This promotional material for UK healthcare professionals has been developed and funded by CSL Vifor

FILSPARI® ▼
(sparsentan) tablets 200 mg/400 mg

Formulary application support pack

This document has been created to support healthcare professionals within the NHS who are completing a formulary application for FILSPARI (sparsentan), which is licensed for the treatment of adults with primary immunoglobulin A (IgA) nephropathy with a urine protein excretion ≥1.0 g/day (or urine protein-to-creatinine ratio ≥0.75 g/g)[(FILSPARI SmPC)].

Sparsentan has been authorised as a GB Orphan medicine. Orphan medicines are intended for use in rare conditions that are life-threatening or chronically debilitating[(MHRA, 2024)].

Prescribing information for FILSPARI 200 mg can be found here

Prescribing information for FILSPARI 400 mg can be found here

These external links go to a third party website.

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Adverse events should be reported. Reporting forms and information for the United Kingdom can be found at https://yellowcard.mhra.gov.uk/ or search for MHRA Yellow Card in the Google Play or Apple App Store. Adverse events should also be reported to Vifor Pharma Ltd. Tel +44 1276 853633. Email: MedicalInfo_UK@viforpharma.com

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Contents

Acronyms and abbreviations

ACE inhibitors	Angiotensin-converting enzyme inhibitors
ADR	Adverse drug reaction
AKI	Acute kidney injury
ALT	Alanine aminotransferase
AT_1R	Angiotensin II receptor type 1
ARB	Angiotensin receptor blocker
AST	Aspartate aminotransferase
CKD	Chronic kidney disease
DEARA	Dual endothelin angiotensin receptor antagonist
eGFR	Estimated glomerular filtration rate
ET_AR	Endothelin receptor type A
g/g	gram per gram
ERA	Endothelin receptor antagonists
ESKD	End-stage kidney disease
IgA nephropathy	Immunoglobulin A nephropathy
KDIGO	Kidney Disease: Improving Global Outcomes
NICE	National Institute for Health and Care Excellence
RAAS	Renin-angiotensin-aldosterone system
RAASi	Renin-angiotensin-aldosterone system inhibitors
RaDaR	UK National Registry of Rare Kidney
SGLT2 inhibitor	Sodium-glucose cotransporter-2 inhibitor
uACR	Urine albumin-to-creatinine ratio
ULN	Upper limit of normal
UP/C	Urine protein/creatinine
UPE	Urine protein excretion

Unmet need

Immunoglobulin A (IgA) nephropathy is a rare renal disease requiring dialysis or transplant if not appropriately managed[EMA, 2021]

In IgA nephropathy, the protein immunoglobulin A (IgA) accumulates in the kidneys. This affects the filtering function of the kidney, and blood and protein leak into the urine[NORD, 2023]. IgA nephropathy is a major cause of chronic kidney disease and kidney failure[Lee, 2023; Yeo, 2018].

IgA nephropathy affects:

- Around 4 in 10,000 people (400 people / million population), or ~ 27,000 people across the UK[EMA, 2021; ONS, 2024b]
- Adults of working age: mean age at diagnosis is 42 years[Pitcher, 2023]

Dialysis for end-stage kidney disease (ESKD) costs the NHS up to ~£35,000 per patient per year[Kidney Research UK, 2023; NHS England, 2025]

In 2022, over 1 in 10 (13.7%, n=1,909/3,245) patients having in-centre haemodialysis in the UK had glomerulonephritis[UKKA, 2024], of which IgA nephropathy is the most common form[Lee, 2023; Yeo, 2018].

ESKD leading to dialysis puts a significant cost burden on the NHS and a substantial impact on patients. On average, a patient on haemodialysis requires three sessions a week, for an average of 4 hours per session[Kidney Research UK, 2023]. In-centre haemodialysis costs range from £23,088 to £33,788 per year (based on NHS Payment System best practice tariff costs of £148 to £223 per session [HRG codes LD01A-LD014A])[NHS England, 2025].

Reducing proteinuria as much as possible from baseline is an important part of reducing the risk of kidney failure or death due to IgA nephropathy[KDIGO, 2025]

Proteinuria is the key modifiable risk factor in IgA nephropathy[Pitcher, 2023; Thompson, 2019]. People at risk of progressive loss of kidney function have proteinuria ≥0.5 g/day, while on or off treatment, and treatment/additional treatment should be started in all cases[KDIGO, 2025].

There is the need for a therapy which targets the endothelin and renin-angiotensin-aldosterone system (RAAS) pathways, critical to kidney damage[Komers, 2016]

Endothelin 1 and angiotensin II mediate processes that lead to IgA nephropathy progression through haemodynamic actions and mesangial cell proliferation, increased expression and activity of proinflammatory and profibrotic mediators, podocyte injury, and oxidative stress[FILSPARI SmPC].

People with IgA nephropathy may not achieve adequate proteinuria reduction even with optimised current treatment[Csomor, 2023; Lim, 2024].

A physician-completed questionnaire and patient chart review of 473 people living with IgA nephropathy (carried out between December 2022 – February 2023) observed that despite optimised treatment with an ACE inhibitor or an ARB (92% of patients), combined with an SGLT2 inhibitor (36%), or a systemic steroid (10%), or SLGT2 inhibitor and systemic steroid (5%)[Csomor, 2024]:

- 50% had proteinuria >1 g/day[Csomor, 2023]
- 25% had moderate to fast decline in eGFR[Csomor, 2023]
- 47% had a decrease in eGFR of ≥3 mL/year[Csomor, 2023]

The burden of IgA nephropathy impacts on everyday activities and quality of life of people living with the condition[Bensink, 2024; Kwon, 2021; NICE, 2023]

IgA nephropathy can affect mental health and emotional wellbeing[NICE, 2023; Kwon, 2021]. People with IgA nephropathy are impacted by the fear of progression to ESKD, the requirement for dialysis or transplantation, and the risk of IgA nephropathy recurrence post-transplant[Kwon, 2021]. Around 3 in 10 people living with IgA nephropathy experience anxiety (31%) or depression (31%)[Bensink, 2024]. Pain and fatigue impact on physical activity, with 27% of people with IgA nephropathy reporting impaired activity[Kwon, 2021; Bensink, 2024].

People with IgA nephropathy may need to spend time in hospital, especially when having dialysis; this can limit their capacity to stay in work, maintain relationships and fulfil day-to-day responsibilities[NICE, 2023]. Of people with IgA nephropathy who are employed, 13% report absenteeism, 18% report presenteeism, and 18% report an overall work productivity loss due to IgA nephropathy-related reasons[Bensink, 2024].

International guidelines

Kidney Disease: Improving Global Outcomes (KDIGO)Treatment guidelines (2025)

The mission of Kidney Disease: Improving Global Outcomes (KDIGO) is to "improve the care and outcomes of people with kidney disease worldwide through promoting coordination, collaboration, and integration of initiatives to develop and implement clinical practice guidelines"[(KDIGO, 2025)].

Practice points (PP) are consensus-based statements representing the expert judgment of the Work Group. They are issued when a clinical question did not have a systematic review performed, to help the implementation of the guidance from graded recommendations[(KDIGO, 2025)].

The strength of the Recommendations (R) are indicated as Level 1 or Level 2, with the certainty of the supporting evidence also graded:[(KDIGO, 2025)]

Grade	Implications for Clinicians	Implications for Policy
Level 1 "KDIGO recommend"	Most patients should receive the recommended course of action.	The recommendation can be evaluated as a candidate for developing a policy or a performance measure
Level 2 "KDIGO suggest"	Different choices will be appropriate for different patients. each patient needs to arrive at a management decision consistent with his or her values and preferences.	The recommendation is likely to require substantial debate and involvement of stakeholders before policy can be determined.

Grade	Certainty of evidence	Meaning
A	High	KDIGO are confident that the true effect is close to the estimate of the effect
B	Moderate	The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
C	Low	The true effect may be substantially different from the estimate of the effect.
D	Very low	The estimate of the effect is very uncertain, and often it will be far from the true effect.

Treatment of patients with IgA nephropathy who are at risk of progressive loss of kidney function and do not have a variant form of primary IgA nephropathy[(KDIGO, 2025)]	
PP 1.4.1.1	Because patients with IgA nephropathy are at risk of progressive loss of kidney function if they have proteinuria ≥0.5 g/d (or equivalent) while on or off treatment of IgAN, treatment or additional treatment should be considered in all such cases.
PP 1.4.2.1	The treatment goal in patients with IgA nephropathy at risk of progressive loss of kidney function is to reduce the rate of loss of kidney function to the physiological state (i.e., <1 ml/min/year for most adults) for the rest of the patient's life. The only validated early biomarker to help guide clinical decision making is urine protein excretion, which should be maintained at a minimum of <0.5 g/d (or equivalent), and ideally at <0.3 g/d (or equivalent), accepting that in

	some patients with extensive kidney scarring, this may not be possible and that multiple treatment strategies, including nonpharmacologic interventions, may be needed to achieve this.
PP 1.4.2.2	The primary focus of management should be to simultaneously: • Prevent or reduce IgA-containing immune complex (Ig-A-IC) formation and Ig-A-IC-mediated glomerular injury • Manage the consequences of existing IgAN-induced nephron loss (likely lifelong) Management of the consequences of IgA nephropathy-induced nephron loss should include: • Lifestyle advice, including information on dietary sodium restriction (<2 g/day), smoking and vaping cessation, weight control, and endurance exercise, as appropriate • Control of blood pressure with a target ≤120/70 mm Hg • Measures to reduce glomerular hyperfiltration and the impact of proteinuria on the tubulointerstitium, using renin-angiotensin system (RAAS) blockade or dual endothelin angiotensin receptor antagonism, singly or in combination with a sodium-glucose cotransporter-2 inhibitor (SGLT2i), and • A thorough cardiovascular risk assessment and commencement of appropriate interventions as per local guidelines, as necessary

Managing the IgA nephropathy-specific drivers for nephron loss[KDIGO, 2025]	
R 1.4.3.1	KDIGO suggest treatment with a 9-month course of targeted-release budesonide for patients who are at risk of progressive kidney function loss with IgA nephropathy *(2B)*.
PP 1.4.3.1	Factors to consider before using targeted-release budesonide: • A 9-month treatment course of targeted-release budesonide, may not result in a sustained clinical response in terms of proteinuria reduction or eGFR stabilisation • Data on the safety and efficacy of additional courses of targeted-release budesonide are awaited

Managing the response to IgA nephropathy-induced nephron loss[KDIGO, 2025]	
R 1.4.4.1	KDIGO recommend all patients with IgA nephropathy be treated with an optimised maximally tolerated dose of either an ACE inhibitor or an ARB *(1B)*.
R 1.4.4.2	KDIGO suggest all patients who are at risk of progressive kidney function loss with IgA nephropathy be treated with sparsentan *(2B)*.
PP 1.4.4.3	Sparsentan is a DEARA and should not be prescribed together with a RAAS inhibitor because sparsentan already combines RAASi with an endothelin antagonist in a single molecule.

R 1.4.4.3	KDIGO suggest all patients who are at risk of progressive kidney function loss with IgA nephropathy be treated with a SGLT-2i *(2B)*.
PP 1.5.4.	Preconception counselling should include a discussion on cessation of RAASi, SGLT2i, sparsentan, targeted-release budesonide, and systemic glucocorticoids. Blood pressure control should be optimised with alternative antihypertensive medications prior to conception.

Supporting information in the KDIGO guidelines states: "The PROTECT trial required all patients to have persistent proteinuria, despite first taking optimised maximally tolerated RAASi. The observed greater proteinuria reduction and eGFR preservation with combined dual blockade of the renin-angiotensin and endothelin systems with sparsentan suggest that this approach may be an appropriate first-line approach to manage the responses of IgAN-induced nephron loss in contrast to the RAASi-first approach"[(KDIGO, 2025)].

NICE technology appraisals

NOTE: The NICE technology appraisals for dapagliflozin and empagliflozin are for treating chronic kidney disease, not specifically IgA nephropathy.

NICE Technology Appraisal TA1074 (2025): Sparsentan for treating primary IgA nephropathy[NICE TA1074]

Sparsentan can be used as option to treat primary immunoglobulin A nephropathy (IgAN) in adults with a:

- urine protein excretion of 1.0 g/day or more, or
- urine protein-to-creatinine ratio (UPCR) of 0.75 g/g or more.

Sparsentan should be stopped after 36 weeks if a person's UPCR:

- is 1.76 g/g or more and
- has not reduced by 20% or more since starting sparsentan

It can only be used if the company provides it according to the commercial arrangement

These recommendations are not intended to affect treatment with sparsentan that was started in the NHS before this guidance was published. People having treatment outside this recommendation may continue without change to the funding arrangements in place for them before this guidance was published, until they and their NHS healthcare professional consider it appropriate to stop.

NICE technology appraisal TA775 (2022): Dapagliflozin for treating chronic kidney disease[NICE TA775, 2022]

Dapagliflozin is recommended as an option for treating chronic kidney disease (CKD) in adults. It is recommended only if:

- it is an add-on to optimised standard care including the highest tolerated licensed dose of ACE inhibitors or ARBs, unless these are contraindicated, and
- people have an estimated glomerular filtration rate (eGFR) of 25 ml/min/1.73 m^2 to 75 ml/min/1.73 m^2 at the start of treatment and:
  - have type 2 diabetes or
  - have a urine albumin-to-creatinine ratio (uACR) of 22.6 mg/mmol or more

NICE technology appraisal TA942 (2023): Empagliflozin for treating chronic kidney disease[NICE TA942, 2023]

Empagliflozin is recommended as an option for treating CKD in adults only if:

- it is an add-on to optimised standard care including the highest tolerated licensed dose of ACE inhibitors or ARBs, unless these are contraindicated, and
- people have an eGFR of:
  - 20 mL/min/1.73m^2 to <45 mL/min/1.73m^2 or
  - 45 mL/min/1.73m^2 to 90 mL/min/1.73m^2 and either:
    - A uACR ratio of 22.6 g/mmol or more, or Type 2 diabetes
- If people with the condition and their clinicians consider empagliflozin to be one of a range of suitable treatments (including dapagliflozin), after discussing the advantages and disadvantages of all the options, use the least expensive. Take account of administration costs, dosage, price per dose and commercial arrangements

NICE technology appraisal TA937 (2023): Targeted-release budesonide for treating primary IgA nephropathy[NICE TA937, 2023]

Targeted-release budesonide is recommended as an option for treating primary immunoglobulin A nephropathy when there is a risk of rapid disease progression in adults with a urine protein-to-creatinine ratio of 1.5 g/g or more. Targeted-release budesonide is recommended only if:

- it is an add-on to optimised standard care including the highest tolerated licensed dose of ACE inhibitors or ARBs, unless these are contraindicated
- the company provides it according to the commercial arrangement

Relationship among categories for albuminuria and proteinuria[KDIGO, 2025]

Measure	Normal to mildly increased	Moderately increased	Severely increased
Albumin-to-creatinine ratio			
mg/mmol	<3	3-30	>30
mg/g	<30	30-300	>300
Protein-to-creatinine ratio			
mg/mmol	<15	15-50	>50
mg/g	<150	150-500	>500

Relationships among measurement methods within a category are not exact. The conversions are rounded for pragmatic reasons. For an exact conversion from mg/g of creatinine to mg/mmol of creatinine, multiply by 0.113. Creatinine excretion varies with age, sex, race and diet; therefore, the relationship among these categories is approximate only[KDIGO, 2025].

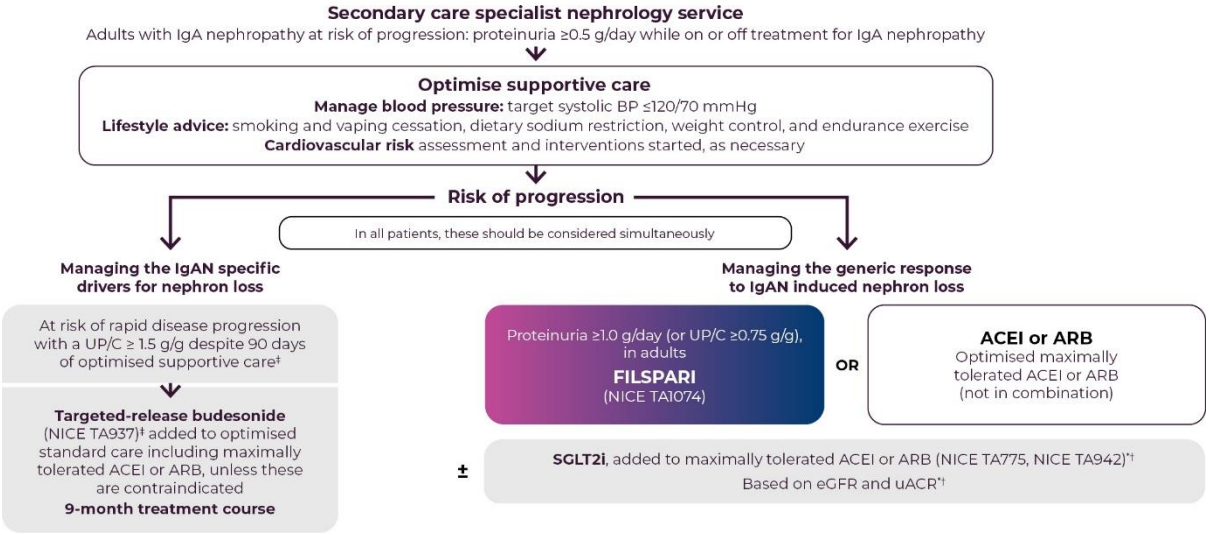
To convert mg/mmol to g/mmol, divide by 1,000; e.g. 3 mg/mmol = 0.003 g/mmol; 50 mg/mol = 0.05 g/mmol

To convert mg/g to g/g, divide by 1,000; e.g. 30 mg/g = 0.03 g/g; 150 mg/g = 0.15 g/g

ACR: albumin-to-creatinine ratio. PCR: protein-to-creatinine ratio.

Treatment pathway for local adaptation

In general, patients have clinic appointments every 3-6 months, or more frequently if they require monitoring and follow-up.



Based on KDIGO guidelines 2025[KDIGO, 2025], NICE technology appraisals[NICE TA1074; NICE TA937, 2023; NICE TA775, 2022; NICE TA942, 2023], and FILSPARI Summary of Product Characteristics[FILSPARI SmPC]

*NICE TA942: Empagliflozin is recommended as an option for treating CKD in adults only if: (a) it is an add-on to optimised standard care including the highest tolerated licensed dose of ACE inhibitors or ARBs, unless these are contraindicated, and (b) people have an eGFR of: 20 mL/min/1.73m^2 to <45 mL/min/1.73m^2 or 45 mL/min/1.73m^2 to 90 mL/min/1.73m^2 and either: a uACR ratio of 22.6 g/mmol or more, or type 2 diabetes. If people with the condition and their clinicians consider empagliflozin to be one of a range of suitable treatments (including dapagliflozin), after discussing the advantages and disadvantages of all the options, use the least expensive. Take account of administration costs, dosage, price per dose and commercial arrangements[NICE TA942, 2023]

†NICE TA775 : Dapagliflozin is recommended as an option for treating CKD in adults. It is recommended only if: (a) it is an add-on to optimised standard care including the highest tolerated licensed dose of ACE inhibitors or ARBs, unless these are contraindicated, and (b) people have an eGFR of 25 ml/min/1.73 m^2 to 75 ml/min/1.73 m^2 at the start of treatment and have type 2 diabetes or have a urine albumin-to-creatinine ratio (uACR) of 22.6 mg/mmol or more. This recommendation is not intended to affect treatment with dapagliflozin that was started in the NHS before this NICE guidance was published. People having treatment outside this recommendation may continue without change to the funding arrangements in place for them before this guidance was published, until they and their NHS clinician consider it appropriate to stop[NICE TA775, 2022]

‡NICE TA937: Targeted-release budesonide is recommended as an option for treating primary immunoglobulin A nephropathy when there is a risk of rapid disease progression in adults with a UPCR of 1.5 g/g or more. Targeted-release budesonide is recommended only if: (a) it is an add-on to optimised standard care including the highest tolerated licensed dose of ACEI or ARBs, unless these are contraindicated, and (b) the company provides it according to the commercial arrangement. This recommendation is not intended to affect treatment with targeted-release budesonide that was started in the NHS before this guidance was published. People having treatment outside this recommendation may continue without change to the funding arrangements in place for them before this guidance was published, until they and their NHS clinician consider it appropriate to stop. The course of treatment with targeted-release budesonide is 9 months. The marketing authorisation states that retreatment may be considered at the discretion of the treating physician, but the safety and efficacy of retreatment with targeted-release budesonide has not been established[NICE TA937, 2023]

ACEI: angiotensin-converting enzyme inhibitors. ARB: angiotensin receptor blockers. CKD: chronic kidney disease. eGFR: estimated glomerular filtration rate. IgA: immunoglobulin A. KDIGO: Kidney Disease Improving Global Outcomes. RAASi: renin-angiotensin-aldosterone system inhibitors. SGLT2i: sodium-glucose cotransporter-2 inhibitor. TA: technology appraisal. uACR: urine albumin-to-creatine ratio. UPCR: urine protein-to-creatinine ratio.

Sparsentan

Sparsentan is the first dual endothelin angiotensin receptor antagonist (DEARA) indicated for the treatment of adults with primary IgA nephropathy with a urine protein excretion ≥1.0 g/day (or urine protein-to-creatinine ratio ≥0.75 g/g). Sparsentan is taken as a once-daily oral tablet[(FILSPARI SmPC; Campbell, 2023)].

Sparsentan inhibits activation of both endothelin receptor type A (ET_AR) and angiotensin II receptor (AT_1R), and thereby reduces proteinuria and slows the progression of kidney disease[(FILSPARI SmPC)]. Sparsentan is the first and only non-immunosuppressive IgA nephropathy therapy that targets both pathways[(Campbell, 2023; Syed, 2023)].

For full prescribing information, see the FILSPARI Summary of Product Characteristics[(FILSPARI SmPC)].

Place in therapy

Sparsentan is a long-term foundational therapy option for patients with IgA nephropathy who are at risk of progressive kidney function loss[(FILSPARI SmPC; Rovin, 2023a)].

Sparsentan can be used as option to treat primary immunoglobulin A nephropathy (IgAN) in line with the NICE recommendation (TA1074), in adults with a:[(NICE TA1074)]

- urine protein excretion of 1.0 g/day or more, or
- urine protein-to-creatinine ratio (UPCR) of 0.75 g/g or more.

Sparsentan should be stopped after 36 weeks if a person's UPCR:[(NICE TA1074)]

- is 1.76 g/g or more and
- has not reduced by 20% or more since starting sparsentan

Co-administration of sparsentan, a dual endothelin angiotensin receptor antagonist, with ARBs or endothelin receptor antagonists is contraindicated. The use of sparsentan in combination with ACE inhibitors should be done with caution, and blood pressure, potassium and kidney function should be monitored. Co-administration of sparsentan with mineralocorticoid (aldosterone) receptor inhibitors is expected to be associated with an increased risk of hyperkalaemia[(FILSPARI SmPC)].

Sparsentan has a different mechanism of action to SGLT2 inhibitors and targeted-release budesonide[(Barratt, 2024)]. By inhibiting activation of both ET_AR and AT_1R, sparsentan targets a different part of the treatment pathway to SGLT2 inhibitors and targeted-release budesonide[(FILSPARI SmPC; Barratt, 2024)]. In clinical practice these may be used in combination[(Barratt, 2024)].

Prescribers and Red-Amber-Green status

Sparsentan is suitable for initiation and prescribing by specialists experienced in the treatment of IgA nephropathy, within secondary care clinics. Primary care prescriber initiation or continuation of therapy is not recommended: specialist knowledge, monitoring, dose adjustment and further evaluation in use is required.

Sparsentan: Key drug details

Refer to the FILSPARI Summary of Product Characteristics for full prescribing information[(FILSPARI SmPC)].

Product name	FILSPARI (sparsentan) 200 mg film-coated tablets[(FILSPARI SmPC)] FILSPARI (sparsentan) 400 mg film-coated tablets[(FILSPARI SmPC)]
Licensed indication	The treatment of adults with primary immunoglobulin A nephropathy (IgA nephropathy) with a urine protein excretion ≥1.0 g/day (or urine protein-to-creatinine ratio ≥ 0.75 g/g)[(FILSPARI SmPC)] Sparsentan has been authorised as a GB Orphan medicine. Orphan medicines are intended for use against rare conditions that are life-threatening or chronically debilitating. To qualify as an orphan medicine, certain criteria, for example concerning the rarity of the disease and the lack of currently available treatments, must be fulfilled [(MHRA, 2024)]
Pharmaceutical form	200 mg film-coated tablets; 400 mg film-coated tablets[(FILSPARI SmPC)]
Mechanism of action	Sparsentan is a single molecule that functions as a high affinity, dual antagonist of both the ET_AR and AT_1R. Endothelin 1, via ET_AR and angiotensin II, via AT_1R_l, mediate processes that lead to IgA nephropathy progression through haemodynamic actions and mesangial cell proliferation, increased expression and activity of proinflammatory and profibrotic mediators, podocyte injury and oxidative stress[(FILSPARI SmPC)]
Dose and method of administration	RAAS inhibitors must be discontinued prior to sparsentan initiation[(FILSPARI SmPC)] For oral use[(FILSPARI SmPC)] Sparsentan should be initiated at a dose of 200 mg once daily for 14 days, then increased to a maintenance dose of 400 mg once daily, dependent upon tolerability[(FILSPARI SmPC)] Sparsentan tablets should be swallowed whole with water to avoid the bitter taste. Sparsentan can be taken with or without food[(FILSPARI SmPC)] For patients experiencing tolerability issues (systolic blood pressure ≤100 mmHg, diastolic blood pressure ≤60 mmHg, worsening oedema, or hyperkalaemia), adjustment of concomitant medicinal products, followed by a temporary down-titration or discontinuation of sparsentan is recommended[(FILSPARI SmPC)] When resuming treatment with sparsentan after interruption, repeating the initial dosing schedule may be considered. Interruption of treatment preceded, or not, by dose reduction of sparsentan, may be considered based on persisting hypotension or changes in liver function[(FILSPARI SmPC)]
Missed dose	If a dose is missed, the dose should be skipped and the next dose taken at the regularly scheduled time. Double or extra doses should not be taken[(FILSPARI SmPC)]

Monitoring	**Exclude pregnancy** before, during and for 1 month after treatment with sparsentan has stopped. The frequency of recommended pregnancy testing should be determined by the method of contraception use and the associated likelihood of contraceptive failure. Women of childbearing potential have to use reliable contraception during and up to 1 month after treatment has stopped[(FILSPARI SmPC)] **Periodic monitoring of serum creatinine and serum potassium** levels should be performed in patients at risk[(FILSPARI SmPC)] **Serum aminotransferase levels and total bilirubin** should be monitored prior to initiation of treatment and then continued monitoring every 3 months[(FILSPARI SmPC)] Patients should be **monitored for signs of hepatic injury**. If patients develop sustained, unexplained, clinically significant ALT and/or AST elevation, or if elevations are accompanied by an increase in bilirubin >2 x ULN, or if ALT and/or AST elevation is accompanied by signs or symptoms of hepatic injury (e.g., jaundice), sparsentan therapy should be discontinued. Consider re-initiation of sparsentan only when hepatic enzyme levels and bilirubin return to pretreatment values, and only in patients without clinical symptoms of hepatoxicity[(FILSPARI SmPC)] An additional risk minimisation measure will be in place for sparsentan, namely a patient card within the pack to alert patients to the risks with pregnancy and the need for regular monitoring of liver function. This card will also be available on the electronic medicines compendium (eMC).
Special populations	**Elderly:** No dose adjustment is required in elderly patients[(FILSPARI SmPC)] **Hepatic impairment:** No dose adjustment of sparsentan is required in patients with mild or moderate hepatic impairment (Child-Pugh A or Child-Pugh B). Clinical experience in patients with moderate hepatic impairment is limited; sparsentan should be used with caution in these patients. Sparsentan has not been studied in patients with severe hepatic impairment (Child-Pugh C) and is therefore not recommended for use in these patients. Clinical experience with aspartate aminotransferase (AST) / alanine aminotransferase (ALT) values >2 x upper limit of normal (ULN) is limited; therefore, sparsentan should not be initiated in patients with AST or ALT >2 x ULN[(FILSPARI SmPC)] **Renal impairment:** No dose adjustment is required in patients with mild or moderate kidney disease. Clinical experience in patients with severe kidney disease is limited; therefore sparsentan is not recommended in these patients. Sparsentan has not been studied in patients who have received a kidney transplant; therefore sparsentan should be used with caution in these patients. Sparsentan has not been studied in patients undergoing dialysis. Initiation of sparsentan is not recommended in these patients[(FILSPARI SmPC)] **Paediatric population**: The safety and efficacy of sparsentan in children <18 years of age with IgA nephropathy has not been established. No data are available[(FILSPARI SmPC)]

Contraindications	• Hypersensitivity to the active substance or excipients[(FILSPARI SmPC)] • Pregnancy[(FILSPARI SmPC)] • Coadministration of ARBs, endothelin receptor antagonists or renin inhibitors[(FILSPARI SmPC)]
Special warnings and precautions for use	**Women of childbearing potential:** Sparsentan treatment must only be initiated in women of childbearing potential when the absence of pregnancy has been verified. Exclude pregnancy before, during and for 1 month after treatment with sparsentan has stopped. The frequency of recommended pregnancy testing should be determined by the method of contraception used and the associated likelihood of contraceptive failure. Women of childbearing potential have to use effective contraception during and up to 1 month after treatment has stopped (see above: Monitoring)[(FILSPARI SmPC)] **Hypotension:** Hypotension has been associated with the use of RAAS inhibitors, including sparsentan. Hypotension may occur during treatment with sparsentan and is reported more frequently in elderly patients[(FILSPARI SmPC)] In patients at risk of hypotension, consider elimination or adjusting other antihypertensive medicinal products and maintaining appropriate volume status. If hypotension develops despite elimination or reduction of other antihypertensive medicinal products, dose reduction or dose interruption of sparsentan should be considered. A transient hypotensive response is not a contraindication to further dosing of sparsentan; treatment can be resumed once blood pressure has stabilised[(FILSPARI SmPC)] If hypotension persists despite elimination or reduction of antihypertensive medicinal products, sparsentan dosing should be reduced to the initial starting dose until blood pressure stabilises. Dose interruption of treatment with sparsentan should be considered if symptoms of hypotension persist after 2 weeks of dose reduction. Sparsentan should be used with caution in patients with systolic blood pressure values ≤ 100 mmHg. Sparsentan should not be uptitrated in patients with systolic blood pressure values ≤ 100 mmHg[(FILSPARI SmPC)] **Impaired kidney function:** A transient increase in serum creatinine has been associated with RAAS inhibitors, including sparsentan. A transient increase in creatinine may occur, especially when initiating sparsentan. Periodic monitoring of serum creatinine and serum potassium should be performed in patients at risk. Sparsentan should be used with caution in patients with bilateral renal artery stenosis. Due to limited clinical experience in patients with an eGFR <30 mL/min/1.73m^2, sparsentan is not recommended in these patients[(FILSPARI SmPC)] **Fluid retention:** Fluid retention has been associated with medicinal products that antagonise endothelin type A receptor (ETAR), including sparsentan. If fluid retention develops during treatment with sparsentan, treatment with diuretics is recommended, or the dose of existing diuretics should be increased before modifying the sparsentan dose. Treatment with diuretics can be considered in patients with

evidence of fluid retention before the start of sparsentan treatment(FILSPARI SmPC)

Sparsentan has not been studied in patients with heart failure; therefore sparsentan should be used with caution in patients with heart failure(FILSPARI SmPC)

Liver function: Elevations in ALT or AST of at least 3 x ULN have been observed with sparsentan. No concurrent elevations in bilirubin >2 x ULN or cases of liver failure have been observed in sparsentan-treated patients. Therefore, to reduce the risk of potential serious hepatotoxicity, serum aminotransferase levels and total bilirubin should be monitored prior to initiation of treatment and then continue monitoring every three months(FILSPARI SmPC)

Patients should be monitored for signs of hepatic injury. If patients develop sustained, unexplained, clinically significant ALT and/or AST elevation, or if elevations are accompanied by an increase in bilirubin >2 x ULN, or if ALT and/or AST elevation is accompanied by signs or symptoms of hepatic injury (e.g., jaundice), sparsentan therapy should be discontinued(FILSPARI SmPC)

Consider re-initiation of sparsentan only when hepatic enzyme levels and bilirubin return to pretreatment values and only in patients without clinical symptoms of hepatotoxicity. Avoid initiation of sparsentan in patients with elevated aminotransferase (>2 x ULN) prior to drug initiation(FILSPARI SmPC)

There is limited clinical experience with moderate hepatic impairment. Therefore, sparsentan should be used with caution in these patients(FILSPARI SmPC)

Dual blockade of the renin-angiotensin-aldosterone system (RAAS): There is evidence that the concomitant use of ACE inhibitors, angiotensin II receptor blockers or aliskiren increases the risk of hypotension, hyperkalaemia and decreased renal function (including acute renal failure). Dual blockade of RAAS through the combined use of ACE inhibitors, angiotensin II receptor blockers (partly a mechanism of sparsentan) or renin inhibitors is therefore not recommended. If dual blockade therapy is considered absolutely necessary, this should only occur under specialist supervision and subject to frequent close monitoring of renal function, electrolytes and blood pressure(FILSPARI SmPC)

Hyperkalaemia: Treatment should not be initiated in patients with serum potassium >5.5 mmol/L. As with other medicinal products that affect the RAAS, hyperkalaemia may occur during treatment with sparsentan, especially in the presence of renal impairment and/or heart failure. Close monitoring of serum potassium in patients at risk is recommended. If patients experience clinically significant hyperkalaemia adjustment of concomitant medicinal products, or temporary down–titration or discontinuation is recommended. If serum potassium level is >5.5 mmol/L discontinuation should be considered(FILSPARI SmPC)

Lactose: Patients with rare hereditary problems of galactose intolerance, total lactase deficiency, or glucose-galactose malabsorption should not take FILSPARI(FILSPARI SmPC)

	Sodium: FILSPARI contains less than 1 mmol sodium (23 mg) per tablet; that is to say essentially 'sodium-free'(FILSPARI SmPC)
Pregnancy, breastfeeding and fertility	**Pregnancy:** There are no or limited data from the use of sparsentan in pregnant women. Studies in animals have shown reproductive toxicity. Sparsentan is contraindicated during pregnancy(FILSPARI SmPC) **Breastfeeding:** Physicochemical data suggest excretion of sparsentan in human milk. A risk to the newborn/infant cannot be excluded. Sparsentan should not be used during breastfeeding(FILSPARI SmPC) **Fertility:** There are no data on the effects of sparsentan on human fertility. Animal data did not indicate any impairment of male or female fertility(FILSPARI SmPC)
Interactions with other medicinal products	**Refer to the FILSPARI Summary of Product Characteristics for full details of drug-drug interactions.** **Concomitant use with ARBs, ERAs and renin inhibitors:** Concomitant use with ERAs such as bosentan, ambrisentan, macitentan, ARBs such as irbesartan, losartan, valsartan, candesartan, telmisartan or renin inhibitors such as aliskiren, is contraindicated(FILSPARI SmPC) **Concomitant use with ACE and mineralocorticoid receptor inhibitors:** Coadministration of sparsentan with mineralocorticoid (aldosterone) receptor inhibitors such as spironolactone and finerenone is expected to be associated with increased risk of hyperkalaemia(FILSPARI SmPC) There are no data on the combination of sparsentan and ACE inhibitors such as enalapril or lisinopril. Dual blockade of the RAAS system through the combined use of ACE inhibitors, angiotensin II blockers or aliskiren, is associated with a higher frequency of adverse events such as hypotension, hyperkalaemia and decreased renal function, compared to the use of a single RAAS-acting agent(FILSPARI SmPC) The use of sparsentan in combination with ACE inhibitors should be done with caution, and blood pressure, potassium and kidney function should be monitored(FILSPARI SmPC) **Concomitant use with potassium supplements and potassium-sparing diuretics:** Hyperkalaemia may occur in patients treated with medicinal products that antagonise the AT_1R; concomitant use of potassium supplements, potassium-sparing diuretics such as spironolactone, eplerenone, triamterene or amiloride, or salt substitutes containing potassium may increase the risk of hyperkalaemia and is not recommended(FILSPARI SmPC) **Effects of other medicinal products on sparsentan** Sparsentan is primarily metabolised by cytochrome P450 (CYP) 3A(FILSPARI SmPC) **Strong and moderate CYP3A4 inhibitors:** Co-administration of sparsentan with strong CYP3A inhibitors is not recommended(FILSPARI SmPC) Co-administration of sparsentan with a moderate CYP3A inhibitors should be done with caution(FILSPARI SmPC)

	CYP3A4 inducers: Sparsentan is a CYP3A substrate; co-administration with a moderate or strong CYP3A inducer is not recommended[FILSPARI SmPC] **Gastric acid reducing agents:** Gastric pH modifying agents such as antacids, proton pump inhibitors, and histamine 2 receptor agonists can be used with sparsentan[FILSPARI SmPC] **Effects of sparsentan on other medicinal products** *In vitro,* sparsentan both inhibited and induced CYP3A, and induced CYP2B6, CYP2C9 and CYP2C19[FILSPARI SmPC] No dose adjustment is required when combining sparsentan at *steady state* with a CYP3A4 or CYP2B6 substrate[FILSPARI SmPC] Coadministration of sparsentan with a CYP2C9 substrate or a CYP2C19 substrate should be done with caution[FILSPARI SmPC] *Initiation* of sparsentan with a CYP3A4 substrate should be done with caution[FILSPARI SmPC] *In vitro,* sparsentan is an inhibitor of P-gp, BCRP, OATP1B3 and OAT3 transporters at relevant concentrations[FILSPARI SmPC] Coadministration of sparsentan with P-gp inhibition substrates should be done with caution if it is known that P-gp inhibition has a significant effect on the absorption[FILSPARI SmPC] No dose adjustment is required when combining sparsentan at steady state with a OATP1B1, OATP1B3 or BCRP substrate[FILSPARI SmPC]
Effects on ability to drive and use machines	Sparsentan may have minor influence on the ability to drive and use machines. Dizziness may occur while taking sparsentan; patients with dizziness should be advised to refrain from driving or using machines until symptoms have subsided[FILSPARI SmPC]
Overdose	Sparsentan has been administered in doses of up to 1600 mg/day in healthy subjects without evidence of dose limiting toxicities. Patients who experience overdose (possibly experiencing signs and symptoms of hypotension) should be monitored closely and appropriate symptomatic treatment given[FILSPARI SmPC]
Shelf life and storage conditions	Shelf life: 4 years[FILSPARI SmPC] No special storage conditions are required[FILSPARI SmPC]

Service implications

Generally, patients with IgA nephropathy have clinic appointments every 3 months, which are increased to a monthly basis for those patients with proteinuria or who require more frequent monitoring.

Monitoring

- Pregnancy must be excluded before, during and for 1 month after treatment with sparsentan has stopped. The frequency of recommended pregnancy testing should be determined by the method of contraception use and the associate likelihood of contraceptive failure. Women of childbearing potential have to use reliable contraception during and up to 1 month after treatment has stopped[(FILSPARI SmPC)]
- Periodic monitoring of serum creatinine and serum potassium levels should be performed in patients at risk[(FILSPARI SmPC)]
- Serum aminotransferase levels and total bilirubin should be monitored prior to initiation of treatment and then continued monitoring every 3 months. Patients should be monitored for signs of hepatic injury. If patients develop sustained, unexplained, clinically significant ALT and/or AST elevation, or if elevations are accompanied by an increase in bilirubin >2 x ULN, or if ALT and/or AST elevation is accompanied by signs or symptoms of hepatic injury (e.g., jaundice), sparsentan therapy should be discontinued. Consider re-initiation of sparsentan only when hepatic enzyme levels and bilirubin return to pretreatment values, and only in patients without clinical symptoms of hepatoxicity[(FILSPARI SmPC)]

Financial implications

Sparsentan is listed as a high cost drug excluded from the NHS England Payment System price calculations[(NHS England, 2025)], and is commissioned by Integrated Care Boards (ICBs).

Sparsentan is not listed on the NHS England specialised commissioning list of high cost drugs for specialised services, meaning that funding is the responsibility of ICBs.

Sparsentan UK pricing and purchasing

The NHS list price of FILSPARI (sparsentan) is £3,401.71 per pack of 30 x 200 mg tablets or 30 x 400 mg tablets.

A discount is available for NHS organisations. The Patient Access Scheme (PAS) price can be obtained via the NHS England Commercial Access and Pricing (CAP) portal.

Orders can be made through Alloga UK using the following codes:

- Sparsentan (FILSPARI) 200 mg: APC0850
- Sparsentan (FILSPARI) 400 mg: APC0857

Estimated patient numbers

The eligible population based on the indication - the treatment of adults with primary immunoglobulin A nephropathy with a urine protein excretion (UPE) ≥1.0 g/day (or UP/C ≥0.75 g/g) has been calculated as follows:

- The proportion of the adult population (18+ years old) in derived from ONS national population projection data(ONS, 2024a)
- An estimate of the proportion of this population with IgA nephropathy, 0.04%, was based on the prevalence of IgA nephropathy across Europe (4 cases per 10,000)(EMA, 2021)
- Due to the limited clinical experience in patients with severe kidney disease (eGFR < 30 mL/min/1.73 m^2; CKD stage 4), it is not recommended to initiate sparsentan in these patients(FILSPARI SmPC); therefore, only patients in CKD stages 1-3 will commence treatment(CSL Vifor, 2024). Patients may continue on treatment should they progress to CKD stage 4. Based on pharmacokinetic data, no dose adjustment can be recommended for patients with severe kidney disease (CKD stage 4, eGFR <30 mL/min/1.73 m^2)(FILSPARI SmPC)
- The proportion of adults with IgA nephropathy in CKD stages 1-3 at diagnosis, with UPE ≥1.0 g/day has been estimated at 47.2%(CSL Vifor, 2024)

Table 1: Estimated eligible patient population for sparsentan(CSL Vifor, 2024)

	England	Wales	Scotland	Northern Ireland
Population (mid-2023)(ONS, 2024a)	57,690,323	3,164,404	5,490,100	1,920,382
Adult population (≥18 years)(ONS, 2024a)	45,691,677	2,544,436	4,476,570	1,483,760
Population with IgA nephropathy (0.04%)(EMA, 2021)	18,277	1,107	1,791	594
IgA nephropathy population with CKD 1-3 (48%)(CSL Vifor, 2024)	8,773	489	860	285
IgA nephropathy, CKD 1-3 population with UPE ≥1 g/day (total eligible population for sparsentan as per licensed indication) (47%)(CSL Vifor, 2024)	4,123	230	404	134
Eligible population for sparsentan as per licensed indication per 1 million population (estimated)	**72**	**72**	**73**	**70**

CKD: chronic kidney disease. IgA nephropathy: immunoglobulin A nephropathy. UPE: urine protein excretion.

Clinical efficacy: PROTECT phase 3 trial

PROTECT was a double-blind, randomised, active-controlled, phase 3 trial evaluating the effect of sparsentan on proteinuria and kidney function[(Rovin, 2023a; FILSPARI SmPC)]. PROTECT is one of the largest interventional trials in patients with IgA nephropathy, comparing a novel therapeutic (sparsentan) to an active control (irbesartan)[(Rovin, 2023a)].

Study design

PROTECT included a 114-week double-blind period (up to 110 weeks of randomly assigned drug, followed by 4 weeks without study drug), followed by a 156-week open-label extension period (total 270 weeks)[(Rovin, 2023a)].

Patients

A total of 404 patients ≥18 years of age with biopsy-proven primary IgA nephropathy, with an eGFR ≥30 mL/min/1.73 m^2 and total urine protein excretion ≥1.0 g/day were enrolled. Prior to enrolment, patients were on the maximum tolerated dose of an ACE inhibitor and/or ARB for at least 3 months. ACE inhibitors and ARBs were discontinued prior to initiation of sparsentan. Patients with a baseline serum potassium value ≥5.5 mmol/L were excluded[(FILSPARI SmPC; Rovin, 2023a)].

Baseline characteristics for eGFR and proteinuria were comparable between the two groups. The overall population had a mean eGFR of 57 mL/min/1.73 m^2, and a median urine protein/creatinine (UP/C) ratio of 1.24 g/g. The mean age was 46 years (range 18-76 years), 70% were male, 67% white, 28% Asian, 1% Black or African American, and 3% other race[(FILSPARI SmPC)].

Interventions

Patients were randomised 1:1 to sparsentan (N=202) or irbesartan (N=202). Randomisation was stratified by screening eGFR (30 to <60 or ≥60 mL/min/1.73 m^2), and screening urine protein excretion (≤1.75 or >1.75 g/day)[(Rovin, 2023a)].

Treatment was initiated with sparsentan 200 mg once daily or irbesartan 150 mg once daily. After 14 days, the doses were titrated, as tolerated, to sparsentan 400 mg once daily or irbesartan 300 mg once daily. Dose tolerance was defined as systolic blood pressure >100 mmHg and diastolic blood pressure >60 mmHg after 2 weeks and no adverse events (e.g. worsening oedema), or laboratory findings (e.g. potassium >5.5 mmol/L)[(FILSPARI SmPC)].

Inhibitors of the RAAS or endothelin system were prohibited during the trial. Other classes of antihypertensives were permitted to achieve target blood pressure. Treatment with immunosuppressives were allowed at the discretion of the investigator[(FILSPARI SmPC)].

Study completers and discontinuation

The full analysis set consisted of 202 patients treated with sparsentan and 202 patients treated with irbesartan. In total, 174 (86%) patients treated with sparsentan and 154 (76%) patients treated with irbesartan completed 110 weeks of treatment, and 199 (98%) and 191 (94%) completed the double-blind study period. A higher number of patients discontinued treated with irbesartan (n=48; 24%) than with sparsentan (n=28; 14%)[(Rovin, 2023a)].

Primary endpoint: Change from baseline at Week 36 in urine protein-creatinine (UP/C)

Sparsentan delivered significant and superior proteinuria reduction at Week 36 vs. irbesartan, meeting the primary endpoint[(FILSPARI SmPC; Heerspink, 2023)]

- Geometric mean UP/C at Week 36:
  0.62 g/g with sparsentan vs. 1.07 g/g with irbesartan[(FILSPARI SmPC)]
- Least-squares (LS) mean percent change in UP/C from baseline to Week 36:
  -49.8% with sparsentan vs. -15.1% with irbesartan, p<0.0001[(Heerspink, 2023)]
- Absolute reduction: 34.7%; relative reduction: 41% (geometric LS mean ratio: 0.59; 95% CI: 0.51 to 0.69)[(Heerspink, 2023)]

Key secondary endpoints: Chronic eGFR slope at Week 110 and total slope at Week 110

Long term benefits of sparsentan were confirmed by eGFR chronic slope from week 6 to week 110[(Rovin, 2023a)]*

There is an initial acute effect of randomised therapy on eGFR, defined as the first 6 weeks of randomised treatment with study medication. Analysis is carried out from 6 weeks post-randomisation to a defined time[(Rovin, 2023b)].

The rate of change in eGFR over a 104-week period following the initial acute effect of randomised therapy is the **chronic slope**, i.e. the mean rate of change in eGFR from the time the drug effect has stabilised to the end of the follow-up period, discounting the acute drug effect (Week 6 to Week 110)[(Rovin, 2023b; Greene, 2019)]. This was the confirmatory endpoint for the EMA.

The rate of change in eGFR over a 110-week period following the initiation of randomised therapy is the **total slope**, i.e. the mean rate of change in eGFR from the start of the study period, including the acute drug effects (day 1 to Week 110) [(Rovin, 2023b; Greene, 2019)]. This was the confirmatory endpoint for the FDA.

Table 2: Key secondary endpoints - change in eGFR over time[(CSL Vifor; Rovin, 2023a)]

Annual eGFR slope (95% CI), mL/min/1.73 m^2/year*	Sparsentan (N=202)	Irbesartan (N=202)	Difference (95 %CI), p value
Chronic slope (over approx. 2 years [Weeks 6-110]) [(Rovin, 2023a)]	**-2.7** (-3.4 to -2.1)	**-3.8** (-4.6 to -3.1)	1.1 (0.1 to 2.1) p=0.037
Total slope (Day 1 to Week 110)[(Rovin, 2023a)]	**-2.9** (-3.6 to -2.2)	**-3.9** (-4.6 to -3.1)	1.0 (-0.03 to 1.94) p=0.058 (not significant)

*Assessed in the full analysis set. Analysis includes eGFR data for patients on treatment; off-treatment and missing data imputed using the multiple imputation procedure.

Other secondary endpoints and exploratory/post-hoc endpoints

Under the hierarchical testing procedure, the study did not formally test the statistical hypotheses for 'other' prespecified secondary efficacy endpoints and exploratory/post-hoc endpoints. No definite conclusions can be drawn from these data. Statistical hypotheses for other prespecified secondary efficacy endpoints were not formally tested under the hierarchical testing procedure because the p value for the eGFR total slope was more than 0.05[(Rovin, 2023a)].

Secondary endpoint: Mean change from baseline up to Week 110 in proteinuria variables

The reduction in UP/C at Week 26 was sustained through Week 110 with sparsentan vs. irbesartan[(FILSPARI SmPC)].

- Geometric mean UP/C at Week 110:
  0.64 g/g with sparsentan vs. 1.09 g/g with irbesartan[(FILSPARI SmPC)]
- Mean reduction in UP/C from baseline to Week 110:
  -42.8% with sparsentan vs. -4.4% with irbesartan[(Rovin, 2023a)]

Secondary endpoint: The absolute change from baseline in eGFR at 2 years

Sparsentan slowed the rate of eGFR decline vs. irbesartan from Week 6 to Week 110[(Rovin, 2023a)].

- Absolute change from baseline in eGFR at 2 years, mL/min/1.73 m^2:
  -5.8 with sparsentan vs. -9.5 with irbesartan; difference: 3.7 (95% CI: 1.5 to 6.0)[(Rovin, 2023a)]

Secondary composite endpoint: Kidney failure endpoint (confirmed 40% eGFR reduction, end-stage kidney disease, or all-cause mortality)

Fewer sparsentan-treated patients progressed to the composite kidney failure endpoint vs. irbesartan-treated patients up to Week 110[(Rovin, 2023a)]:

- Composite kidney endpoint 18/202 (9%) patients treated with sparsentan vs. 26/202 (13%) treated with irbesartan[(Rovin, 2023a)]
- Absolute risk reduction: 4%; relative risk reduction: 30% (relative risk: 0.7; 95% CI: 0.4 to 1.2)[(Rovin, 2023a)]

Within this endpoint:

- 18/202 (9%) patients treated with sparsentan and 22/202 (11%) treated with irbesartan had confirmed 40% eGFR reduction[(Rovin, 2023a)]
- 9/202 (4%) patients treated with sparsentan and 11/202 (5%) treated with irbesartan had ESKD[(Rovin, 2023a)]
- One death was reported, in a patient treated with irbesartan[(Rovin, 2023a)]

Exploratory endpoint: remission of proteinuria

- Complete proteinuria remission (urine protein excretion <0.3 g/day) was observed in 62/202 (31%) patients treated with sparsentan and 23/202 (11%) patients treated with irbesartan; absolute risk reduction: 20%; relative risk: 2.5 (95% CI: 1.6 to 4.1)[(Rovin, 2023a)]
- Partial proteinuria remission (urine protein excretion <1.0 g/day) was observed in 157/202 (78%) patients treated with sparsentan and 106/202 (53%) patients treated with irbesartan; absolute risk reduction: 25%; relative risk: 1.5 (95% CI: 1.1 to 1.9)[(Rovin, 2023a)]

Exploratory endpoint: use of rescue immunosuppressants

Rescue immunosuppressants were initiated sooner and more frequently in patients treated with irbesartan (16/202; 8%) than in those treated with sparsentan (6/202; 3%)[(Rovin, 2023a)].

Post-hoc analysis: remission of proteinuria

- Urine protein excretion <0.5 g/day) was observed in 103/202 (51%) patients treated with sparsentan and 48/202 (24%) patients treated with irbesartan; relative risk: 2.1, 95% CI: 1.5 to 2.9[(Rovin, 2023a)]

Treatment-emergent and serious adverse events were well balanced between treatment groups, except for dizziness and hypotension, which were more frequent in the sparsentan arm[(Rovin, 2023a)]

The safety population in PROTECT consisted of 202 patients treated with sparsentan and 202 patients treated with irbesartan[(Rovin, 2023a)].

Dizziness was reported by 15% and hypotension by 13% of patients treated with sparsentan, and 6% and 4% of patients respectively treated with irbesartan[(Rovin, 2023a)].

Table 3: Treatment-emergent adverse events to Week 110[(Rovin, 2023a)]

Treatment-emergent adverse events, n (%)	Sparsentan (N=202)	Irbesartan (N=202)
Any TEAE	187 (93%)	177 (88%)
Most common TEAEs (≥10% of patients in either group)		
COVID-19	53 (26%)	46 (23%)
Hyperkalaemia	32 (16%)	26 (13%)
Peripheral oedema	31 (15%)	24 (12%)
Dizziness	30 (15%)	13 (6%)
Headache	27 (13%)	26 (13%)
Hypotension	26 (13%)	8 (4%)
Hypertension	22 (11%)	28 (14%)
Transaminase elevations >3 x ULN	5 (2%)	7 (3%)
Serious TEAEs	75 (37%)	71 (35%)
Serious hepatic TEAEs	0	2 (1%)
Drug-induced liver injury	0	0
Serious TEAEs in ≥5 patients in either group		
COVID-19	42 (21%)	38 (19%)
Chronic kidney disease	6 (3%)	6 (3%)
TEAEs leading to treatment discontinuation	21 (10%)	18 (9%)
TEAEs leading to death	0	1 (<1%)

Sparsentan safety profile

The most commonly reported adverse drug reactions (ADRs) were hypotension (10.8%), hyperkalaemia (9.6 %), dizziness (7.8%), and peripheral oedema (5.4%). The most common serious adverse reaction reported was acute kidney injury (0.9%)[FILSPARI SmPC].

Table 4: Adverse drug reactions observed during clinical trials[FILSPARI SmPC]

System organ class	Very common (≥1/10)	Common (≥1/100 to <1/10)	Uncommon (≥1/1,000 to <1/100)
Blood and lymphatic system disorders		-	Anaemia
Metabolism and nutrition disorders		Hyperkalaemia	-
Nervous system disorders		Dizziness, headache	-
Vascular disorders	Hypotension	Orthostatic hypotension	-
Renal and urinary disorders		Renal impairment, acute kidney injury	-
General disorders and administration site conditions		Oedema peripheral, fatigue	-
Investigations		Blood creatinine increased, elevated transaminase*	-

*Elevated transaminase includes preferred terms of alanine aminotransferase increased, aspartate aminotransferase increased, gamma-glutamyltransferase increased and hepatic enzyme increased

Description of selected adverse events

Haemoglobin decrease

In PROTECT, anaemia or decreased haemoglobin was reported as an ADR in 2 (1%) subjects treated with sparsentan compared to 4 (2%) irbesartan-treated subjects. Overall, haemoglobin ≤9 g/dL was reported at any time post treatment in 7 (3%) subjects in the sparsentan treatment arm and 4 (2%) subjects in the irbesartan treatment arm. This decrease is thought to be in part due to haemodilution. There were no treatment discontinuations due to anaemia[FILSPARI SmPC].

Hepatic associated adverse events

In PROTECT, 6 (3%) patients treated with sparsentan and 4 (2%) patients treated with irbesartan had raised liver transaminases ≥3 x ULN without elevation of total bilirubin, after receiving study medication for 168-407 days respectively. All events were non-serious and asymptomatic. The majority were mild to moderate in intensity, all were reversible, and other reasons have been identified as potential causal factors or as potentially contributing to transaminase elevations. No clinical symptoms of hepatic injury were observed. Three patients treated with sparsentan discontinued treated after positive challenge, while in two other patients sparsentan was restarted with no repeated hepatic enzyme elevations[FILSPARI SmPC].

Acute kidney injury (AKI)

In PROTECT, acute kidney injury ADRs were reported in four (2%) patients treated with sparsentan and three (1%) patients treated with irbesartan. Four (2%) patients treated with sparsentan reported serious AKI, all of which were reversible. None of the serious AKI required dialysis. Three patients discontinued treatment in the sparsentan group[(FILSPARI SmPC)].

Hyperkalaemia

In PROTECT, hyperkalaemia was reported as an ADR in 20 (10%) of patients treated with sparsentan and 16 (8%) of patients treated with irbesartan. All events were non-serious in patients treated with sparsentan, the majority were mild to moderate in intensity, and all were reversible. There were no treatment discontinuations due to hyperkalaemia. The risk of hyperkalaemia is increased for patients with a lower eGFR[(FILSPARI SmPC)].

Hypotension

Hypotension was reported during treatment with sparsentan. In PROTECT, a systolic blood pressure (SBP) ≤100 mmHg or a reduction in SBP >30 mmHg was reported in 12% and 10% of patients on sparsentan, respectively, versus 11% and 10% on irbesartan. In subjects treated with sparsentan only 15 subjects (7.4%) were ≥65 years old. Hypotension was reported in 20 (11%) subjects <65 years of age and in 6 (40%) subjects 65 to 74 years of age[(FILSPARI SmPC)].

Economic modelling on prevention of dialysis and transplant

Extrapolated data using economic modelling based on the PROTECT and real world data of patients with IgA nephropathy using the UK National Registry of Rare Kidney (RaDaR) database (Pitcher, 2023; Rovin, 2023a), shows that the use of sparsentan has the potential to reduce the number of patients requiring dialysis or kidney transplantation, both of which have associated burdens and cost to the patient and the NHS.

Treating 72 eligible adults* with IgA nephropathy with sparsentan over 5 years instead of standard of care irbesartan, leads to an **estimated 4 fewer adults on dialysis at Year 5**(CSL Vifor, 2025; CSL Vifor, 2024).

*Adults with IgA nephropathy in CKD stages 1-3 at diagnosis, with UPE ≥1.0 g/day(CSL Vifor, 2024)

Table 5: Estimated number and proportion of adults receiving a kidney transplant each year since treatment initiation(CSL Vifor, 2025)

	Kidney transplant	
	Sparsentan (N=72)	**Irbesartan (N=72)**
Year 1	0.0 (0.02%)	0.0 (0.03%)
Year 2	0.1 (0.10%)	0.1 (0.18%)
Year 3	0.2 (0.33%)	0.4 (0.62%)
Year 4	0.5 (0.64%)	0.9 (1.19%)
Year 5	**0.8 (1.05%)**	**1.4 (1.95%)**

Table 6: Estimated number and proportion of adults receiving dialysis each year since treatment initiation(CSL Vifor, 2025)

	Sparsentan (N=72)	**Irbesartan (N=72)**	**Difference**
Year 1	0.2 (0.31%)	0.4 (0.53%)	0.2
Year 2	1.0 (1.34%)	1.8 (2.46%)	0.8
Year 3	2.5 (3.45%)	4.6 (6.46%)	2.1
Year 4	4.0 (5.55%)	7.4 (10.35%)	3.4
Year 5	**5.6 (7.82%)**	**10.3 (14.40%)**	**4.7**

Treating 72 eligible adults* with IgA nephropathy with sparsentan over 5 years instead of standard of care irbesartan, leads to an **estimated 9.3 fewer patients-years of in-centre haemodialysis (ICHD) and an estimated1,451 fewer ICHD sessions over a 5-year period.** This is based on three ICHD sessions a week, equivalent to 156.5 ICHD sessions per patient per year[(CSL Vifor, 2025)].

*Adults with IgA nephropathy in CKD stages 1-3 at diagnosis, with UPE ≥1.0 g/day[(CSL Vifor, 2024)]

Table 7: Estimated patient-years of in-centre haemodialysis over 5 years[(CSL Vifor, 2025)]

	Sparsentan (N=72)	Irbesartan (N=72)	Difference
Year 1	0.2	0.3	0.1
Year 2	0.8	1.4	0.7
Year 3	2.0	3.8	1.8
Year 4	3.3	6.0	2.8
Year 5	4.6	8.5	3.9
Patient years of ICHD (over 5 years)	**10.9**	**20.2**	**9.3**

Table 8: Estimated in-centre haemodialysis sessions over 5 years[(CSL Vifor, 2025)]

	Sparsentan (N=72)	Irbesartan (N=72)	Difference
Year 1	28	49	21
Year 2	123	227	103
Year 3	319	596	278
Year 4	512	954	443
Year 5	722	1,329	607
ICHD sessions (over 5 years)	**1,704**	**3,155**	**1,451**

Extrapolated data use a baseline mean eGFR of 57 mL/min/1.73 m^2, reflecting the baseline mean eGFR in PROTECT, with change in mean chronic slope of -2.7 mL/min/1.73 m^2 with sparsentan and -3.8 mL/min/1.73 m^2 with irbesartan, as seen in the PROTECT trial[(Rovin, 2023a)].

Assumptions: The reduction in dialysis and transplantation rates is based on clinical trial data, real-world data (RaDaR) or modelled projections of sparsentan's efficacy. Assumes that the results observed in clinical trials are replicated in real-world settings. The use of irbesartan as a comparator reflects the actual standard of care in the eligible population. Outcomes assume consistent patient adherence to sparsentan and irbesartan treatment regimens.

Patient benefits

Sparsentan has an innovative non-immunosuppressive dual mechanism of action[(FILSPARI SmPC)]

Sparsentan, a dual endothelin angiotensin receptor antagonist, targets two critical pathways, the endothelin and angiotensin pathways, involved in disease progression in one molecule[(FILSPARI SmPC)].

Sparsentan delivered significant and superior proteinuria reduction at Week 36 vs. irbesartan[(Heerspink, 2023)]

- Geometric mean UP/C at baseline: 1.3 g/g with sparsentan vs. 1.2 g/g with irbesartan[(Heerspink, 2023)]
- Geometric mean UP/C at Week 36: 0.62 g/g with sparsentan vs. 1.07 g/g with irbesartan[(FILSPARI SmPC)]
- Least-squares (LS) mean percent change in UP/C from baseline to Week 36: -49.8% with sparsentan vs. -15.1% with irbesartan, p<0.0001[(Heerspink, 2023)]
- Absolute reduction: 34.7%; relative reduction: 41% (geometric LS mean ratio: 0.59; 95% CI: 0.51 to 0.69)[(Heerspink, 2023)]

Sparsentan preserves kidney function by slowing the rate of change in eGFR (chronic slope over approximately 2 years) vs. irbesartan[(Rovin, 2023a)]:

Absolute difference of 1.1 mL/min/1.73 m^2 per year (95% CI: 0.1 to 2.1; p=0.0372) in the chronic slope with sparsentan vs. irbesartan (-2.7 vs -3.9 mL/min/1.73 m^2 per year, respectively) [(Rovin, 2023a)].

Sparsentan is an oral tablet taken once daily and is generally well tolerated[(FILSPARI SmPC)]

The most commonly reported adverse drug reactions were hypotension (9%), hyperkalaemia (7%), dizziness (7%), and peripheral oedema (5%). The most common serious adverse reaction reported was acute kidney injury (1%)[(FILSPARI SmPC)].

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