SMC2847

sparsentan film-coated tablet (Filspari®)

CSL Vifor

08 May 2026

The Scottish Medicines Consortium (SMC) has completed its assessment of the above product and advises NHS Boards and Area Drug and Therapeutic Committees (ADTCs) on its use in NHSScotland. The advice is summarised as follows:

ADVICE: following a full submission assessed under the orphan medicine process

sparsentan (Filspari®) is accepted for restricted use within NHSScotland.

Indication under review: treatment of adults with primary immunoglobulin A nephropathy (IgAN) with a urine protein excretion ≥1.0 g/day (or urine protein-to-creatinine ratio ≥0.75 g/g*).

*equivalent to ≥85 mg/mmol

SMC restriction: patients whose condition has not responded adequately to current standard of care that is; maximally tolerated angiotensin converting enzyme inhibitor or angiotensin receptor blocker and sodium-glucose cotransporter-2 inhibitor, as appropriate. Patients should stop sparsentan at week 24 if no response to treatment.

In a double-blind phase III study, sparsentan, compared with an angiotensin receptor blocker, significantly reduced proteinuria and decline in renal function measured via annualised slope of estimated glomerular filtration rate (eGFR).

This advice applies only in the context of an approved NHSScotland Patient Access Scheme (PAS) arrangement delivering the cost-effectiveness results upon which the decision was based, or a PAS/ list price that is equivalent or lower.

This advice takes account of the views from a Patient and Clinician Engagement (PACE) meeting.

Chair
Scottish Medicines Consortium

1. Clinical Context

1.1. Medicine background

Sparsentan is a dual endothelin angiotensin receptor antagonist at both the ET_AR and AT_1R, thereby blocking the effects of endothelin I, and angiotensin II, respectively, which mediate processes that lead to immunoglobulin A nephropathy (IgAN) progression through haemodynamic actions and mesangial cell proliferation, increased proinflammatory and profibrotic mediators, podocyte injury, and oxidative stress. Sparsentan thereby reduces proteinuria and slows the progression of kidney disease. It should be initiated at a dose of 200 mg orally once daily for 14 days and then increased to a maintenance dose of 400 mg once daily, dependent upon tolerability. Further details are included in the summary of product characteristics.[1]

1.2. Disease background

Immunoglobulin A nephropathy is the most common form of primary glomerulonephritis. It is characterised by deposition in the glomeruli of immune complexes containing polymeric galactose-deficient IgA1 (Gd-IgA1) and associated autoantibodies, leading to inflammation and scarring. Patients can present with symptoms including, haematuria, proteinuria, impaired kidney function, oedema and hypertension. It often has a chronic and progressive course. Persistent proteinuria is a predictor of future kidney failure for patients with IgAN. Approximately 30% of patients with IgAN will progress to end-stage kidney disease in 10 to 25 years from diagnosis and may then be considered for kidney transplantation. IgAN affects nearly all ages, but peak incidence is in the second and third decades of life. [2-4]

1.3. Company proposed position

The company agreed to SMC restricting use to patients whose condition has not responded adequately to current standard of care. That is, maximally tolerated angiotensin converting enzyme inhibitor or angiotensin receptor blocker and sodium-glucose cotransporter-2 inhibitor, as appropriate. Patients should stop sparsentan at week 24 if no response to treatment.

1.4. Treatment pathway and relevant comparators

The Kidney Disease: Improving Global Outcomes (KDIGO) guideline notes that as patients with IgAN are at risk of progressive loss of kidney function if they have proteinuria ≥0.5 g/day, they should receive treatment to maintain it below this level. It recommends that management should simultaneously: (a) prevent or reduce IgA-containing immune complex formation and complex-mediated glomerular injury; and (b) manage the consequences of existing IgAN-induced nephron loss. The latter includes: lifestyle advice, including dietary sodium restriction; control of blood pressure; cardiovascular risk assessment and intentions; and reduction of glomerular hyperfiltration and the impact of proteinuria on tubule interstitium, using renin-angiotensin system (RAS) blockade (with optimised maximally tolerated angiotensin converting enzyme [ACE] inhibitor or angiotensin II receptor blocker [ARB]) or dual endothelin angiotensin receptor antagonism, singly or in combination with a sodium-glucose cotransporter-2 (SGLT2) inhibitor. The SGLT2 inhibitors dapagliflozin (SMC2428, SMC2763) and empagliflozin (SMC2642) are accepted for restricted use by SMC for the treatment of chronic kidney disease in patients on optimised standard care. The KDIGO guideline notes that as ACEi or ARB do not mitigate the IgAN-specific drivers of nephron loss, their use should not preclude concomitant therapies that target the

drivers of IgAN or glomerular inflammation for patients who will likely benefit from them. [5] The latter may include corticosteroid and immunosuppressants, with clinical experts consulted by SMC noting that these are particularly used for patients with high risk or rapidly progressing disease.

1.5. Category for decision-making process

Eligibility for a PACE meeting

Sparsentan meets SMC orphan criteria.

2. Summary of Clinical Evidence

2.1. Evidence for the licensed indication under review

Evidence is from the PROTECT study, detailed in Table 2.1. [6-8]

Table 2.1. Overview of relevant study[6-8]

Criteria	PROTECT
Study design	International, double-blind, phase III study.
Eligible patients	Adults (≥18 years) with primary IgAN and proteinuria ≥1.0 g/day despite maximised RAS inhibition for ≥12 weeks and eGFR ≥30 mL/min/1.73 m^2.
Treatments	ACE inhibitor and/or ARB therapy was discontinued before randomisation, then, patients were equally assigned to once daily sparsentan (target dose 400 mg) or irbesartan (target dose 300 mg) for 110 weeks.
Randomisation	Patients randomised equally, stratified by eGFR (30 to <60 or ≥ 60 mL/min/1.73 m^2) and urine protein excretion (≤1.75 or >1.75 g/day).
Primary outcome	At interim analysis, GLSM change from baseline to 36 weeks in urine protein-creatinine ratio based on 24-hour urine sample.
Key secondary outcomes in non-US statistical plan	At interim analysis: eGFR slope from week 6 to week 58 (chronic slope). At final analysis: eGFR slope from week 6 to week 110 (chronic slope); eGFR slope from day 1 to week 110 (total slope); change from baseline in eGFR at week 110.
Statistical analysis	Efficacy and safety assessed in full analysis set, which comprised all randomised patients who received at least one dose of randomly assigned study drug. Testing hierarchy for secondary outcomes were different in US and non-US countries. In non-US, the hierarchy of secondary outcomes is detailed above.

Abbreviations: ACE = angiotensin converting enzyme; ARB = angiotensin receptor blocker; eGFR = estimated glomerular filtration rate; GLSM = geometric least square mean; IgAN = immunoglobulin A nephropathy; United States.

Within the non-United States (US) country statistical analysis plan, at the interim analysis (1 August 2021), the primary outcome, which assessed proteinuria, was significantly improved with sparsentan compared with irbesartan, with a similar result at the final analysis (7 September 2023). At the interim analysis, the first key secondary outcome, estimated glomerular filtration rate (eGFR) slope from week 6 to week 58 (eGFR chronic slope at one year), was not significantly different between the groups at α=0.01. Therefore, the first key secondary outcome at the final analysis, eGFR slope from week 6 to week 110 (eGFR chronic slope at two years) was tested at an α=0.04. This was significantly reduced with sparsentan compared with irbesartan. There was no significant difference between the groups for the next key secondary outcome in the hierarchy, eGFR slope from day 1 to week 110 (eGFR total slope at two years), and this ended formal testing. Results are detailed in Table 2.2.[6, 9] At the final analysis, the relative risk was 0.7 (95% confidence interval [CI]: 0.4 to 1.2) for the composite outcome of death (zero versus one with sparsentan versus irbesartan), initiation of renal replacement therapy (9 [4.4%] versus 11 [5.4%]) or ≥40% reduction in eGFR (18 [8.9%] versus 22 [11%]). [8]

Table 2.2: Results of PROTECT study. [6-8]

	Sparsentan	Irbesartan
Interim Analysis (1 August 2021)	**N=140**	**N=140**
GLSM % change in urine protein-creatinine ratio at week 36	-49.8	-15.1
Ratio (95% CI), p-value	0.59 (0.51 to 0.69), p<0.001	
eGFR slope from week 6 to week 58, mL/min/1.73 m^2/year	-3.4	-4.9
Difference (95% CI), p-value	1.4 (-0.36 to 3.26), p=0.117	
Final Analysis (7 September 2023)	**N=202**	**N=202**
GLSM % change in urine protein-creatinine ratio at week 110	-42.8	-4.4
Ratio (95% CI)	0.60 (0.50 to 0.72)	
eGFR slope from week 6 to week 110, mL/min/1.73 m^2/year	-2.7	-3.8
Difference (95 % CI), p-value	1.1 (0.07 to 2.12), p=0.037	
eGFR slope from day 1 to week 110, mL/min/1.73 m^2/year	-2.9	-3.9
Difference (95 % CI)	1.0 (-0.03 to 1.94), p=0.058	
eGFR change from baseline to week 110, mL/min/1.73 m^2	-5.8	-9.5
Difference (95 % CI)	3.7 (1.45 to 5.99)	
Patients achieving urine protein excretion <0.3 g/day, n (%)	62 (31%)	23 (11%)
Relative risk (95% CI)	2.5 (1.6 to 4.1)	
Patients achieving urine protein excretion <0.5 g/day, n (%)	103 (51 %)	48 (24 %)
Relative risk (95% CI)	2.1 (1.5 to 2.9)	

Abbreviations: CI = confidence interval; eGFR = estimated glomerular filtration rate; GLSM = geometric least square mean.

2.2. Health-related quality of life outcomes

Health-related quality of life was assessed using kidney disease quality of life-36 (KDQoL-36) survey and the EQ-5D-5L questionnaire at baseline and week 24, 48, 70, 94, and 110. Over the course of the study, there was no consistent pattern of substantial differences between the groups for these outcomes.[10]

2.3. Supportive studies

An exploratory, open-label, single-arm, multicentre, phase II study (SPARTACUS) recruited adults with IgAN, urine albumin-creatinine ratio ≥0.3 g/g, eGFR ≥25mL/min/1.73 m^2, who were taking a stable dose of SGLT2 inhibitor and ACE inhibitor or ARB for ≥12 weeks. All 48 patients continued taking their SGLT2 inhibitor throughout and, at the start of the study, discontinued their ACE inhibitor or ARB and commenced sparsentan 400 mg daily for 24 weeks. The primary outcome was change from baseline to week 24 in urine albumin-creatinine ratio. At 24 weeks, this was reduced by 56%.[11, 12]

3. Summary of Safety Evidence

At the September 2023 cut, median duration of treatment in PROTECT was 110 weeks in both groups. Within the sparsentan and irbesartan groups, adverse events were reported by 93% (187/202) and 88% (177/202) of patients, respectively, which were treatment-related in 46% and 35%, were serious in 37% and 35% and led to treatment discontinuation in 10% and 8.9%.[8, 9] Rates of the following adverse events were higher in the sparsentan group, compared with irbesartan: dizziness (15% versus 6.4%), hypotension (13% versus 4.0%), fatigue (8.4% versus 5.4%), anaemia (7.9% versus 4.4%), cough (7.4% versus 3.5%), acute kidney injury (5.9% versus 2.5%), nausea (4.9% versus 2.5%) and myalgia (4.9% versus 2.0%). Within the sparsentan group the following

adverse events were reported at lower rates: hypertension (11% versus 14%), diarrhoea (4.9% versus 9.4%), renal impairment (3.5% versus 5.9%), urinary tract infection (3.5% versus 5.9%), hyperuricaemia (3.5% versus 5.4%) and pain in extremity (3.0% versus 5.9%). [8]

Overall, one of the main differences between sparsentan and irbesartan is hypotension-associated adverse events (hypotension, orthostatic hypotension and systolic blood pressure decreased), which were reported by 16% versus 6.4% of patients in the respective groups and led to treatment discontinuation in three patients (1.5%) in the sparsentan group. Long-term safety data for sparsentan in IgAN are limited, especially for detecting rare issues. [6, 8]

4. Summary of Clinical Effectiveness Considerations

4.1. Key strengths

- In PROTECT, sparsentan, compared with irbesartan, significantly improved proteinuria assessed via the primary outcome (change from baseline to 36 weeks in urine protein-creatinine ratio). The antiproteinuric effect was maintained up to week 110. A regulator considered this was clinically relevant and noted that proteinuria, which is used in clinical practice to monitor disease severity, is an acceptable biomarker to evaluate the early onset of treatment effect.[6]
- The regulator considered the differences in total eGFR slope over 2 years between sparsentan and irbesartan (assessed as the key secondary outcome) were clinically meaningful, as they exceeded the level (0.75 mL/min/1.73 m^2/year) regarded as a clinically meaningful predictor of benefit in chronic kidney disease (CKD) progression. Support was provided by the absolute difference in eGFR at 2 years showing less decline with sparsentan.[6]

4.2. Key uncertainties

- Current treatment of IgAN in Scotland typically includes, in addition to RAS blockade, a SGLT2 inhibitor, dapagliflozin or empagliflozin. This differs from the comparator in the PROTECT study, where only 5.4% (22/404) of patients at baseline were receiving a SGLT2 inhibitor in addition to the ARB, irbesartan. The SPARTACUS study[11] has provided some evidence that the addition of sparsentan to optimised therapy with ACE inhibitor or ARB plus SGLT2 inhibitor reduced proteinuria at 24 weeks compared with baseline. However, it is limited by small sample size and lack of active control, leading to uncertainty in the magnitude of benefit expected with sparsentan when used in Scottish practice.
- The sample size of PROTECT was estimated based on between treatment differences in 2-year total and chronic eGFR rate slopes of approximately 2.9 and 3.2 mL/min/1.73 m^2/year, respectively. Observed differences were smaller, around 1.0 mL/min/1.73 m^2/year, and not statistically significant for the total slope. The company noted that, in contrast to previous studies of irbesartan, a higher proportion of patients (95%) were titrated to the maximum labelled dose and so the relative treatment of sparsentan was lower than expected; a larger study may have been necessary to significantly detect this smaller difference. [6] In a post hoc analysis that adjusted for intercurrent events, a similar treatment effect for 2-year eGFR total slope (1.2 mL/min/1.73 m^2/year) was statistically significant.[1]

- There is uncertainty around the magnitude of long-term clinical outcomes, such as renal failure. Regulatory guidance notes that proteinuria is not accepted as a surrogate for long-term kidney damage, with eGFR slope preferred as the primary outcome in pivotal studies.[6, 13] Although there was a time to event analysis for the composite outcome of death, initiation of renal replacement therapy or ≥40% reduction in eGFR,[8] it does not provide robust evidence about the relative effects of sparsentan versus irbesartan on the development of renal failure, as the number of events was small and the majority were reductions in eGFR. The magnitude of the relative effects on development of renal failure of sparsentan versus the current standard of care, ACE inhibitor or ARB, is uncertain.
- The PROTECT study excluded patients who were taking any systemic immunosuppressive medications (including corticosteroids) for >2 weeks within 3 months prior to screening. At baseline, 21 (5.2%) of patients (10 and 11 in sparsentan and irbesartan groups, respectively) reported a history of taking an immunosuppressive agent with a renal indication. During the double-blind period, 6 (3.0%) and 16 (7.9%) in the respective groups used systemic immunosuppressive medications with a renal indication while on treatment.[9] It is not clear how this would affect the generalisability of the results to the Scottish population.

4.3. Clinical expert input

Clinical experts consulted by SMC considered that sparsentan fills an unmet need in this therapeutic area, namely it provides improved efficacy in controlling proteinuria and renal function decline compared with the current standard of care, ACE inhibitor or ARB and SGLT2 inhibitor. Therefore, it was considered a therapeutic advancement. The clinical experts noted that sparsentan would be used in place of ACE inhibitor or ARB, especially for patients who do not achieve adequate control of proteinuria with these.

4.4. Service implications

Clinical experts consulted by SMC advised that sparsentan would be initiated and monitored in secondary care but is not expected to be associated with substantial service implications. They noted that it would be possible to implement in practice the stopping rule that supports the economic analysis, that is, discontinuation in patients with urine protein-creatinine ratio greater than 199 mg/mmol that had reduced less than 20% from treatment initiation at week 24.

5. Patient and clinician engagement (PACE)

A patient and clinician engagement (PACE) meeting with patient group representatives and clinical specialists was held to consider the added value of sparsentan, as an orphan medicine, in the context of treatments currently available in NHSScotland.

The key points expressed by the group were:

- When IgAN nephropathy progresses to kidney failure and associated dialysis or transplant, patients' health and ability to live a normal life substantially deteriorates. They suffer debilitating fatigue and oedema plus side effects from dialysis that limit their ability to participate in education and sport, to work (leading to financial difficulties), travel, and care for family. As patients are often younger adults, this has an immense impact on their mental health.
- Patients often rely on family and carers to manage their condition and attend dialysis and healthcare appointments. The carer responsibilities can be substantial and may limit carers' ability to work or care for other family members. Overall, it can put a strain on families, and the mental health of carers can suffer.
- Clinical experts advised that sparsentan has a novel mechanism of action and is considered a breakthrough in the management of this condition. They noted that a reduction in proteinuria with sparsentan would be likely to be associated with a reduction in the decline of renal function.
- By delaying the development of kidney failure, sparsentan would give patients longer when they are well and able to live their life normally, to work, socialise and care for family. It would reduce the psychological and practical burden of carer's responsibilities. It may give hope of improved renal function and allow patients to feel in control of their condition and possibly plan for a transplant or dialysis. These involve major life upheaval, such as reorganising work and childcare or making home modifications for home dialysis, if required. It may allow time for assessment of the patient and potential donor for transplant. It would give patients and those involved in their care more time to learn about lifestyle changes associated with dialysis and transplant as well as to prepare psychologically. Overall, it could have a positive impact on the patient and their carer's physical and mental health.
- Clinicians advised that sparsentan would be particularly useful for patients who have proteinuria despite treatment with ACE inhibitor or ARB and SGLT2 inhibitor, which are included in the current standard of care. In these patients, it would be exchanged for the ACE inhibitor or ARB for a trial period and only continued in those who achieve a specified level of improvement of proteinuria.

Additional Patient and Carer Involvement

We received patient group submissions from Kidney Care UK, Kidney Research UK and National Kidney Federation. All three organisations are registered charities. Kidney Care UK has received 3.6% pharmaceutical company funding in the past two years, including from the submitting company. Kidney Research UK has received 5.3% pharmaceutical company funding in the past two years, including from the submitting company. National Kidney Federation has received 9% pharmaceutical company funding in the past two years, including from the submitting company. Representatives from all three patient groups participated in the PACE meeting. The key points of their submissions have been included in the full PACE statement considered by SMC.

6. Summary of Comparative Health Economic Evidence

6.1. Economic case

An overview of the economic analysis is presented in Table 6.1

Table 6.1 Description of economic analysis

Criteria	Overview
Analysis type	Cost-utility analysis
Time horizon	Lifetime (55 years), with a mean patient starting age of 46 years.
Population	Adult patients with primary IgAN with a urine protein excretion (UPE) ≥1.0 g/day, or urine protein-to-creatinine ratio (UP/C) ≥0.75 g/g.
Comparators	Irbesartan
Model description	A sixteen health states cohort-level state transition model was used. The model component consisted of 12 health states defined according to categories of UP/C level (<0.44 g/g; 0.44 to <0.88 g/g; 0.88 to <1.76 g/g and ≥1.76 g/g) and within each UP/C state CKD stage (CKD1/2 i.e., eGFR ≥60; CKD3 i.e. eGFR 30-59 and CKD4 i.e. eGFR15-29), and a dead health state. The ESRD state (CKD stage 5 i.e., eGFR <15) included separate sub-states for pre-RRT (renal replacement therapy), dialysis, and transplant, regardless of the patient's UP/C level. Model cycle length was 12-week.
Clinical data	Transitions between UP/C state for sparsentan and irbesartan were derived from the PROTECT study separately for week 0-12 and then uniform per cycle transition probabilities were applied for weeks 12-108 (study end). Missing UP/C data was handled using last observation carried forward (LOCF). No treatment waning was assumed. CKD stage transition probabilities were primarily informed by data from the PROTECT study, but due to the limited patients in CKD stages 4 and 5 in the study, supplementary data for these transitions were sourced from the UK National Registry of Rare Kidney Diseases (RaDaR). [14] The RaDaR data was matched to the population in the PROTECT trial. A uniform set of CKD stage transition probabilities were applied for both treatment arms, with an initial transition matrix from Week 0 to Week 12, followed by a uniform transition matrix per cycle from Week 12 to week 108. The transition probabilities to ESRD (CKD5), and the transition between pre-RRT, transplant, and dialysis, were derived from RaDaR and NICE TA937. [15] Mortality estimates by CKD stage were based on published sources (KDIGO guidelines 2024, and Neovius *et al*). [16, 17] Adverse events (AEs) of ≥5% were included in the economic analysis. Treatment discontinuation for sparsentan was estimated from the PROTECT study with a constant rate per cycle applied in the model. A stopping rule for non-response (patient UP/C > 1.76 g/g with less than 20% reduction from baseline) was applied for sparsentan at week 36. Zero discontinuation was assumed for irbesentan as it was assumed that patients would always remain on a RAASi treatment, also when discontinuing sparsentan (proxied by irbesartan).
Extrapolation	Treatment specific UP/C transition probabilities were extrapolated beyond week 108 of the PROTECT study to the end of the model time horizon using the treatment specific averaged per cycle transition probability matrix for weeks 12-108 of the PROTECT study, and for CKD transitions beyond week 108 based on applying the averaged uniform per cycle transition probability matrix for weeks 12-108 of the PROTECT/RaDaR data.
Quality of life	The EQ-5D-5L was included in the PROTECT study but was not used in the economic model due to lack of observations. Therefore, the company used the utility estimates obtained from a published SLR of utility values for CKD stages (not IgAN specific) that had been used in a previous NICE appraisal in IgAN (TA937). [15] The utilities from this source were all based on the

	EQ-5D-3L instrument, with values for CKD1&2, CKD3, CKD4, CKD5 pre-renal replacement therapy (RRT), CKD5 dialysis, and CKD5 transplant. Disutilities were also estimated for AEs based on a published source, [18] or assumption.
Costs and resource use	Drug acquisition costs were included for all medicines included in the economic analysis. All treatments are administered orally, so no costs included for drug administration. Drug wastage is included in the base case. Additional treatment cost for an SGLT2 inhibitor was also incorporated in the model, assuming 60% of patients in both arms would receive dapagliflozin as a concomitant treatment, based on clinical expert opinion. Costs were also included for disease management, costs of dialysis, and transplantation costs. For disease management across CKD stages, the model incorporated primary and secondary care costs. Dialysis were assumed to be 31.9% in hospital-based, 50.8% in satellite units, 4.7% for home dialysis, and 12.6% for peritoneal dialysis derived from the UK Renal Registry (UKRR) 26th Annual Report (2024). [19] Within CKD5 transplant-related costs included immunosuppressive therapy (hospitalisations and procedural costs of pre-assessment), the transplant procedure, and post-transplant assessment. AE costs were included.
PAS	A Patient Access Scheme (PAS) was submitted by the submitting company and assessed by the Patient Access Scheme Assessment Group (PASAG) as acceptable for implementation in NHSScotland. Under the PAS, a discount was offered on the list price.

Abbreviations: AE = adverse event; CKD = chronic kidney disease; eGFR = estimated glomerular filtration rate; ESRD = end-stage renal disease; IgAN = immunoglobulin A nephropathy; KDIGO = Kidney Disease: Improving Global Outcomes; LOCF = last observation carried forward; NICE = National Institute for Health and Care Excellence; PAS = Patient Access Scheme; PASAG = Patient Access Scheme Assessment Group; RaDaR = National Registry of Rare Kidney Diseases; RAASi = renin-angiotensin-aldosterone system inhibitor; RRT = renal replacement therapy; SLR = systematic literature review; SLTG2 = sodium-glucose co-transporter 2; UKRR = United Kingdom Renal Registry; UP/C = urine protein-to-creatinine ratio; UPE = urine protein excretion.

6.2. Results

The base case results are presented in Table 6.2.

Table 6.2: Base case results (PAS price)

Technologies	Total			Incremental			ICER (£/QALY)
	Costs	LYs	QALYs	Costs	LYs	QALYs	
Sparsentan	CIC	CIC	CIC	-	-	-	-
Irbesartan	CIC	CIC	CIC	CIC	CIC	CIC	£17,716

Abbreviations: CIC = commercial in confidence; ICER = incremental cost-effectiveness ratio; LYs, life years; PAS = patient access scheme; QALY = quality adjusted life years.

The efficacy benefit for sparsentan was driven by rapid reductions in UP/C within the first model cycle which was maintained over the 108 weeks PROTECT study duration. Sparsentan was associated with higher drug acquisition costs compared with irbesartan. There were additional costs in earlier CKD stages due to prolonged time spent in less severe disease states, offset by delayed progression to ESRD and reduced need for higher-cost dialysis and renal transplant therapies with sparsentan.

Quality adjusted life year (QALY) gains for sparsentan were driven by reduced UP/C relative to irbesartan estimated to produce slower progression to later CKD stages and renal failure and need for dialysis with higher mortality and quality of life impact.

6.3. Sensitivity analyses

Deterministic sensitivity analysis demonstrated the top three most influential parameters to the incremental cost effectiveness ratio (ICER) were, the cost of dialysis given the high cost associated with the state, baseline age, and the health state utility in CKD1&2. The highest ICER range was associated with varying baseline age from 41 to 51 years (see Table 6.3). The ICER range for varying dialysis per cycle costs by +/- 10% were £13,242 to £22,909.

Various scenario analyses were performed by the company or requested. The ICER was most sensitive to assuming no stopping rule for non-response (Scenario 1), if the PROTECT study was used to populate all CKD transitions (Scenario 2), and a short time horizon is applied (Scenario 6).

The results of key selected scenarios are presented in Table 6.3. In addition, sub-group analyses were performed to explore inclusion of different patient populations at baseline (Table 6.4).

Table 6.3: Selected scenario analyses (PAS price)

	Parameter	Base case	Scenarios	ICER (£/QALY)
1a	Non-responder stopping rule	Non-responders discontinue at 36-weeks	Non-responders continue treatment	35,540
1b			Non-responders discontinue at 24-weeks	17,209
2a	CKD Transition Source	Combined Transitions	PROTECT (Weeks 0-108): inform CKD transitions, applied until the end of the PROTECT trial period	19,128
2b			PROTECT (All Cycles): inform CKD transitions, applied for the whole model	32,228
2c			The model uses RaDaR to inform CKD transitions	16,771
3	Dialysis Mortality	Age-based Hazard Ratio	Mortality for dialysis uses a Fixed Rate	20,213
4	Transplant Mortality	Age-based Hazard Ratio	Mortality for transplanted patients uses a Fixed Rate	18,372
5	Drug Wastage	Included	Not included	17,260
6a	Time Horizon	lifetime (55 years)	10 years	92,282
6b			20 years	24,877
7a	Types of Dialysis	Hospital, 31.9%; Satellite, 50.8%; Home, 4.7%; Peritoneal, 12.6%	Satellite dialysis (lowest cost), 100%	20,338
7b			Peritoneal dialysis (highest cost), 100%	6,981
8a	Baseline age	Baseline age: 46	Baseline age: 41 (-10%)	12,858
8b			Baseline age: 51 (+10%)	23,320
9a	Proportion of having SGLT2 inhibitor as a concomitant treatment in both arms (costs only)	60% of patients in both arms receiving dapagliflozin	0% of patient in sparsentan arm receiving dapagliflozin	15,491
9b			100% of patient in sparsentan arm receiving dapagliflozin	19,199

10a	Health state utility values	Sourced from Cooper *et al.* (2020)	10% lower utility values	19,743
10b			Sourced from the PROTECT trial	14,393
11	Annual discontinuation rate	An annual discontinuation rate of 7.08% was applied	No annual discontinuation rate in patients with sparsentan	24,222
12	Long run benefit	None	50% efficacy reduction between sparsentan and irbesartan by end of time horizon from week 108 onwards	19,314
13	Combined scenario	Scenario 6 and 8	Time horizon of 20 years + baseline age of 51 years	29,358

Abbreviations: CIC, commercial in confidence; CKD, chronic kidney disease; ICER, incremental cost-effectiveness ratio; PAS, patient access scheme; QALYs, quality adjusted life years; UP/C, urine protein-to-creatinine ratio.

Table 6.4: Subgroup analysis scenario results (PAS price)

Subgroup scenarios	**ICER (£/QALY)**
Original baseline distribution in PROTECT trial	16,198
UP/C ≥ 0.7 g/g (≥79mg/mmol)	15,237
UP/C ≥ 0.7 g/g (≥79mg/mmol)and in CKD 1-3	16,794

Abbreviations: ICER = incremental cost-effectiveness ratio; PAS = patient access scheme; QALY = quality adjusted life years; UP/C=urine protein/creatinine ratio; CKD =chronic kidney disease

6.4. Key strengths

- Data from the PROTECT study, a double-blind, randomised phase III study were used.
- The estimation of resource use and associated costs appears to have been appropriately conducted.

6.5. Key uncertainties

- The economic analysis used irbesartan as a proxy for the ACEi/ ARBs comparator treatment class, which seemed to be a reasonable proxy for the ACEi/ARB treatment class costs and outcomes. However, Scottish clinical practice for IgAN includes an SGLT2 inhibitor (dapagliflozin or empagliflozin) alongside RAS blockade, which is different from the PROTECT trial comparator arm. A comparison of the costs and outcomes of sparsentan plus an SGLT2 inhibitor versus standard of care plus an SGLT2 inhibitor has not been performed by the company.
- The eGFR and CKD data from the PROTECT study were limited to inform the economic model. This was a particular issue for CKD stages 4 and 5 and hence other observational registry data (RaDaR) were used to supplement PROTECT study data which necessitated patient matching. This increased the uncertainty associated with the ICER results. A scenario that only used the PROTECT study data to estimate CKD transitions increased the ICER (Scenario 2, Table 6.3).

- Only two years follow-up data were available from the PROTECT study, presenting limitations for understanding the long-term UP/C and associated CKD progression for use in the economic analysis. There was uncertainty over the long-term outcomes and benefits for sparsentan which were assumed to be maintained over the entire model time horizon. A scenario assuming 50% reduction in treatment effect from the end of the PROTECT study by the model time horizon had a modest upward impact on the ICER (Scenario 12, Table 6.3). Applying shorter time horizons led to increased ICERs illustrating the inherent sensitivity associated with long-term projections of benefit (Scenario 6, Table 6.3). The results were also sensitive to starting age (Scenarios 8 and 13, Table 6.3).
- The model applied a one-off discontinuation rate (stopping rule) for patients receiving sparsentan at week 36 associated with non-response. There was an upward impact on the ICER for a scenario assuming no one-off discontinuation at week 36 (Scenario 1a, Table 6.3). SMC clinical experts were supportive of the feasibility of implementing a stop rule in practice. A scenario was also provided by the company exploring where response to treatment was assessed at 24-weeks and patients who were found to have non-response discontinued treatment as this may have been more aligned with routine clinical practice (Scenario 1b). This scenario had a small downward impact on the ICER.
- The PROTECT study was reported to provide insufficient EQ-5D data to support utility estimates by CKD stage for the economic model. Therefore, utility values were sourced from a published study for CKD stages, but these were not specific to IgAN. The values were potentially high for CKD stages 1/2 to 4 which could have favoured sparsentan. The company provided a scenario analysis based on PROTECT study EQ 5D-5L utilities which reduced the ICER (Scenario 10b, Table 6.3) but it was uncertain as to what the utility values were for each health state from this source.

7. Conclusion

The Committee considered the benefits of sparsentan in the context of the SMC decision modifiers that can be applied when encountering high cost-effectiveness ratios and agreed that as sparsentan is an orphan medicine, SMC can accept greater uncertainty in the economic case.

After considering all the available evidence and the output from the PACE process, the Committee accepted sparsentan for restricted use in NHSScotland.

8. Guidelines and Protocols

In 2025, the Kidney Disease: Improving Global Outcomes (KDIGO) organisation published 'KDIGO 2025 Clinical Practice Guideline for the Management of Immunoglobulin A Nephropathy (IgAN) and Immunoglobulin A Vasculitis (IgAV)'.[5]

9. Additional Information

9.1. Product availability date

July 2025

Table 9.1 List price of medicine under review

Medicine	Dose regimen	Cost per year (£)
Sparsentan	**200 mg orally once daily for 14 days, then, 400 mg once daily**	**41,274**

Costs from BNF online on 17 December 2025. Costs do not take any patient access schemes into consideration.

10. Company Estimate of Eligible Population and Estimated Budget Impact

The submitting company estimated there would be 407 patients eligible for treatment with sparsentan in year 1 and 411 patients in year 3. The estimated uptake rate was 2% (7 patients) in year 1 and 12% (51 patients) in year 3 with a discontinuation rate of 7% applied each year. This resulted in 6 patients estimated to receive treatment in year 1 rising to 48 patients in year 3.

SMC is unable to publish the with PAS budget impact due to commercial in confidence issues. A budget impact template is provided in confidence to NHS health boards to enable them to estimate the predicted budget with the PAS.

*Other data were also assessed but remain confidential.**

References

1. Vifor Fresenius Medical Care Renal Pharma UK Ltd. Sparsentan film-coated table (Filspari®) Summary of Product Characteristics. Electronic Medicines Compendium www.medicines.org.uk/emc/ Last updated 29 April 2025.
2. Stamellou E, Seikrit C, Tang SCW, et al. IgA nephropathy. Nat Rev Dis Primers 2023; 9: 67.
3. Glassock RJ. An expert opinion on current and future treatment approaches in IgA nephropathy. Adv Ther 2025; 42: 2545-58.
4. British Medical Journal. BMJ Best Practice: IgA nephropathy, last updated 1 February 2022.
5. Kidney Disease: Improving Global Outcomes (KDIGO) IgAN and IgAV Work Group et al. KDIGO 2025 Clinical Practice Guideline for the Management of Immunoglobulin A Nephropathy (IgAN) and Immunoglobulin A Vasculitis (IgAV). Kidney International 2025; 108 (4): S1 - S71.
6. European Medicines Agency (EMA). Sparsentan film-coated table (Filspari®) Assessment Report, EMEA/H/C/005783/0000, 22 February 2024.
7. Heerspink HJL, Radhakrishnan J, Alpers CE, et al. Sparsentan in patients with IgA nephropathy: a prespecified interim analysis from a randomised, double-blind, active-controlled clinical trial. Lancet 2023; 401: 1584-94.
8. Rovin BH, Barratt J, Heerspink HJL, et al. Efficacy and safety of sparsentan versus irbesartan in patients with IgA nephropathy (PROTECT): 2-year results from a randomised, active-controlled, phase 3 trial. Lancet 2023; 402:2077-90.
9. Travere Therapeutics. Clinical study report for 021IGAN17001 (PROTECT), 8 February 2024.
10. Travere Therapeutics. Clinical study report for 021IGAN17001 (PROTECT), additional report TVTX-RE021-TR023.
11. Ayoub I, Tang S, Kooienga L, et al. Concomitant sparsentan and sodium-glucose cotransporter-2 inhibitors in adults with IgA nephropathy in the ongoing phase 2 SPARTACUS trial. Poster FR-P0849 presented at the American Society of Nephrology (ASN) Kidney Week 2024, 23-27 October 2024, San Diego, USA.
12. Ayoub I, Tang SCW, Kooienga LA, et al. Sparsentan added to stable sodium-glucose cotransporter-2 inhibitors in adults with IgA nephropathy in the Phase 2 SPARTACUS Trial. European Renal Association (ERA) Congress 2025. Nephrol Dial Transplant 2025; 40(S3): i616-i618.
13. European Medicines Agency (EMA). Guideline on the clinical investigation of medicinal products to prevent development/slow progression of chronic renal insufficiency, EMA/CHMP/500825/2016, 15 September 2016.
14. Travere Therapeutics. RADAR: Data on file, 2022.
15. National Institute for Health and Care Excellence (NICE). Targeted-release budesonide for treating primary IgA nephropathy [ID1434] Committee Papers, 2023.
16. Kidney Disease: Improving Global Outcomes Glomerular Diseases Work Group. KDIGO 2024 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. Kidney Int 2024; 105(4S): S117-S314.
17. Neovius M, Jacobson SH, Eriksson JK, et al. Mortality in chronic kidney disease and renal replacement therapy: a population-based cohort study. BMJ Open 2014; 4(2): e004251.
18. Sullivan PW, Slejko JF, Sculpher MJ, Ghushchyan V. Catalogue of EQ-5D scores for the United Kingdom. Med Decis Making 2011; 31(6): 800-4.
19. UK Kidney Association. UK Renal Registry 26th Annual Report, 2024.

This assessment is based on data submitted by the applicant company up to and including 13 March 2026.

*Agreement between the Association of the British Pharmaceutical Industry (ABPI) and the SMC on guidelines for the release of company data into the public domain during a health technology appraisal:*https://www.scottishmedicines.org.uk/about-us/policies-publications/

Medicine prices are those available at the time the papers were issued to SMC for consideration. SMC includes Scottish national contract prices in its decision-making. These contract prices are commercial in confidence and cannot be put in the public domain, including via the SMC Detailed Advice Document.

Patient Access Schemes (PAS): A PAS is a scheme proposed by a pharmaceutical company in order to improve the cost-effectiveness of a medicine and enable patients to receive access to cost-effective innovative medicines. The Patient Access Scheme Assessment Group (PASAG), established under the auspices of Public Services Delivery Scotland, reviews and advises NHS Scotland on the feasibility and acceptability on implementing proposed schemes. PASAG operates separately from SMC to maintain the integrity and independence of the assessment process of the SMC. When SMC accepts a medicine for use in NHS Scotland on the basis of a PAS that has been considered acceptable for implementation by PASAG, a set of guidance notes on the operation of the scheme will be circulated to health boards' Area Drugs and Therapeutics Committees prior to publication of SMC advice.

Advice context:

No part of this advice may be used without the whole of the advice being quoted in full.

This advice represents the view of the Scottish Medicines Consortium and was arrived at after careful consideration and evaluation of the available evidence. It is provided to inform the considerations of Area Drug and Therapeutics Committees and NHS Boards in Scotland in determining medicines for local use or local formulary inclusion. This advice does not override the individual responsibility of health professionals to make decisions in the exercise of their clinical judgement in the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.