PRIOR AUTHORIZATION POLICY

POLICY: Nephrology – Voyxact Prior Authorization Policy
- Voyxact® (sibeprenlimab-szsi subcutaneous injection – Otsuka)

REVIEW DATE: 12/10/2025

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

Voyxact, an A Proliferation Inducing Ligand (APRIL) blocker, is indicated to reduce proteinuria in adults with **primary immunoglobulin A nephropathy** (IgAN) at risk of rapid disease progression.[1]

Voyxact was approved under accelerated approval based on reduction of proteinuria.[1] It has not been established whether Voyxact slows kidney function decline over the long-term in patients with IgAN. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory clinical trial.

Disease Overview

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.[2] 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) [2025] note that proteinuria reduction to < 0.5 g/day, a surrogate marker of improved kidney outcomes in IgAN, is a reasonable target.

Clinical Efficacy

The efficacy of Voyxact was evaluated in a Phase III trial in adults with biopsy-proven IgAN, proteinuria at screening (defined as a urine protein to creatinine ratio [UPCR] ≥ 0.75 g/g or urine protein ≥ 1.0 g/day), and estimated glomerular filtration rate (eGFR) ≥ 30 mL/min/1.73 m^2 (VISONARY, n = 510).[1,3] Additionally, patients were receiving the maximum tolerated dose of an angiotensin converting enzyme inhibitor (ACEI) or angiotensin receptor blocker (ARB) with or without a sodium-glucose co-transporter 2 (SGLT2) inhibitor for ≥ 12 weeks prior to study entry. Patients who were receiving immunosuppressive medications (including corticosteroids within 16 weeks of screening), and patients with CKD in addition to IgAN, or IgAN secondary to other conditions were excluded. The majority of patients remained on a renin-angiotensin system (RAS) inhibitor throughout the study.[1]

The primary efficacy endpoint was the change from baseline in UPCR (based on 24-hour urine sample) at Month 9.[1,3] In the interim analysis set (comprised of the first 320 patients randomized in the study, who completed 9 months of the trial), the change in UPCR from baseline to Month 9 was significantly greater with Voyxact compared with placebo. The geometric least squares mean percent change in UPCR from baseline was -50% for Voyxact vs. 2% for placebo. This resulted in a statistically significant relative reduction from baseline in UPCR for the Voyxact group, corresponding to a 51% relative reduction with Voyxact (P < 0.0001). In the exploratory analysis, the percent of patients achieving remission of proteinuria (total urine protein < 0.5 g/day at Month 12) was 34.3% for Voyxact (n = 99) and 12.7% for placebo (n = 118).[3]

Guidelines

KDIGO clinical practice guidelines for the management of IgAN and immunoglobulin A vasculitis (2025) recommend patients who are at risk of progressive kidney function loss with IgAN to be treated with RAS inhibitor or Filspari (sparsentan tablets) with or without a SGLT2 inhibitor.[4] Filspari should not be prescribed with a RAS inhibitor. It is also recommended that a 9-month course of Tarpeyo (budesonide delayed-release capsules) be considered for patients with a risk of progressive kidney function loss with IgAN. Therapeutic strategies that minimize or avoid systemic glucocorticoid exposure are considered areas of priority for research to improve treatment and outcomes in patients with IgAN. Voyxact, Fabhalta (iptacopan capsules), and Vanrafia (atrasentan tablets) were noted as investigative treatments with no guideline recommendations.

The goal of treatment is to prevent progressive kidney function loss. The only validated biomarker to guide clinical decision-making is urine protein excretion, which should be maintained < 0.5 g/day and ideally < 0.3 g/day. Following a biopsy-confirmed diagnosis of IgAN, the primary focus of treatment should include RAS inhibitors or Filspari with or without SGLT2 inhibitor, blood pressure control, cardiovascular risk minimization, and adherence to lifestyle advice. Additional treatment should be considered if the patient has proteinuria ≥ 0.5 g/day while on or off treatment. In patients who remain at high risk of progressive CKD despite maximal supportive care, a 6- to 9-month course of glucocorticoid therapy should be considered. However, the guidelines recommend that glucocorticoid use in IgAN should be used with extreme caution or avoided in patients with an eGFR < 30 mL/minute/1.73 m^2, diabetes, obesity (body mass index > 30 kg/m^2), latent infections (e.g., tuberculosis, viral hepatitis), secondary disease (e.g., cirrhosis), active peptic ulceration, uncontrolled psychiatric illness, and severe osteoporosis.

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of Voyxact. 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 Voyxact as well as the monitoring required for adverse events and long-term efficacy, approval requires Voyxact to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Voyxact® (sibeprenlimab-szsi subcutaneous injection - Otsuka) 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 Indication

1. **Primary Immunoglobulin A Nephropathy.** Approve for 9 months 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 ≥ 0.5 g/day; OR
         - **(2)** Urine protein-to-creatinine ratio ≥ 0.8 g/g; AND

b) Patient has received or is currently receiving the maximum or maximally tolerated dose of ONE of the following for ≥ 12 weeks prior to starting Voyxact [(1) or (2)]:
(1) Angiotensin converting enzyme inhibitor; OR
(2) Angiotensin receptor blocker; AND

iv. According to the prescriber, patient has received ≥ 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 ≥ 30 mL/min/1.73 m^2; AND

vi. The medication is prescribed by or on consultation with a nephrologist; OR

B) Patient is Currently Receiving Voyxact. 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 Voyxact,; 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 COVERED

Voyxact® (sibeprenlimab-szsi subcutaneous injection - Otsuka) is(are) considered not medically necessary for ANY other use(s) including the following. Criteria will be updated as new published data are available.

REFERENCES

1. Voyxact® subcutaneous injection [prescribing information]. Rockville, MD: Otsuka; November 2025.
2. 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 December 1, 2025.
3. Perkovic V, Trimarchi H, Tesar V, et al. Sibeprenlimab in IgA Nephropathy - Interim analysis of a Phase 3 trial. *N Engl J Med*. Published online November 8, 2025.

HISTORY

Type of Revision	Summary of Changes	Review Date
New Policy	--	12/10/2025