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. Atrasentan (Vanrafia) is an orally administered endothelin (ET_AR) antagonist. Sibeprenlimab (Voyxact) is an injectable administered A Proliferation Inducing Ligand (APRIL) blocker. Atacicept (Trutakna) is an injectable administered B-lymphocyte stimulator (BLyS)-specific inhibitor [also known as B-cell activating factor (BAFF)] and APRIL blockers.

Length of Authorization

- Initial: Six months
- Renewal: 12 months

Quantity Limits

Product Name	Indication	Dosage Form	Quantity Limit*
sparsentan (Filspari)	Focal segmental glomerulosclerosis (FSGS) without nephrotic syndrome	400 mg tablet	60 tablets/30 days
	Primary IgA nephropathy; at risk of disease progression	200 mg tablet	30 tablets/30 days
atrasentan (Vanrafia)	Primary IgA nephropathy; at risk of disease progression	0.75 mg tablet	30 tablets/30 days
sibeprenlimab (Voyxact)		400 mg/2mL prefilled syringe	2 mL (1 syringe)/28 days
atacicept (Trutakna)		150 mg/mL prefilled syringe	4 mL (4 syringes)/28 days

**Quantity limit exceptions are not allowed.*

Initial Evaluation

I. **Sparsentan (Filspari), atrasentan (Vanrafia), sibeprenlimab (Voyxact), and atacicept (Trutakna)** may be considered medically necessary when the following criteria are met:
   A. Medication is prescribed by, or in consultation with, a nephrologist or immunologist; **AND**
   B. Member has an eGFR greater than or equal to 30 mL/min/1.73m^2; **AND**
   C. Member is not currently receiving dialysis; **AND**
   D. Member has not undergone a kidney transplant; **AND**
   E. A diagnosis of one of the following:
      1. A diagnosis of **Primary immunoglobulin A nephropathy (IgAN)**; **AND**
         i. Medication requested will not be used in combination with another targeted medication for the treatment of the condition (i.e., atrasentan

[Vanrafia], budesonide [Tarpeyo], sparsentan [Filspari], iptacopan [Fabhalta], sibeprenlimab [Voyxact] or atacicept [Trutakna]); **AND**

ii. The member trialed each of the following groups at therapeutic doses for at least three months:
    a. Group 1: renin-angiotensin system (RAS) inhibitor (e.g., angiotensin converting enzyme inhibitor [ACEi] [e.g., enalapril, lisinopril]; angiotensin receptor blocker [ARB] [e.g., valsartan, irbesartan])
    b. Group 2: sodium-glucose cotransporter-2 inhibitor (SGLT2i) [e.g. dapagliflozin (Farxiga), empagliflozin (Jardiance)]; **AND**

iii. Diagnosis of Primary immunoglobulin A nephropathy (IgAN) has been confirmed by a kidney biopsy; **AND**

iv. Documentation of elevated protein levels in urine as indicated by proteinuria greater than or equal to 0.5 g/day or urine protein to creatinine ratio (UPCR) greater than or equal to 0.5 g/g; **AND**

v. The request is for sparsentan (Filspari) or atrasentan (Vanrafia); **OR**

vi. The request is for sibeprenlimab (Voyxact) or atacicept (Trutakna); **AND**
    a. Treatment with oral corticosteroids [e.g., targeted-release budesonide (Tarpeyo)*, prednisone, methylprednisolone, etc.] has been ineffective, not tolerated, or all are contraindicated; **AND**
    b. Treatment with at least one of the following medications has been ineffective, not tolerated, or all are contraindicated
        i. sparsentan (Filspari)*
        ii. atrasentan (Vanrafia)*; **OR**

2. The request is for treatment of **focal segmental glomerulosclerosis (FSGS)**; **AND**

i. Member is 8 years of age or older; **AND**

ii. Diagnosis is confirmed by a biopsy; **OR**
    a. There is documentation of a pathogenic variant likely associated with focal segmental glomerulosclerosis (FSGS); **AND**
        i. Provider attestation that secondary causes of FSGS have been evaluated and ruled out (e.g., viral infections, drug-induced, etc.,); **AND**

iii. There is documentation of elevated protein levels in urine as indicated by proteinuria greater than or equal to 1 g/day or urine protein to creatinine ratio (UPCR) greater than or equal to 1.5 g/g; **AND**

iv. Provider attestation member does <u>not</u> have current nephrotic syndrome defined as presence of edema at baseline, proteinuria greater than 3.5 g/24 hours (adults) or UPCR greater than 2.0 g/g (pediatric patients less than 18 years of age), and serum albumin less than 3.0 g/dL; **AND**

v. 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**

vi. The request is for sparsentan (Filspari)

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

II. Sparsentan (Filspari), atrasentan (Vanrafia), sibeprenlimab (Voyxact) and atacicept (Trutakna) are considered investigational when used for all other conditions, including but not limited to:
   A. Multi-drug regimens [e.g., atrasentan (Vanrafia), sparsentan (Filspari), budesonide (Tarpeyo), iptacopan (Fabhalta), sibeprenlimab (Voyxact), atacicept (Trutakna), used in combination with each other]
   B. Secondary IgA nephropathy
   C. Newly diagnosed IgAN without high risk of disease progression
   D. Chronic kidney disease (CKD) other than primary IgAN
   E. Sjögren's syndrome
   F. Improvements in histological biomarkers overtime, (biopsy results)
   G. Rheumatoid arthritis
   H. Systemic lupus erythematous

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 targeted medication for the treatment of the condition (i.e., atrasentan [Vanrafia], budesonide [Tarpeyo], sparsentan [Filspari], iptacopan [Fabhalta], or sibeprenlimab [Voyxact], or atacicept [Trutakna]); **AND**
IV. Member has an eGFR greater than or equal to 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 less than 1 g/day or urine protein to creatinine ratio (UPCR) less than 1.5 g/g).

Supporting Evidence

Primary immunoglobulin A nephropathy (IgAN)

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. In April 2026

sparsentan (Filspari) received FDA-approval for the treatment of segmental glomerulosclerosis (FSGS) in adults and pediatrics 8 years of age and older. 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. Atacicept (Trutakna) is a B-lymphocyte stimulator (BLyS)-specific inhibitor [also known as B cell activating factor (BAFF)] and APRIL blocker that received accelerated FDA-approval in July 2026 for the reduction of proteinuria in adults with primary IgAN at risk of disease progression. Full approval of atacicept (Trutakna) is expected in 2027. Sparsentan (Filspari), atrasentan (Vanrafia), and sibeprenlimab (Voyxact) and atacicept (Trutakna) have not been studied in a pediatric population for the treatment of IgAN.

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 2025 KDIGO IgAN guideline does not currently include formal recommendations for newer agents such as atrasentan (Vanrafia), iptacopan (Fabhalta), or sibeprenlimab (Voyxact) or atacicept (Trutakna) 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." A March 2026 KDIGO commentary article subsequently recognized the expanding role of newer targeted therapies in IgAN, including endothelin, compliment, APRIL and dual APRIL/BAFF pathway agents, without providing formal recommendations for treatment selection, sequencing or combination therapy. 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 targeted IgAN 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 August 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 targeted 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, VISIONARY and ORIGIN-3 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), sibeprenlimab (Voyxact) or atacicept (Trutakna) in this selected population have not been evaluated and are 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%).

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 two-year eGFR results were released by the manufacturer August 2026, demonstrating an annualized eGFR slope of +0.3 mL/min/1.73m^2 vs -4.2 mL/min/1.73m^2 for placebo, a treatment effect of +4.5 mL/min/1.73m^2; however, results have not formally been published and Voyxact has not yet received full FDA-approval. Lastly, efficacy as monotherapy is unknown, as sibeprenlimab (Voyxact) was studied in combination with RASis and SGLT2is, consistent with expected real-world use.

XXIV. Atacicept (Trutakna) received accelerated FDA approval July 2026 based on the interim results of the ORIGIN-3 trial, which included 203 patients who were optimized with RASi +/- SGLT2i in a Phase 3, randomized, double-blind, placebo-controlled trial with biopsy confirmed IgAN at risk of progression. The primary efficacy endpoint was reduction of 24-hr UPCR at week 36; 41.8% (95% CI; 28.9% to 52.3%). For the key secondary endpoint, investigators are evaluating the annualized eGFR slope at week 104, in 428 patients and topline results are expected late 2026. Other secondary endpoints evaluated, although not powered for confirmatory evidence, were

reduction in galactose-deficient IgA1 (Gd-IgA1) 67.4% (95% CI: 63.8% to 70.6%) and resolution of hematuria in patients who presented with hematuria at baseline, OR 19.1 (95% CI; 7.3 to 50).

XXV. The safety profile of atacicept (Trutakna) is similar to other APRIL- and BAFF/APRIL- blockers FDA-approved [e.g., sibeprenlimab (Voyxact)] or povetacicept (under FDA review as of August 2026) for the treatment of IgAN. In the ORIGIN-3 trial, 214 patients received atacicept (Trutakna) and 214 patients received placebo. Any infection occurred in 31.8% for atacicept (Trutakna) vs 28% for placebo. Most common adverse events for atacicept (Trutakna) vs placebo, respectively, were injection-site reactions (19% vs 2%), upper respiratory tract infection (12% vs 9%), and injection-site erythema (6% vs 1%).

XXVI. 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. Favorable topline results of the annualized eGFR slope at Week 104 were released by the manufacturer September 2026 and noted their intent to file for full approval Q4 2026 with potential full approval in 2027; -0.6 mL/min/1.73m^2/year vs -5.6 for placebo, demonstrating a treatment effect of 5.0, (95% CI, 3.6 to 6.5, $p < 0.0001$). Currently, dual APRIL/BAFF inhibition has not demonstrated an advantage over selective APRIL inhibition [e.g., sibeprenlimab (Voyxact)] and comparative efficacy is unknown given the lack of head-to-head trials with current FDA-approved IgAN-specific therapies. Lastly, efficacy as monotherapy is unknown, as atacicept (Trutakna) was studied in combination with RASis and SGLT2is, consistent with expected real-world use.

XXVII. Systemic corticosteroids are required to be tried and failed unless ineffective, not tolerated, or contraindicated prior to authorizing access to targeted-release budesonide (Tarpeyo), sibeprenlimab (Voyxact), atacicept (Trutakna) or povetacicept (Brand). 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.

XXVIII. The 2025 KDIGO IgAN guidelines have not been updated to include atrasentan (Vanrafia), sibeprenlimab (Voyxact) or atacicept (Trutakna). 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.

Focal segmental glomerulosclerosis (FSGS)

XXIX. Focal segmental glomerulosclerosis (FSGS) is a kidney condition where distinct patterns of scaring or injury are noted within the glomeruli by microscopic findings and may be accompanied by nephrotic syndrome (proteinuria >3.5g/day plus hypoalbuminemia (<30 g/L).

XXX. The FDA-approved indication for sparsentan (Filspari) in FSGS is limited to patients without nephrotic syndrome. Because nephrotic syndrome may fluctuate over time and requires assessment of multiple clinical features, including proteinuria, hypoalbuminemia, and edema, the policy requires prescriber attestation that the member does not have current nephrotic syndrome at the time of the request.

XXXI. FSGS is classified by either primary, secondary and genetic forms of FSGS—primary, no other identifiable causes and secondary, usually caused by some viral infections or certain drugs. Of note, the guidelines state that currently the appropriate use of genetic testing is unclear, citing unavailability or costly expertise to evaluate the results.

XXXII. Therapy for FSGS is mainly supportive care for all patients with persistent proteinuria—optimizing BP, RAS inhibition and limiting salt intake; however, immunosuppressants—glucocorticoids (first-line) and calcineurin inhibitors (second-line) are recommended for patients with primary FSGS presenting with nephrotic syndrome. For glucocorticoids, KDIGO guidelines recommend specific treatment with high-dose prednisone 1mg/kg/day up to 80 mg max (or every-other day dosing 2mg/kg up to 120 mg max) for at least 4 weeks and until remission is achieved with a max duration of 16 weeks. Prednisone may be discontinued if patients are experiencing significant side effects from prednisone and/or proteinuria is unremitting.

XXXIII. KDIGO guidelines suggests the following values as a indicators of remission, resistance or relapse in adults with FSGS: complete remission—*reduction of proteinuria to <0.3 g/d or PCR <300 mg/g (or <30 mg/mmol), stable serum creatinine and serum albumin >3.5 g/dl (or 35 g/l),* partial remission—*reduction of proteinuria to 0.3-3.5 g/d or PCR 300-3500 mg/g (or 30-350 mg/mmol) and a decrease >50% from baseline* and relapse—*proteinuria >3.5 g/d or PCR >3500 mg/g (or 350 mg/mmol) after complete remission has been achieved or an increase in proteinuria by >50% during partial remission.* For calcineurin inhibitors (CNI), treatment with cyclosporine or tacrolimus should be dose-adjusted to their corresponding trough levels, 100-175 ng/mL (83-146 nmol/L) and 5-10 ng/mL (6-12 nmol/L), respectively, for at least 4 to 6 months prior to determining the patient is resistant to CNI treatment.

XXXIV. Sparsentan (Filspari) was studied in a multicenter, randomized, double-blind, active-controlled Phase 3 trial comparing sparsentan at a target dose of 800 mg with irbesartan at a target dose of 300 mg in patients ages 8-75 for the treatment of primary and genetic FSGS (DUPLEX). Eligible patients had a biopsy-confirmed or a documented pathogenic variant in a podocyte protein associated with FSGS (genetic FSGS), a urinary protein-to-creatinine ratio (UPCR) of ≥ 1.5 g/g and an eGFR of ≥ 30 mL/min/1.73m^2, patients with FSGS from another cause were excluded; essentially only patients with primary FSGS or genetic FSGS were included. The key baseline characteristics were: mean age for both groups was 41 years of age, mostly White, mean eGFR of 63 mL/min/1.73m^2, median UPCR of 3.1 g/g, mean blood potassium level of 4.3 mmol/L, about 30% had a history of nephrotic syndrome and about 20% were noted to have genetic FSGS. Participants were required to undergo a two-week washout of renin-angiotensin system inhibitors (RASi) and were stratified by urinary protein-to-creatinine ratio of ≤3.5 or >3.5 for

patients ≥18 years of age, ≤2 or >2 for patients <18 years of age and eGFR ≥30 to <60 or ≥60 mL/min/1.73m^2 at screening then underwent treatment with the trial agent for 108 weeks.

XXXV. The DUPLEX trial was conducted in a two-part fashion. The endpoint for the first part was a prespecified interim analysis at 36 weeks to measure partial remission of proteinuria, "defined as a urinary protein-to-creatinine ratio of ≤1.5 [with protein and creatinine both measured in grams] and a >40% reduction in the ratio from baseline." Following the interim prespecified analysis, the primary efficacy endpoints for the DUPLEX trial were an annualized rate of change in eGFR from day 1 to week 108 for the United States, used as a secondary endpoint elsewhere and an annualized rate of change in eGFR slope from week 6 to week 108 (chronic slope) outside of the United States, and used as a secondary endpoint in the U.S. The results of the endpoint for the first part—remission of proteinuria at 36 weeks 42% (sparsentan) vs 26% (irbesartan) RR 1.55 (95% CI, 1.1 to 2.18; p =0.009). Neither primary efficacy endpoint was found to be statistically significant: -5.4 mL/min/1.73 m2 (sparsentan) vs -5.7 mL/min/1.73 m2 (irbesartan) with a treatment difference of 0.3 (95% CI, −1.7 to 2.4; p = 0.75) for the total eGFR slope and -4.8 mL/min/1.73 m2 (sparsentan) vs -5.7 mL/min/1.73 m2 (irbesartan) with a treatment difference of 0.9 (95% CI, −1.3 to 3; p = 0.42) for the chronic slope. Of note, not meeting statistical significance of an endpoint lends itself to interpreting all remaining subsequent endpoints with caution. The secondary endpoints studied were: complete remission of proteinuria at any time 18.5% (sparsentan; 34/184) vs 7.5% (irbesartan; 14/187) RR 2.47 (95% CI, 1.37 to 4.45), confirmed ≥ 40% reduction in eGFR, kidney failure or death 20.1% (sparsentan; 37/184) vs 23% (irbesartan; 43/187) RR 0.87 (95% CI, 0.6 to 1.26), confirmed ≥ 50% reduction in eGFR, kidney failure or renal death 11.4% (sparsentan; 21/184) vs 16.6% (irbesartan; 31/187) RR 0.68 (95% CI, 0.43 to 1.10) and kidney failure 6.5% (sparsentan; 12/184) vs 11.2% (irbesartan; 21/187) RR 0.58 (95% CI, 0.31 to 1.07). Adverse events were similar between groups except for hyperkalemia 31 (16.8%) for sparsentan group vs 20 (10.7%) for irbesartan, muscle spasms 25 (13.6) for sparsentan vs 15 (8%) irbesartan, hypotension 33 (17.9%) for sparsentan vs 21 (11.2%) irbesartan and anemia 24 (13%) for sparsentan vs 10 (5.3%). Of note, the adverse events leading to treatment discontinuation occurred more frequently in the sparsentan group, 26 patients (14.1%) than in the irbesartan group, 22 (11.8%) in the irbesartan group. It should be noted that improvement in eGFR would be considered the gold standard for assessing an impact a drug may have since it is the key marker used to determine renal function; however, it has been noted that studying eGFR is likely impractical due to sample size in relation to the duration of the study, where a duration of at least 3 years is needed for a true assessment of eGFR. Lastly, the minimal clinically important difference (MCID) has not been well established. The FDA notes proteinuria or UPCR may be used as a surrogate endpoint for investigating glomerular diseases associated with significant proteinuria.

XXXVI. In DUPLEX, patients without nephrotic syndrome had a 48% reduction in UPCR with sparsentan vs 27% with irbesartan, representing an adjusted 29% reduction (95% CI, 9% to 44%). However, in patients with nephrotic syndrome, UPCR reductions were similar between sparsentan and irbesartan, 39% vs 37%; an adjusted difference 3% (95% CI, -54% to 39%). Nephrotic syndrome was defined as a previous documented event in the medical history or currently presenting with nephrotic syndrome with the following: the concurrent presence of proteinuria >3.5 g/24 hours

(adults) or UPCR >2.0 g/g (pediatric patients <18 years of age), serum albumin <3.0 g/dL, and edema at baseline.

XXXVII. The DUPLEX trial was a well-designed multi-center, international, randomized, double-blind, active-controlled Phase 3 trial which compared sparsentan vs irbesartan for the treatment of FSGS. The trial design allows for strong internal validity; however, the reliance on surrogate endpoints lends itself to uncertainty for patient-important outcomes. The trial utilized proteinuria reduction as a surrogate efficacy endpoint during the first part of the study, which was statistically significant. The overall quality of evidence is considered moderate due to a lack of well-established MCID thresholds for the endpoints studied, although this is a recognized limitation within the glomerular disease space. While MCID thresholds in FSGS remain incompletely defined, the FDA has recently accepted proteinuria reduction as a surrogate endpoint in the treatment of FSGS, the DUPLEX trial being the first to utilize the endpoint. The exploratory composite endpoints provide optimistic insight for patient-important outcomes but fall short of usability, as the trial was not powered for statistical significance for these measures. Generalizability may be limited by underrepresented patient populations, specifically for Asian and Black ancestry.

Investigational or Not Medically Necessary Uses

I. Sparsentan (Filspari), atrasentan (Vanrafia) have not been FDA-approved, or sufficiently studied for safety and efficacy for the following conditions or settings listed below:
   A. Multi-drug regimens (e.g., atrasentan (Vanrafia), sparsentan (Filspari), budesonide (Tarpeyo), iptacopan (Fabhalta), sibeprenlimab (Voyxact), used in combination with each other)
   B. Secondary IgA nephropathy
   C. Newly diagnosed IgAN without high risk of disease progression
   D. Chronic kidney disease (CKD) other than primary IgAN
   E. Rheumatoid arthritis
      i. Atacicept (Trutakna) was evaluated in two Phase 2 trials in patients with rheumatoid arthritis between 2007 and 2010 (NCT00595413 and NCT00664521). Neither trial demonstrated meaningful clinical benefit despite expected biologic effects. Requests for this indication are considered experimental and investigational at this time.
   F. Systemic lupus erythematous
      i. Atacicept (Trutakna) was evaluated in a Phase 2b, randomized, placebo-controlled trial in patients with systemic lupus erythematous between 2013 and 2016 (NCT01972568). The study did not meet its primary efficacy endpoint despite demonstrating improvement in subgroup analyses. Requests for this indication are considered experimental and investigational at this time.

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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
Proximal Complement Inhibitors	Primary IgA nephropathy; at rapid risk of progression

Policy Implementation/Update

Action and Summary of Changes	Date
Added atacicept (Trutakna) and povetacicept (Brand) to policy.	11/2026
Amended policy name to "Targeted Agents for Glomerular Disease." Updated ">, ≥, <" symbols to text. Updated criteria to rephrase and assess adequate trials of supportive care (RAS inhibition and SGLT2 inhibitors). Removed attestation that the member does not have severe disease as indicated by MEST or MEST C score. Updated supportive evidence and experimental and investigational references.	10/2026
Corrected criteria for sparsentan (Filspari) in FSGS—removed requirement of immunosuppressants.	09/2026
Added criteria for sparsentan (Filspari) in focal segmental glomerulosclerosis (FSGS) without nephrotic syndrome; updated supporting evidence. Updated QL table, reformatted criteria.	05/2026
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