eocco sparsentan (Filspari®), atrasentan (Vanrafia™) and sibeprenlimab (Voyxact®)

EOCCO POLICY

Policy Type:PA/SP Pharmacy Coverage Policy: EOCCO278

Description

Sparsentan (Filspari) is an orally administered dual endothelin (ET_AR) and angiotensin II (AT_1R) receptor antagonist (DEARA) and inhibits endothelin-1 and angiotensin II, which may contribute to pathogenesis of immunoglobulin A nephropathy (IgAN). Atrasentan (Vanrafia) is an orally administered endothelin (ET_AR) antagonist. Sibeprenlimab (Voyxact) is an injectable administered A Proliferation Inducing Ligand (APRIL) blocker.

Length of Authorization

- Initial: Six months
- Renewal: 12 months

Quantity Limits

Product Name	Indication	Dosage Form	Quantity Limit*
sparsentan (Filspari)	Primary IgA nephropathy; at risk of disease progression	200 mg tablet	30 tablets/30 days
		400 mg tablet	30 tablets/30 days
atrasentan (Vanrafia)		0.75 mg tab	30 tablets/30 days
sibeprenlimab (Voyxact)		400 mg/2mL prefilled syringe	2 mL (1 syringe)/ 28 days

**Quantity limit exceptions are not allowed.*

Initial Evaluation

I. **Sparsentan (Filspari), atrasentan (Vanrafia), and sibeprenlimab (Voyxact)** may be considered medically necessary when the following criteria are met:
   A. Member is 18 years of age or older; **AND**
   B. Medication is prescribed by, or in consultation with, a nephrologist or immunologist; **AND**
   C. Member has an eGFR > 30 mL/min/1.73m^2; **AND**
   D. Member is not currently receiving dialysis; **AND**
   E. Member has not undergone a kidney transplant; **AND**
   F. Medication requested will not be used in combination with another specialty medication for the treatment of the condition (i.e., atrasentan [Vanrafia], budesonide [Tarpeyo], sparsentan [Filspari], iptacopan [Fabhalta] or sibeprenlimab [Voyxact]); **AND**
   G. Treatment with a renin-angiotensin system (RAS) inhibitor (e.g., angiotensin converting enzyme inhibitor [ACEi] [e.g., enalapril, lisinopril]; angiotensin receptor blocker [ARB] [e.g., valsartan, irbesartan]) for at least 3 months has been ineffective, not tolerated, or all are contraindicated; **AND**

H. Treatment with a sodium-glucose cotransporter-2 inhibitor (SGLT2i) [e.g. dapagliflozin (Farxiga), empagliflozin (Jardiance)], for at least 3 months has been ineffective, not tolerated, or all are contraindicated; **AND**
I. Treatment with a sodium-glucose cotransporter-2 inhibitor (SGLT2i) [e.g. dapagliflozin (Farxiga), empagliflozin (Jardiance)], will be used in combination with the requested drug, unless not tolerated or contraindicated; **AND**
J. A diagnosis of **Primary immunoglobulin A nephropathy (IgAN)** when the following are met:
    1. Diagnosis of Primary immunoglobulin A nephropathy (IgAN) has been confirmed by a kidney biopsy; **AND**
    2. Documentation of elevated protein levels in urine as indicated by proteinuria ≥ 0.5 g/day or urine protein to creatinine ratio (UPCR) ≥ 0.5 g/g; **AND**
K. If the request is for **sparsentan (Filspari)**: Medication will not be used in combination with an ACEi (e.g., enalapril, lisinopril), ARB (e.g., valsartan, irbesartan); **OR**
L. If the request is for **atrasentan (Vanrafia):** Medication will be used in combination with an ACEi (e.g., enalapril, lisinopril), ARB (e.g., valsartan, irbesartan) unless not tolerated or contraindicated; **OR**
M. If the request is for **sibeprenlimab (Voyxact)**; **AND**
    1. Treatment with systemic corticosteroids (e.g., prednisone, prednisolone, methylprednisolone) has been ineffective, not tolerated or contraindicated; **AND**
    2. Treatment with the following medications has been ineffective, not tolerated, or all are contraindicated:
        i. A nine-month course of targeted-release budesonide (Tarpeyo)*; **AND**
        ii. One of the following for at least three months:
            a. sparsentan (Filspari)*; **OR**
            b. atrasentan (Vanrafia)*; **AND**
    3. Provider attestation the member does not have severe disease as indicated by MEST or MEST-C score of T2 or C2, the presence of >50% tubulointerstitial fibrosis, or the presence of crescents in >25% of glomeruli; **AND**
    4. Medication will be used in combination with an ACEi (e.g., enalapril, lisinopril), ARB (e.g., valsartan, irbesartan), unless not tolerated or contraindicated.

*Please note: medications notated with an asterisk may require additional review.

II. Sparsentan (Filspari) is considered investigational when used for all other conditions, including but not limited to:
    A. Secondary IgA nephropathy
    B. Newly diagnosed IgAN without high risk of disease progression
    C. Multi-drug regimens (e.g., atrasentan (Vanrafia), sparsentan (Filspari), budesonide (Tarpeyo), iptacopan (Fabhalta), sibeprenlimab (Voyxact) used in combination with each other)
    D. Focal segmental glomerulosclerosis (FSGS)

E. Chronic kidney disease (CKD) other than primary IgAN

III. Atrasentan (Vanrafia) is considered investigational when used for all other conditions, including but not limited to:
   A. Secondary IgAN
   B. Newly diagnosed IgAN without high risk of disease progression
   C. Chronic kidney disease (CKD) or proteinuric glomerular diseases other than primary IgAN
   D. Multi-drug regimens (e.g., atrasentan (Vanrafia), sparsentan (Filspari), budesonide (Tarpeyo), iptacopan (Fabhalta), sibeprenlimab (Voyxact) used in combination with each other)

IV. Sibeprenlimab (Voyxact) is considered investigational when used for all other conditions, including but not limited to:
   A. Secondary IgAN or IgA vasculitis
   B. Newly diagnosed IgAN without high risk of disease progression
   C. Chronic kidney disease (CKD) or proteinuric glomerular diseases other than primary IgAN
   D. Multi-drug regimens (e.g., atrasentan (Vanrafia), sparsentan (Filspari), budesonide (Tarpeyo), iptacopan (Fabhalta), sibeprenlimab (Voyxact) used in combination with each other)
   E. Sjögren's syndrome
   F. Improvements in histological biomarkers overtime, (biopsy results)

Renewal Evaluation

I. Member has received a previous prior authorization approval for this agent through this health plan or has been established on therapy from a previous health plan; **AND**
II. Member is not continuing therapy based off being established on therapy through samples, manufacturer coupons, or otherwise. If they have, initial policy criteria must be met for the member to qualify for renewal evaluation through this health plan; **AND**
III. Medication will not be used in combination with another specialty medication for the treatment of the condition (i.e., atrasentan [Vanrafia], budesonide [Tarpeyo], sparsentan [Filspari], iptacopan [Fabhalta] or sibeprenlimab [Voyxact]); **AND**
IV. Member has an eGFR > 30 mL/min/1.73m^2; **AND**
V. Member is not currently receiving dialysis; **AND**
VI. Member has not undergone a kidney transplant; **AND**
VII. Member has exhibited improvement or stability of disease symptoms (e.g., reduction in proteinuria <1 g/day or urine protein to creatinine ratio (UPCR) < 1.5 g/g); **AND**
VIII. If the request is for **sparsentan (Filspari):** Medication will not be used in combination with angiotensin converting enzyme (ACE) inhibitor (e.g., enalapril, lisinopril), angiotensin receptor blocker (ARB) (e.g., valsartan, irbesartan); **OR**
IX. If the request is for **atrasentan (Vanrafia)** or **sibeprenlimab (Voyxact):** Medication will be used in combination with a renin-angiotensin system (RAS) inhibitor [e.g., angiotensin converting enzyme (ACE) inhibitor (e.g., enalapril, lisinopril); angiotensin receptor blocker (ARB) (e.g., valsartan, irbesartan)], unless not tolerated or contraindicated; **AND**

X. Medication will be used in combination with a sodium-glucose cotransporter-2 inhibitor (SGLT2i) [e.g. dapagliflozin (Farxiga), empagliflozin (Jardiance)], unless not tolerated or contraindicated

Supporting Evidence

I. Sparsentan (Filspari) is a novel Dual Endothelin Angiotensin Receptor Antagonist (DEARA) that received accelerated FDA-approval in February 2023 for the reduction of proteinuria in adults with primary immunoglobulin A nephropathy (IgAN) at risk of rapid disease progression. Full approval was granted in September 2024 after positive confirmatory eGFR data. Atrasentan (Vanrafia) is a selective endothelin type A receptor (ET_AR) antagonist that received FDA accelerated approval in April 2025 to reduce proteinuria in adults with primary IgAN at risk of rapid disease progression. Full approval of atrasentan (Vanrafia) is expected in 2026. Sibeprenlimab (Voyxact) is an A Proliferation Inducing Ligand (APRIL) blocker that received accelerated FDA-approval in November 2025 for the reduction of proteinuria in adults with primary IgAN at risk of disease progression. Full approval of sibeprenlimab (Voyxact) is expected in 2027. Sparsentan (Filspari), atrasentan (Vanrafia) and sibeprenlimab (Voyxact) have not been studied in a pediatric population.

II. Primary immunoglobulin A nephropathy, also called Berger's disease, is a rare kidney disorder characterized by deposits of immune complexes containing galactose-deficient IgA in the glomerular mesangium leading to glomerulosclerosis, and renal failure. Although previously considered a benign condition, IgAN is now recognized to cause end-stage renal disease (ESRD) in 30% of affected individuals.

III. The Kidney Disease Improving Global Outcomes (KDIGO) guideline indicates IgAN can only be diagnosed with a kidney biopsy. While there are several prognostic scoring tools that have been developed to assist in predicting kidney outcomes of IgAN patients (i.e., MEST-C, International IgAN Prediction Tool, etc.) there are currently no validated diagnostic serum or urine biomarkers.

IV. Due to the complexities related to diagnosis monitoring and management of IgAN patients, therapy for this disease space should be initiated by or in consultation with a specialist such as nephrologist or immunologist.

V. The 2025 KDIGO IgAN guideline update reflects a shift towards earlier treatment of IgAN, recognizing that clinically meaningful kidney damage may occur at lower levels of proteinuria. Evidence indicates that proteinuria ≥ 0.5 g/day is associated with increased long-term risk of kidney failure, supporting earlier intervention rather than reliance on supportive care until later stages of disease progression. Evidence in favor of the lowered proteinuria threshold in IgAN is supported by two large observational cohort studies that demonstrated even proteinuria thresholds of < 1 g/g, which were once considered low risk of progression, led to significantly high rates of kidney failure. Specifically, kidney failure resulted in 10 years for 20% of patients who maintained time-averaged proteinuria of < 0.44 g/g, vs. 30% of patients who maintained time-averaged proteinuria of 0.44 to 0.88 g/g. Notably, for every 10% decrease in proteinuria from baseline resulted in an 11% decreased risk of kidney failure. The KDIGO IgAN guideline does not yet address newer agents such as atrasentan (Vanrafia), iptacopan (Fabhalta), or

sibeprenlimab (Voyxact) due to their data collection cutoff of August 2024; however, it acknowledges the surge of new therapies for IgAN and clarifies utilizing mechanistically unique agents provides an opportunity for synergistic combinations "to achieve the newly articulated goals of treatment to preserve kidney function for a patient's lifetime.". The policy criterion specific to the lowered proteinuria threshold of ≥ 0.5 g/day for the treatment of IgAN is in alignment with the current KDIGO guidelines.

VI. For IgAN, guidelines recommend a treatment approach that addresses both immune-mediated disease and the downstream effects of IgAN-induced nephron loss simultaneously—treatment with a 9-month course of targeted-release budesonide (Tarpeyo) where available (or systemic glucocorticoids if not available), in addition to ACEi/ARB or DERRA (e.g., sparsentan) ± SGLT2i (e.g., dapagliflozin, empagliflozin) in addition to lifestyle modifications such as sodium restriction, smoking cessation, weight management, regular exercise, and a blood pressure target of ≤ 120/70 mmHg.

VII. The 2025 KDIGO guidelines include renin-angiotensin system (RAS) blockade (e.g., ACEi/ARB), alone or in combination with SGLT2i, as part of supportive care in patients with IgAN at risk of progressive loss of kidney function. This approach reflects guideline-based management intended to reduce glomerular hyperfiltration and the harmful effects of persistent proteinuria that contribute to ongoing nephron loss. This criterion is intended to ensure optimization of guideline-based supportive care before or alongside the use of IgAN-specific specialty therapy.

VIII. Sparsentan (Filspari) is the first DEARA and the second drug approved for the treatment of IgAN. It follows IgAN-indicated budesonide (Tarpeyo). A nine-month course of glucocorticoids (e.g., prednisone, methylprednisolone) and/ or other immunosuppressants (e.g., hydroxychloroquine, mycophenolate) have been used for the treatment of high-risk IgAN. However, their use may be limited by other prognostic factors (e.g., eGFR > 30 mL/min/ 1.73 m^2), lack of strong clinical evidence, and considerations of treatment-related toxicities. Additionally, the KDIGO guideline recommends enrollment in a clinical trial for this patient population. Sparsentan (Filspari) may be considered a steroid-sparing alternative for the treatment of high-risk IgAN.

IX. The accelerated FDA approval for sparsentan (Filspari) was based on interim analysis of a randomized, double-blind, active-controlled Phase 3 trial where patients were randomized 1:1 to either sparsentan (Filspari) 400 mg or irbesartan 300 mg once daily (PROTECT, N = 404). Adults with biopsy proven primary IgAN, proteinuria ≥ 1 g/day, eGFR ≥ 30 mL/min/1.73 m^2, and supportive therapy with an ACEi and/or ARB for ≥ 12 weeks were included in the study. Patients with secondary IgAN, documented history of immunosuppressants (including corticosteroids) use for ≥ 2 weeks within 3 months before screening, active CVD, hepatic or immune conditions were excluded. Baseline median proteinuria and mean eGFR in the sparsentan (Filspari) treatment arm were 1.8 g/day, and 56.9 mL/min/1.73m^2, respectively. Half (51.5%) of patients in the treatment arm had urinary protein excretion >1.75 g/day at baseline. The primary endpoint was met for the reported change in UPCR at week 36 versus baseline, which was -49.8% and -15% for sparsentan (Filspari) versus irbesartan (OR 0.6; 95% CI .5, 0.7; p <0.0001). Additionally, 55% of patients in the treatment arm achieved proteinuria < 1 g/day at week 36. A supportive secondary endpoint: change in UPCR at week 94 was also reported to be statistically significant (52% versus 11%; p=0.0002).

X. Conversion to full approval of sparsentan (Filspari) was based on the 2-year eGFR results from the PROTECT Study, where sparsentan (Filspari) delivered superior long-term kidney function preservation compared to irbesartan. The two-year efficacy data contained in the FDA-approved label was a modified intention to treat (ITT) analysis, as preferred by the FDA, evaluated data from all patients regardless of treatment discontinuation. In the final analysis of the 404 randomized patients, sparsentan (Filspari) significantly reduced the rate of decline in kidney function from baseline to Week 110 compared to irbesartan. In the ITT analysis included in the label, the mean eGFR slope from baseline to Week 110 was -3.0 mL/min/1.73 m^2/year for sparsentan (Filspari) and -4.2 mL/min/1.73 m^2/year for irbesartan, corresponding to a statistically significant treatment effect of 1.2 mL/ min/1.73 m^2/year (p=0.0168). The positive treatment effects on proteinuria compared to irbesartan that were observed at Week 36 were durable out to the two-year measurement period. Additional results from the PROTECT Study demonstrated the benefit of sparsentan (Filspari) on absolute eGFR accrued over time and by Week 110 resulted in a 3.8 mL/min/1.73 m^2 difference in the mean change from baseline between sparsentan (Filspari) and irbesartan.

XI. During PROTECT clinical trial for sparsentan (Filspari), patients with a history of immunosuppressants, including corticosteroids, for more than 2 weeks within 3 months of screening were excluded. Efficacy and safety of sparsentan (Filspari) in combination with IgAN-indicated budesonide (Tarpeyo) and other systemic corticosteroids has not been evaluated. Due to the very high risk of adverse events, concurrent use of ACE inhibitors and ARB agents with sparsentan (Filspari) is contraindicated.

XII. During PROTECT clinical trial, a higher percentage of sparsentan (Filspari) treated patients reported treatment-emergent adverse event (TEAE) than irbesartan group (82.2% versus 73.3%), with dizziness (13%), peripheral edema (13%), hyperkalemia (10%), hypotension (10%), fatigue (8%), upper respiratory tract infections (6%), and acute kidney injury (4%) reported as the most common TEAE in the treatment arm. Kidney and urinary disorders were the most common severe adverse event (AE) reported in both arms leading to discontinuations (7.9% and 4.5% in the sparsentan (Filspari) and irbesartan arms, respectively). Results from the two-year trial showed that sparsentan (Filspari) was well tolerated with a clearly defined safety profile that has been consistent across all clinical trials conducted to date. Following engagement with the FDA, the Travere Therapeutics expects to submit an sNDA for a potential modification to the liver-monitoring REMS.

XIII. The real-world utility of sparsentan (Filspari) is limited by exclusion of patients with cardiovascular disorders, anemia (Hb< 9 g/dL), and pre-existing CKD, which are considered major prognostic concerns related to renal impairment and are critical risk factors associated with mortality in CKD. An open-label extension (OLE) for the PROTECT clinical trial is currently ongoing along with two additional clinical trials to evaluate sparsentan (Filspari) for the treatment of focal segmental glomerulosclerosis (FSGS).

XIV. The accelerated approval of atrasentan (Vanrafia) was based on the prespecified interim analysis of the ALIGN trial, a Phase 3, randomized, double-blind, placebo-controlled study involving 270 patients with biopsy-confirmed IgAN, persistent proteinuria ≥1.0 g/day, on a stable dose of maximally tolerated RASi. The study included two cohorts: a main cohort (340

patients) and an exploratory cohort (64 patients who were also on a stable dose of SGLT2i at baseline), which was independent of the main stratum and analyzed separately. Baseline mean eGFR in the atrasentan (Vanrafia) treatment arm was 1.5g/g and 59 mL/min/1.73m^2. The geometric mean baseline UPCR was 1.5g/g samples from a 24-hour urine and 15% of patients had proteinuria >3.5 g/day. The trial excluded participants on chronic dialysis or kidney transplantation for end-stage kidney disease as these are considered clinical outcomes of interest. The efficacy analysis used to support the accelerated approval included the first 270 patients in the main cohort who reached the primary endpoint at week 36: was the percent change in urine protein-to-creatinine ratio (UPCR) from baseline. In the interim analysis, the geometric mean percentage change in the UPCR relative to baseline was significantly greater with atrasentan (Vanrafia) (−38.1%) than with placebo (−3.1%), This resulted in a statistically significant relative reduction from baseline in UPCR for the atrasentan (Vanrafia), corresponding to a 36% relative reduction with atrasentan (Vanrafia) (P < 0.001).

XV. Proteinuria reduction was evident at week 6 and sustained through week 36. This treatment effect at Week 36 was also consistent in the exploratory SGLT2i cohort. Exploratory efficacy endpoints for changes in UPCR from baseline to Week 36 in the SGLT2i cohort was -39.6% for atrasentan (Vanrafia) (14 patients) compared to -3.4% for placebo (15 patients). This corresponds to a relative reduction of 37.4% in UPCR from baseline.

XVI. The expected place in therapy for atrasentan (Vanrafia) is as an adjunct to supportive care that includes renin-angiotensin system inhibitor (RASi) with or without an SGLT2i for patients at high risk of IgAN progression based on sustained proteinuria.

XVII. The safety profile of atrasentan (Vanrafia) was consistent with other endothelin receptor antagonist (ERA) therapies. The most common adverse events (vs. placebo) included peripheral edema (24% vs. 10%), nasopharyngitis (18% vs. 12%), headache (14% vs. 8%), fatigue (13% vs. 7%), and anemia (11% vs. 6%). Adverse events of special interest in the treatment group included anemia, fluid retention, and vasodilation or hypotension. Permanent discontinuation due to AEs occurred in 7% of patients. Dose interruption occurred in 16% of patients on atrasentan (Vanrafia). Atrasentan (Vanrafia) carries a black box warning for embryo-fetal toxicity and warnings and precautions for hepatotoxicity, fluid retention, and decreased sperm count.

XVIII. The quality of evidence for atrasentan (Vanrafia) is considered low. The ALIGN clinical program consists of an ongoing trial, alluding to a short-term indication of efficacy. Reduction in proteinuria < 1 g/day is an objective surrogate marker for IgAN. However, it falls shy of predicting long-term patient outcomes such as progression to ESRD, dialysis dependence and overall mortality in ESRD. The Kidney Health Initiating workgroup and National Kidney Foundation recommend the use of dual (primary and confirmatory) endpoints of proteinuria reduction as well as slope of eGFR decline. At this time, effect of atrasentan (Vanrafia) on eGFR is unknown compared to other agents on the market. Currently, all four approved therapies for IgAN demonstrate comparable reductions in UPCR; but ultimately, confirmatory eGFR data from both iptacopan (Fabhalta) and atrasentan (Vanrafia) will be essential for evaluating their impact on kidney function.

XIX. As of March 2026, no clinical trials support the combined use of multiple novel therapies in IgAN. While it is known that multiple pathophysiologic mechanisms contribute to kidney

function loss in patients with IgAN, particularly those at risk of progressive decline, targeting these mechanisms concurrently may be necessary. In clinical practice, this could mean combining standard of care therapies with one or more agents. In the absence of updated clinical guidelines and supporting evidence to allow combination use of specialty IgAN therapies (e.g., atrasentan (Vanrafia), targeted-release budesonide (Tarpeyo), sparsentan (Filspari), iptacopan (Fabhalta), etc.), concurrent use is contraindicated and considered experimental and investigational.

XX. During the PROTECT, ALIGN and VISIONARY clinical trials, patients with an eGFR $\leq$ 30 mL/min/1.73m^2, patients on dialysis, and history of kidney transplant were excluded from participation. Efficacy and safety of sparsentan (Filspari), atrasentan (Vanrafia) and sibeprenlimab (Voyxact) in this selected population has not been evaluated and is therefore considered experimental and investigational.

XXI. Sibeprenlimab (Voyxact) received accelerated FDA approval November 2025 based on the interim results of the VISIONARY trial, which studied 320 patients who were optimized with RASi (e.g. lisinopril, irbesartan) +/- SGLT2i (e.g. dapagliflozin, empagliflozin) in a Phase 3, randomized, double-blind, placebo-controlled trial with biopsy confirmed IgAN at risk for progression. The primary efficacy endpoint was reduction of 24-hr UPCR at 9 months; 51% (96.5% CI; 43% to 58%). For the confirmatory endpoint, (also known as the key secondary endpoint), investigators are evaluating the annualized eGFR slope over 24 months, in 510 patients and results are expected in 2027.

XXII. The safety profile of sibeprenlimab (Voyxact) is similar to placebo. In the VISIONARY trial, 259 patients received sibeprenlimab (Voyxact) and 251 patients received placebo. Any infection occurred in 49% for sibeprenlimab (Voyxact) vs 45% for placebo. Most common adverse events (AEs) for sibeprenlimab (Voyxact) vs placebo, respectively, were upper respiratory infections (15% vs 14%) and injection site erythema (13% vs 12%).

XXIII. The overall evidence is considered low. While the primary endpoint supports accelerated approval, it is a surrogate marker and does not demonstrate improvement in clinical renal outcomes such as decreased risk of ESRD or kidney transplantation. The annualized eGFR slope from baseline to 24 months compared to placebo will provide insight into potential clinical utility. Lastly, efficacy as monotherapy is unknown, as sibeprenlimab (Voyxact) was studied in combination with RASis and SGLT2is, consistent with expected real-world use.

XXIV. Systemic corticosteroids are required to be tried and failed unless ineffective, not tolerated, or contraindicated prior to authorizing access to targeted-release budesonide (Tarpeyo) and sibeprenlimab (Voyxact). Systemic corticosteroids, including prednisone and methylprednisolone have demonstrated reductions in proteinuria comparable to those seen with IgAN-specific agents and have safety profiles similar to targeted-release budesonide (Tarpeyo). Although targeted-release budesonide (Tarpeyo) was developed to target IgA-mediated disease activity in the gut mucosa, it is systemically absorbed and associated with corticosteroid-related adverse effects. Consistent with this, the FDA label states that the relative contribution of local ileal versus systemic effects to its clinical efficacy has not been established.

Both targeted-release budesonide (Tarpeyo) and systemic corticosteroids carry a Level 2B recommendation in the 2025 KDIGO guidelines, reflecting moderate certainty of evidence and recognition that treatment decisions may vary based on clinical context. In light of this evidence and healthcare resource utilization, use of systemic corticosteroids remains clinically appropriate in selected patients, particularly when individual factors such as contraindications, tolerability, and prior response are taken into account.

XXV. The MEST and MEST-C score is a biopsy-based measure of IgAN severity that includes mesangial and endocapillary hypercellularity, segmental sclerosis, interstitial fibrosis/tubular atrophy and crescents, where T2 and C2 lesions represent more advanced disease and likely irreversible kidney scaring. The VISIONARY trial excluded patients with T2 or C2 lesions or with >50% tubulointerstitial fibrosis, or crescents in >25% of glomeruli. It is unknown whether sibeprenlimab (Voyxact) would provide effective and/or meaningful outcomes for patients with these characteristics of advanced disease and is therefore considered experimental and investigational.

XXVI. The 2025 KDIGO IgAN guidelines have not been updated to include sibeprenlimab (Voyxact). As noted above, data to support combination use among the IgAN-specific agents is limited and considering the higher costs and the lack of proven benefit, combination therapy is not allowed.

Investigational or Not Medically Necessary Uses

I. Sparsentan (Filspari) has not been FDA-approved or sufficiently studied for safety and efficacy for the conditions or settings listed below. There are currently ongoing trials in the setting of focal segmental glomerulosclerosis (FSGS). However, no data is available to support efficacy and safety of sparsentan (Filspari) for the treatment of FSGS:
   A. Secondary IgA nephropathy
   B. Newly diagnosed IgAN without high risk of disease progression
   C. Multi-drug regimens (e.g., atrasentan (Vanrafia), sparsentan (Filspari), budesonide (Tarpeyo), iptacopan (Fabhalta), sibeprenlimab (Voyxact) used in combination with each other)
   D. Focal segmental glomerulosclerosis (FSGS)
   E. Chronic kidney disease (CKD) other than primary IgAN

II. Atrasentan (Vanrafia) has not been FDA-approved or sufficiently studied for safety and efficacy for the conditions or settings listed below.
   A. Secondary IgAN
   B. Newly diagnosed IgAN without high risk of disease progression
   C. Chronic kidney disease (CKD) or proteinuric glomerular diseases other than primary IgAN
   D. Multi-drug regimens (e.g., atrasentan (Vanrafia), sparsentan (Filspari), budesonide (Tarpeyo), iptacopan (Fabhalta), sibeprenlimab (Voyxact) used in combination with each other)

III. Sibeprenlimab (Voyxact) has not been FDA-approved or sufficiently studied for safety and efficacy for the conditions or settings listed below.
   A. Secondary IgAN or IgA vasculitis

B. Newly diagnosed IgAN without high risk of disease progression
C. Chronic kidney disease (CKD) or proteinuric glomerular diseases other than primary IgAN
D. Multi-drug regimens (e.g., atrasentan (Vanrafia), sparsentan (Filspari), budesonide (Tarpeyo), iptacopan (Fabhalta), sibeprenlimab (Voyxact) used in combination with each other)
E. Sjögren's syndrome
    i. Sibeprenlimab (Voyxact) is being investigated in a Phase 2, multicenter, randomized, double-blind, placebo-controlled trial for the treatment of Sjögren's disease (NCT06928142). Estimated study completion is in June 2027. Requests for this indication are considered experimental and investigational at this time.
F. Improvements in histological biomarkers overtime (biopsy results)
    i. Sibeprenlimab (Voyxact) is being evaluated in a Phase 2b, multicenter, open-label, single-arm trial to assess kidney histology through repeat kidney biopsies in adolescents and adults with IgAN (NCT06740526). Estimated study completion is in April 2029. Requests for this use indication are considered experimental and investigational at this time.

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12. Kidney Disease: Improving Global Outcomes (KDIGO). KDIGO 2025 Clinical Practice Guideline for the Management of Immunoglobulin A Nephropathy (IgAN) and Immunoglobulin A Vasculitis (IgAV). KDIGO. October 2025. Accessed February 1, 2026. https://kdigo.org/wp-content/uploads/2024/08/KDIGO-2025-IgAN-IgAV-Guideline.pdf
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Related Policies

Policies listed below may be related to the current policy. Related policies are identified based on similar indications, similar mechanisms of action, and/or if a drug in this policy is also referenced in the related policy.

Policy Name	Disease state
budesonide (Tarpeyo)	Primary IgA nephropathy; at risk of progression
Fabhalta: Proximal Complement Inhibitors	Primary IgA nephropathy; at rapid risk of progression

Policy Implementation/Update

Action and Summary of Changes	Date
Added sibeprenlimab (Voyxact) to the policy and updated supporting evidence section to include 2025 KDIGO IgAN guideline updates.	05/2026
Addition of atrasentan (Vanrafia) to policy. Updated initial and renewal criteria to exclude the use of IgAN therapies in combination, exclude use in dialysis and kidney transplant, include eGFR, remove use of corticosteroid requirement, and clarified use of RASi with Vanrafia. Updated E/I, supporting evidence, references, and related policies.	08/2025
Policy created	05/2023