 - (2) Angiotensin receptor blocker; AND
- iv. According to the prescriber, patient has received \geq 3 months of optimized supportive care, including blood pressure management, lifestyle modification, and cardiovascular risk modification; AND
- v. Patient has an estimated glomerular filtration rate \geq 30 mL/min/1.73 m²; AND
- vi. The medication is prescribed by or in consultation with a nephrologist; OR
- B) Patient is Currently Receiving Fabhalta.** Approve if the patient meets ALL of the following (i, ii, iii, iv, and v):
 - i. Patient is \geq 18 years of age; AND
 - ii. The diagnosis has been confirmed by biopsy; AND
 - iii. According to the prescriber, patient has had a response to Fabhalta; 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 \geq 30 mL/min/1.73 m²; AND
 - v. The medication is prescribed by or on consultation with a nephrologist.

CONDITIONS NOT COVERED

- **Fabhalta® (iptacopan capsules – Novartis)** is(are) considered not medically necessary for ANY other use(s) including the following (this list may not be all inclusive; criteria will be updated as new published data are available):

- 1. Concomitant Use with Another Complement Inhibitor.** There is no evidence to support concomitant use of Fabhalta with another complement inhibitor.
Note: Examples of complement inhibitors are Empaveli (pegcetacoplan subcutaneous injection), PiaSky (crovalimab-akkz intravenous infusion or subcutaneous injection), eculizumab intravenous infusion (Soliris, biosimilars), Ultomiris (ravulizumab-cwvz intravenous infusion), and Voydeya (danicopan tablets).
- 2. Concomitant Use with Other Medications Indicated for the Treatment of Immunoglobulin A Nephropathy (e.g., Filspari and Vanrafia).** The requested medication should not be administered in combination with other medications indicated for immunoglobulin A nephropathy. Combination therapy is generally not recommended due to a lack of controlled clinical trial data supporting additive efficacy.

REFERENCES

1. Fabhalta® capsules [prescribing information]. East Hanover, NJ: Novartis; March 2025.
2. Heidenreich K, Goel D, Priyamvada PS, et al. C3 glomerulopathy: a kidney disease mediated by alternative pathway deregulation. *Front Nephrol.* 2024;4:1460146. doi: 10.3389/fneph.2024.1460146.
3. Ayehu G, Atari M, Hassanein M, Jhaveri KD. C3 glomerulopathy. [Updated 2024 November 5]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing. 2026 Jan -. Available at: <https://www.ncbi.nlm.nih.gov/books/NBK609090/#article-169701.s4>. Accessed on March 23, 2026
4. 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.
5. Shah N, Bhatt H. Paroxysmal Nocturnal Hemoglobinuria. [Updated 2023 Jul 31]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan. Available at: <https://www.ncbi.nlm.nih.gov/books/NBK562292/>. Accessed on March 23, 2026.
6. 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.
7. Kidney Diseases: Improving Global Outcomes (KDIGO) 2025 clinical practice guidelines for the management of immunoglobulin A nephropathy (IgAN) and immunoglobulin A vasculitis (IgAV). Available at: <https://kdigo.org/wp-content/uploads/2024/08/KDIGO-2025-IgAN-IgAV-Guideline.pdf>. Accessed on March 17, 2026.
8. Kavanagh D, Bomback AS, Vivarelli M, et al. Oral iptacopan therapy in patients with C3 glomerulopathy: a randomized, double-blind, parallel group, multicentre, placebo-controlled, phase 3 study. *Lancet.* 2025;406:1587-1598.
9. Perkovic V, Barratt J, Rovin B, et al. Alternative complement pathway inhibition with iptacopan in IgA nephropathy. *N Engl J Med.* 2025;392(6):531-543.

HISTORY

| Type of Revision | Summary of Changes | Review Date |
|-----------------------|--|-------------|
| Annual Revision | Conditions Not Covered – Concomitant Use with Another Complement Inhibitor: In the Note of examples of complement inhibitors, Soliris biosimilars were added as examples. | 12/11/2024 |
| Early Annual Revision | Complement 3 Glomerulopathy: This condition and criteria for approval were added to the policy. | 04/02/2025 |
| Selected Revision | Conditions Not Covered: Added new condition regarding concomitant use with other medications indicated for the treatment of immunoglobulin A nephropathy. | 07/16/2025 |
| Selected Revision | Complement 3 Glomerulopathy: Initial Therapy: The requirement that the patient has not received a kidney transplant in the past was removed. The requirement regarding use of an angiotensin converting enzyme (ACE) inhibitor or angiotensin receptor blocker (ARB) at a maximum or maximally tolerated dose for ≥ 90 days was changed to state “at least ONE” of ACE inhibitor or ARB. Also, the number of days that a patient should have received either therapy was changed from ≥ 90 days to ≥ 12 weeks. Patient is Currently Receiving Fabhalta: The requirement that the patient has not received a kidney transplant in the past was removed. | 08/06/2025 |
| Annual Revision | Primary Immunoglobulin A Nephropathy: The approval duration was changed to 1 year for both initial therapy and patients currently receiving Fabhalta. | 03/25/2026 |

"Cigna Companies" refers to operating subsidiaries of The Cigna Group. All products and services are provided exclusively by or through such operating subsidiaries, including Cigna Health and Life Insurance Company, Connecticut General Life Insurance Company, Evernorth Behavioral Health, Inc., Cigna Health Management, Inc., and HMO or service company subsidiaries of The Cigna Group.© 2026 The Cigna Group.