iptacopan (Fabhalta®)

Policy # 00876
Original Effective Date: 06/10/2024
Current Effective Date: 06/01/2025

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc. (collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Paroxysmal Nocturnal Hemoglobinuria (PNH)

Based on review of available data, the Company may consider iptacopan (Fabhalta®)‡ for the treatment of paroxysmal nocturnal hemoglobinuria (PNH) to be **eligible for coverage.****

Patient Selection Criteria

Coverage eligibility for iptacopan (Fabhalta) will be considered when the following criteria are met:

I. Initial

A. Patient has received vaccination against meningococcal infections within 2 years prior to, or at the time of initiating the requested drug; AND
B. If the drug is initiated < 2 weeks after meningococcal vaccination, patient will receive prophylactic antibiotics until 2 weeks after vaccination; AND
C. Patient is 18 years of age or older; AND
D. Documentation is provided of peripheral blood high sensitivity flow cytometry results showing a granulocyte or monocyte clone size of ≥ 5%; AND
E. Patient meets ONE of the following (i or ii):
    i. Patient has at least ONE of the following significant disease manifestations caused by hemolysis (a, b, c, d, OR e):
        a. Documented history of a major adverse vascular event (MAVE) from thromboembolism; OR
        b. Presence of organ damage secondary to chronic hemolysis (e.g., worsening renal insufficiency); OR
        c. Patient is transfusion-dependent as evidenced by 2 or more transfusions in the 12 months prior to the initiation of treatment; OR
        d. Patient has a high lactate dehydrogenase (LDH) activity (defined as ≥ 1.5 times the upper limit of normal) with clinical symptoms (e.g., severe fatigue, dyspnea, jaundice, abdominal or chest pain, discolored urine, dysphagia, pulmonary hypertension); OR

e. Patient has symptomatic anemia with a hemoglobin less than the lower limit of normal; OR

ii. Patient has been previously receiving eculizumab (Soliris®)‡ or ravulizumab (Ultomiris™)‡ or pegcetacoplan (Empaveli™)‡, or crovalimab-akkz (PiaSky®)‡ for the treatment of PNH and is switching to iptacopan (Fabhalta); AND

*(Note: These specific patient selection criteria are additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*

F. For a patient transitioning to iptacopan (Fabhalta) from eculizumab (Soliris), ravulizumab (Ultomiris), pegcetacoplan (Empaveli), crovalimab-akkz (PiaSky), or danicopan (Voydeya™)‡; the prescriber attests that these medications will be discontinued within 4 weeks after starting Fabhalta.

II. Continuation

A. Patient has received an initial authorization for Fabhalta; AND

B. Patient has experienced improvement on therapy as evidenced by at least ONE of the following (i, ii, or iii):

i. Decreased serum LDH compared to pretreatment baseline; OR

ii. Decreased need for blood transfusion compared to pretreatment baseline; OR

iii. Stabilization of hemoglobin; AND

*(Note: These specific patient selection criteria are additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*

C. Fabhalta will not be used in combination with Empaveli, Soliris, Ultomiris, PiaSky, or Voydeya.

Immunoglobulin A Nephropathy (IgAN)

Based on review of available data, the Company may consider iptacopan (Fabhalta) for the treatment of immunoglobulin A nephropathy (IgAN) to be **eligible for coverage.****

Patient Selection Criteria

Coverage eligibility for iptacopan will be considered when the following criteria are met:

I. Initial

A. Patient has received vaccination against meningococcal infections within 2 years prior to, or at the time of initiating the requested drug; AND

B. If the drug is initiated < 2 weeks after meningococcal vaccination, patient will receive prophylactic antibiotics until 2 weeks after vaccination; AND

C. Patient is 18 years of age or older; AND

D. Patient has a diagnosis of primary immunoglobulin A nephropathy (IgAN); AND

E. Diagnosis has been confirmed by biopsy; AND

*(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*

F. According to the prescriber, the patient has received > 90 days of optimized supportive care, including blood pressure management, lifestyle modification, and cardiovascular risk modification; AND
*(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*

G. Patient is at high risk of disease progression, defined by meeting the following criteria (i AND ii):
   i. Patient meets ONE of the following (a OR b):
      a. Proteinuria > 1 g/day; OR
      b. Urine protein to creatinine ratio > 1.5 g/g; AND
   ii. Patient has been receiving the maximally tolerated dose of an angiotensin converting enzyme inhibitor (ACEi) (e.g., lisinopril, enalapril, benazepril, captopril, fosinopril, moexipril, perindopril, quinapril, ramipril, trandolapril) or angiotensin receptor blocker (ARB) (e.g., candesartan, irbesartan, losartan, olmesartan, telmisartan, valsartan) for > 90 days; AND
   *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*

H. Patient has an estimated glomerular filtration rate ≥ 20 mL/min/1.73m^2; AND
*(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*

I. Patient has tried and failed (e.g., intolerance or inadequate response) BOTH budesonide (Tarpeyo™)‡ and sparsentan (Filspari™)‡ unless there is clinical evidence or patient history that suggests the use of the alternative agents will be ineffective or cause an adverse reaction to the patient.
*(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*

II. Continuation

A. Patient has received an initial authorization for Fabhalta for IgAN; AND

B. According to the prescribing physician, patient is continuing to derive benefit from Fabhalta. Examples of treatment benefits include reduction in urine protein-to-creatinine ratio from baseline or reduction in proteinuria from baseline.
*(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*

Complement 3 Glomerulopathy (C3G)

Based on review of available data, the Company may consider iptacopan (Fabhalta) for the treatment of complement 3 glomerulopathy to be **eligible for coverage.****

Patient Selection Criteria:

Coverage eligibility for iptacopan (Fabhalta) for the treatment of complement 3 glomerulopathy will be considered when the following criteria are met:

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I. Initial

A. Patient has received vaccination against meningococcal infections within 2 years prior to, or at the time of initiating the requested drug; AND
B. If the drug is initiated < 2 weeks after meningococcal vaccination, patient will receive prophylactic antibiotics until 2 weeks after vaccination; AND
C. Patient is 18 years of age or older; AND
D. Patient has a diagnosis of complement 3 glomerulopathy (C3G) confirmed by kidney biopsy; AND
*(Note: The requirement that diagnosis be confirmed by kidney biopsy is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*
E. Infection-related or post-infectious glomerulonephropathy has been ruled out; AND
*(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*
F. Patient has a urine protein-to-creatinine ration (UPCR) $\geq$ 1 g/g AND an estimated glomerular filtration rate (eGFR) $\geq$ 30 mL/min/1.73 m^2; AND
G. Patient has been receiving the maximally tolerated dose of an angiotensin converting enzyme inhibitor (ACEi) (e.g., lisinopril, enalapril, benazepril, captopril, fosinopril, moexipril, perindopril, quinapril, ramipril, trandolapril) or angiotensin receptor blocker (ARB) (e.g., candesartan, irbesartan, losartan, olmesartan, telmisartan, valsartan) for > 90 days.
*(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*

II. Continuation

A. Patient has received an initial authorization for Fabhalta for C3G; AND
B. According to the prescribing physician, patient is continuing to derive benefit from Fabhalta. Examples of treatment benefits include reduction in urine protein-to-creatinine ratio from baseline or reduction in proteinuria from baseline.
*(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*

When Services Are Considered Not Medically Necessary

Based on review of available data, the Company considers the use of iptacopan (Fabhalta) for PNH when the patient does not have a manifestation of significant disease or has not been previously receiving eculizumab (Soliris), ravulizumab (Ultomiris), pegcetacoplan (Empaveli), or crovalimab-akkz (PiaSky) for PNH to be **not medically necessary.****

Based on review of available data, the Company considers the use of iptacopan (Fabhalta) for IgAN when the diagnosis has not been confirmed by kidney biopsy, the patient has not received > 90 days of optimized supportive care, has not received the maximally tolerated dose of an ACEi or ARB for > 90 days, has an eGFR < 20 mL/min/1.73 m^2, or has not tried and failed both Tarpeyo and Filspari to be **not medically necessary.****

Based on review of available data, the Company considers the use of iptacopan (Fabhalta) for C3G when the patient's diagnosis has not been confirmed by kidney biopsy, infection-related or post-infectious glomerulonephropathy has not been ruled out, or the patient has not been receiving the maximally tolerated dose of an ACEi or ARB for > 90 days to be **not medically necessary.****

Based on review of available data, the Company considers the continued use of iptacopan (Fabhalta) for PNH, IgAN, or C3G when the patient has not experienced an improvement on therapy to be **not medically necessary.****

When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers the use of iptacopan (Fabhalta) when the patient selection criteria are not met (except those denoted above as **not medically necessary****) to be **investigational.***

Background/Overview

Fabhalta is a Factor B inhibitor indicated for the treatment of paroxysmal nocturnal hemoglobinuria (PNH), Immunoglobulin A Nephropathy (IgAN), and Complement 3 Glomerulopathy (C3G) in adults. It works by binding to Factor B to regulate the cleavage of C3 and ultimately downregulate the complement activation that is responsible for many of the manifestations of these conditions. It is an oral treatment dosed as 200 mg twice daily without regard to food. Because it is a complement inhibitor, Fabhalta carries a similar requirement to other complement inhibitors for vaccination against encapsulated bacteria prior to treatment as well as a black box warning regarding the risk for serious infections.

Paroxysmal Nocturnal Hemoglobinuria (PNH)

PNH is an acquired hematopoietic stem cell disorder associated with an acquired somatic mutation of the phosphatidylinositol glycan class A (PIGA) gene. Mutations disrupt the first step in glycophosphatidylinositol (GPI) synthesis, which causes an absence of the GPI anchor and a deficiency of GPI proteins. The absence of GPI proteins on erythrocytes makes them susceptible to attack by complement and intravascular hemolysis. Intravascular hemolysis associated with PNH leads to release of free hemoglobin, leading to anemia, hemoglobinuria, thrombosis, dysphagia, abdominal pain, pulmonary hypertension, renal impairment, and erectile dysfunction. The prevalence of PNH is estimated to be between 0.5-1.5 per million people in the general population, with an approximately equal male to female distribution. Although PNH can affect any age group, the median age at diagnosis is during the fourth decade of life. The primary clinical finding is hemolysis of red blood cells by complement, which leads to hemoglobinuria that is most prominent in the morning. Those with PNH are also susceptible to repeated, potentially life-threatening thromboses. Underlying bone marrow dysfunction may also be present and those who are severely

affected may have pancytopenia. Many patients also have acquired aplastic anemia. Although less common, some patients have concomitant myelodysplasia. For unknown reasons, PNH may rarely develop into acute leukemia.

Signs and symptoms of PNH may vary, with some patients exhibiting mild and stable disease for many years while other patients have severe symptoms that rapidly progress to life-threatening. However, chronic hemolysis is central to all of the symptoms and physical findings associated with PNH. Fatigue, rapid heartbeat, headaches, and chest pain and difficulty breathing while exercising can result from mild hemolysis. With severe hemolysis, disabling fatigue, dysphagia, and painful contractions of the abdomen and esophagus may occur. It is estimated that 15-30% of patients with PNH develop blood clots, particularly venous thrombosis. Diagnosis of PNH is suspected in those with unexplained hemoglobinuria or abnormally high serum lactate dehydrogenase (LDH) levels. However, flow cytometry is the main diagnostic test for the identification of PNH cells.

There are no formal guidelines for treatment of PNH. However, there is an expert opinion for management of PNH published in a journal supported by the American Society of Hematology. Diagnosis of PNH is straightforward based on flow cytometry and specific treatment is recommended based on classification by the PNH interest group. Soliris is recommended for patients with classic PNH characterized by > 50% of GPI-AP-deficient PMNs as well as patients with PNH in the setting of another bone marrow failure syndrome with large PNH clones. No specific PNH therapy is recommended for patients with subclinical PNH with no clinical or biochemical evidence of intravascular hemolysis. This review was published before the approval of Ultomiris, Empaveli, Fabhalta, PiaSky, and Voydeya.

Immunoglobulin A Nephropathy (IgAN)
IgAN is the most common cause of primary glomerulonephritis in resource-abundant settings. Around 25% of patients with this condition have a slow progression to end-stage kidney disease (ESKD) within 25 years of presentation. The remaining patients enter a sustained remission or have persistent low-grade hematuria and/or proteinuria. Some of the proposed risk factors for disease progression include proteinuria above 1 g/day, hypertension, reduced eGFR, hematuria, certain histologic predictors on kidney biopsy, and modifiable factors such as obesity, hypertriglyceridemia, and smoking. The goal of treating IgAN is to prevent disease progression to ESKD by reducing proteinuria to less than 0.5 to 1 g/day and resolving microscopic hematuria. The first-line treatment options to achieve this goal are supportive care with blood pressure control, maximally tolerated renin-angiotensin system blockade, treatment with a sodium-glucose cotransporter-2 (SGLT2) inhibitor, and lifestyle modification. After 3-6 months of optimized supportive care, patients at high risk (e.g., those with proteinuria $\geq$ 1 g/day) may require further therapy with immunosuppressive agents such as glucocorticoids to reduce risk. Prior to the approval of Fabhalta for IgAN, two other specific therapies were approved for IgAN, sparsentan (Filspari) and budesonide delayed release (Tarpeyo). Filspari, Tarpeyo, and Fabhalta have not been directly compared in clinical trials and the optimal place in therapy for each agent is not known.

Complement 3 Glomerulopathy (C3G)
C3G is a rare glomerular kidney disease caused by dysregulation of the alternative complement pathway resulting in C3 deposits within the glomeruli. When the glomeruli are blocked and damaged, they cannot filter the blood, resulting in toxin build-up and kidney damage. Disease presentation can be variable from patient to patient and diagnosis is made based on kidney biopsy. C3G has two forms: dense deposit disease (DDD) and C3 glomerulonephritis (C3GN).

- DDD: refers to the linear-appearing, dense material observed in the glomerular basement membrane upon kidney biopsy and is primarily a disease of children.
- C3GN: characterized by the isolated C3 deposits that are less electron-dense than those in DDD; it is generally diagnosed in an older population than DDD.

Treatment for C3G is stratified based upon the severity of disease, but typically includes immunosuppressive therapy with mycophenolate mofetil and/or glucocorticoids. In select patients who do not respond to these therapies, clinical practice guidelines suggest that a trial of eculizumab is reasonable. These guidelines were published prior to the approval of Fabhalta for C3G and its optimal place in therapy is still unknown.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)
Fabhalta was approved in December 2023 for the treatment of adults with paroxysmal nocturnal hemoglobinuria. In August 2024, the label was expanded to include 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) $\geq$ 1.5 g/g. In March 2025, the label was further expanded to include treatment of adults with complement 3 glomerulopathy (C3G) to reduce proteinuria.

Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, technology evaluation centers, reference to regulations, other plan medical policies, and accredited national guidelines.

Paroxysmal Nocturnal Hemoglobinuria (PNH)
The efficacy of Fabhalta administered orally in adults with PNH was evaluated in a multi-center, open-label, 24-week, active comparator-controlled trial called APPLY-PNH. The trial enrolled 97 adults with PNH and residual anemia (hemoglobin < 10 g/dL) despite previous treatment with a stable regimen of an anti-C5 treatment (either eculizumab or ravulizumab) for at least 6 months prior to randomization. Patients were randomized in an 8:5 ratio to switch to Fabhalta 200 mg orally twice daily (n = 62) or to continue anti-C5 treatment throughout the duration of the 24-week randomized controlled period. Randomization was stratified based on prior anti-C5 treatment and transfusion

history within the last 6 months. Following completion of the 24-week randomized controlled period, all patients were eligible to enroll in a 24-week treatment extension period and receive Fabhalta monotherapy. Subsequently, patients were eligible to enter a separate long-term extension study.

Efficacy was established based on demonstration of superiority of switching to Fabhalta compared to continuing on anti-C5 therapy in achieving hematological response after 24 weeks of treatment, without a need for transfusion, by assessing the proportion of patients demonstrating both a sustained increase of $\geq$ 2 g/dL in hemoglobin levels from baseline and sustained hemoglobin levels of $\geq$ 12 g/dL. Fabhalta was statistically superior to anti-C5 therapy for both endpoints with 82.3% of the Fabhalta group achieving a sustained increase of hemoglobin levels $\geq$ 2 g/dL compared to 0 in the anti-C5 therapy group ($p < 0.0001$). Similarly, 67.7% of patients in the Fabhalta group had a sustained hemoglobin level $\geq$ 12 g/dL compared to 0 of the patients in the anti-C5 therapy arm.

The efficacy of Fabhalta in patients with PNH who were not previously treated with a complement inhibitor was studied in the APPOINT-PNH trial, a single arm study that enrolled a total of 40 adults with PNH. All 40 patients received Fabhalta 200 mg orally twice daily during the 24-week open-label core treatment period. Subsequently, patients were eligible to enroll in a 24-week treatment extension period and continue to receive Fabhalta, followed by a separate long-term extension study. In total, 77.5% (95% CI: 61.5%, 89.2%) of patients achieved a sustained increase in hemoglobin levels from baseline of $\geq$ 2 g/dL in the absence of RBC transfusions, based on central laboratory hemoglobin values. In a sensitivity analysis, 87.5% (95% CI: 73.2%, 95.8%) of patients achieved a sustained increase in hemoglobin levels from baseline of $\geq$ 2 g/dL in the absence of RBC transfusions.

Immunoglobulin A Nephropathy (IgAN)
The effect of Fabhalta was evaluated in a multicenter, randomized, placebo-controlled, double-blind study (APPLAUSE-IgAN) in adults with biopsy-proven IgAN, eGFR $\geq$ 20 mL/min/1.73 m^2, and urine protein-to-creatinine ratio (UPCR) $\geq$ 1 g/g on a stable dose of maximally-tolerated renin-angiotensin system (RAS) inhibitor therapy with or without a stable dose of an SGLT2 inhibitor. Patients with other glomerulopathies or those who had been recently treated with systemic immunosuppressants were excluded. Patients were included in either the Main Study Population (eGFR $\geq$ 30 mL/min/1.73 m^2) or the Severe Renal Impairment population (eGFR $\geq$ 20 and < 30 mL/min/1.73 m^2). Within each group, patients were randomized (1:1) to either Fabhalta 200 mg or placebo twice daily. Rescue immunosuppressive treatment could be initiated per investigator discretion during the trial.

Patients were required to be vaccinated against *Neisseria meningitidis* and *Streptococcus pneumoniae* and were recommended to be vaccinated against *Haemophilus influenzae* type b. If the patient had not been previously vaccinated or if a booster was required, vaccination was administered at least 2 weeks prior to first dosing. If Fabhalta treatment was initiated earlier than 2 weeks after vaccination, antibacterial drug prophylaxis was administered.

The efficacy analysis was based on the first 250 patients with an eGFR ≥ 30 mL/min/1.73 m^2 (Main Study Population), who had completed or discontinued the study prior to the Month 9 visit. At baseline, the mean age of these patients was 39 years (range 18 to 74 years); 52% were male, 44% White, 54% Asian, and < 1% Black or African American; the mean eGFR was 64 mL/min/1.73 m^2; the geometric mean UPCR (sampled from a 24-hr urine collection) was 2.0 g/g, and 12% had a UPCR ≥ 3.5 g/g. At baseline, 99% of patients were treated with an ACEi or ARB and 13% were on an SGLT2i. Approximately 59% had a history of hypertension, 6% had a history of type 2 diabetes, and 75% had hematuria based on urine dipstick.

The primary endpoint was the percent reduction in UPCR (sampled from a 24-hr urine collection) at Month 9 relative to baseline. The mean percent change from baseline in UPCR over time in the Fabhalta group was 44% compared to 9% in the placebo group. This corresponded to a 38% reduction in UPCR at Month 9 in the Fabhalta vs placebo groups (95% CI: 26%, 49%, $p < 0.0001$).

Complement 3 Glomerulopathy (C3G)
The efficacy of Fabhalta in reducing proteinuria in adult patients with native kidney C3G was demonstrated in the APPEAR-C3G trial. Safety and effectiveness of Fabhalta in patients with recurrent C3G following kidney transplant have not been established.

APPEAR-C3G was a randomized, double-blind, placebo-controlled study in 74 adult patients with biopsy confirmed native kidney C3G who had a urine protein-to-creatinine ratio (UPCR) ≥ 1 g/g and eGFR ≥ 30 mL/min/1.73 m^2. Patients were randomized (1:1) to receive either Fabhalta 200 mg orally twice daily (N = 38) or placebo (N = 36) for 6 months, followed by a 6-month open-label treatment period in which all patients received Fabhalta 200 mg orally twice daily.

Patients were required to be on a maximally tolerated renin-angiotensin system (RAS) inhibitor and could be on a corticosteroid and/or mycophenolate mofetil/sodium (MMF/MPS) at baseline. All background therapies (i.e., RAS inhibitors, corticosteroids and MMF/MPS) were required to be at stable doses for 90 days prior to randomization and throughout the study. Randomization was stratified according to whether patients were receiving concomitant immunosuppressive therapy.

Patients were required to be vaccinated against *Neisseria meningitidis* and *Streptococcus pneumoniae* and were recommended to be vaccinated against *Haemophilus influenzae* type b. If the patient had not been previously vaccinated or if a booster was required, vaccination was administered at least 2 weeks prior to first dosing. If Fabhalta treatment was initiated earlier than 2 weeks after vaccination, antibacterial drug prophylaxis was administered.

At baseline, the mean eGFR (mL/min/1.73 m^2) was 89 and 99 in the Fabhalta and placebo groups, respectively, and the geometric mean 24-hour UPCR (g/g) at baseline was 3.3 and 2.6 in the Fabhalta and placebo groups, respectively.

Twenty four percent of patients in the Fabhalta group and 3% in the placebo group had dense deposit disease. Baseline use of corticosteroids and/or MMF/MPS, and RAS inhibitor was balanced among the Fabhalta and placebo groups. Overall, 45% of patients were on corticosteroids and/or MMF/MPS, and 99% of patients were on a RAS inhibitor at baseline.

The primary efficacy endpoint was the log-transformed ratio to baseline in UPCR (sampled from a 24-hour urine collection) at 6 months. At 6 months, the geometric mean UPCR ratio relative to baseline was 0.70 (95% CI: 0.57, 0.85) and 1.08 (95% CI: 0.88, 1.31) in the Fabhalta and placebo groups, respectively, resulting in a 35% reduction in 24-hour UPCR from baseline in the Fabhalta group compared to placebo ($p = 0.0028$).

Following the initial 6-month treatment period, all patients were treated with Fabhalta for an additional 6 months. In patients initially randomized to Fabhalta, the reduction in 24-hour UPCR seen at 6 months was maintained at Month 12. In patients who switched from placebo to Fabhalta, the magnitude of the reduction in 24-hour UPCR from Month 6 to 12 was similar to the reduction seen in patients initially randomized to Fabhalta.

Compared to patients treated with placebo, 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] at 6 months. Although a greater proportion of patients in the Fabhalta arm (30%) as compared to placebo (6%) achieved a $\geq 50\%$ reduction in 24-hour UPCR compared to baseline, there was no difference between arms in the proportion of patients with stable or improved eGFR compared to baseline at 6 months (90% in Fabhalta vs 89% in placebo).

References

1. Fabhalta [package insert]. Novartis Pharmaceuticals, Corp. East Hanover, NJ. Updated March 2025.
2. C3 glomerulopathies: Dense deposit disease and C3 glomerulonephritis. UpToDate. Updated June 2024.
3. Kidney Disease: Improving Global Outcomes (KDIGO). KDIGO 2021 Clinical Practice Guideline for the Management of Glomerular Diseases. Kidney Int. 2021; 100(4S).

Policy History

Original Effective Date: 06/10/2024
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05/02/2024	Medical Policy Committee review
05/08/2024	Medical Policy Implementation Committee approval. New policy.
05/01/2025	Medical Policy Committee review
05/13/2025	Medical Policy Implementation Committee approval. Updated criteria and background information to include two new indications for Immunoglobulin A Nephropathy and complement 3 glomerulopathy.

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
    1. Consultation with technology evaluation center(s);
    2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
    3. Reference to federal regulations.

**Medically Necessary (or "Medical Necessity") - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

A. In accordance with nationally accepted standards of medical practice;
B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, "nationally accepted standards of medical practice" means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

NOTICE: If the Patient's health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.

NOTICE: Federal and State law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage.