NCPE Assessment

Technical Summary

Sparsentan (Filspari®)

24020

26 November 2025

Applicant: CSL Vifor

Sparsentan for the treatment of adults with primary immunoglobulin A nephropathy (IgAN) with a urine protein excretion ≥1.0g/day (or urine protein-to-creatinine ratio ≥0.75g/g)

NCPE
National Centre for Pharmacoeconomics, Ireland

The National Centre for Pharmacoeconomics (NCPE) has issued a recommendation regarding the cost-effectiveness of sparsentan (Filspari®).

Following assessment of the Applicant's submission, the NCPE recommends that sparsentan (Filspari®) not be considered for reimbursement unless cost-effectiveness can be improved relative to existing treatments.*

The Health Service Executive (HSE) asked the NCPE to carry out an evaluation of the Applicant's (CSL Vifor) Health Technology Assessment of sparsentan (Filspari®). The NCPE uses a decision framework to systematically assess whether a technology is cost-effective. This includes comparative clinical effectiveness and health related quality of life benefits, which the new treatment may provide and whether the cost requested by the pharmaceutical company is justified.

Following the recommendation from the NCPE, the HSE examines all the evidence which may be relevant for the decision; the final decision on reimbursement is made by the HSE. In the case of cancer drugs the NCPE recommendation is also considered by the National Cancer Control Programme (NCCP) Technology Review Group.

About the National Centre for Pharmacoeconomics

The NCPE are a team of clinicians, pharmacists, pharmacologists and statisticians who evaluate the benefit and costs of medical technologies and provide advice to the HSE. We also obtain valuable support from clinicians with expertise in the specific clinical area under consideration. Our aim is to provide impartial advice to help decision makers provide the most effective, safe and value for money treatments for patients. Our advice is for consideration by anyone who has a responsibility for commissioning or providing healthcare, public health or social care services.

Summary

In December 2024, CSL Vifor submitted a dossier which investigated the comparative clinical effectiveness, cost-effectiveness and budget impact of sparsentan (Filspari®) for the treatment of adults with primary immunoglobulin A nephropathy (IgAN) with a urine protein excretion ≥1.0g/day (or urine protein-to-creatinine ratio ≥0.75g/g). CSL Vifor is seeking reimbursement of sparsentan on the High-Tech Drug Arrangement.

Sparsentan is a dual endothelin angiotensin receptor antagonist that inhibits the activities of both endothelin type A receptor and angiotensin II type 1 receptor. This dual inhibition reduces proteinuria and slows the progression of kidney disease in patients with IgAN. Sparsentan should be initiated at a dose of 200mg once daily (o.d) for 14 days and then increased to a maintenance dose of 400mg o.d, dependent upon tolerability. A temporary down-titration is recommended if patients experience tolerability issues such as low blood pressure, worsening oedema, or hyperkalaemia. Sparsentan is, potentially, a long-term treatment and the SmPC does not make any recommendation on treatment duration, nor does it recommend a timepoint for assessment of response.

The current standard of care (SOC) for patients with IgAN in Ireland, is renin-angiotensin-aldosterone system inhibitors (RAASi) that includes angiotensin-converting enzyme inhibitors (ACEi) or angiotensin receptor blockers (ARBs). Sodium-glucose cotransporter-2 inhibitors (SGLT2i) such as dapagliflozin and empagliflozin are currently used as an add-on therapy to RAASi in 60% to 70% of patients who have persistent proteinuria. The KDIGO 2025 Clinical Practice Guideline recommends that SGLT2i should be used in combination with sparsentan or RAASi in patients with IgAN who are at risk of progressive kidney function loss.

1. Comparative effectiveness of sparsentan

The clinical trial programme of sparsentan includes PROTECT, a randomised, double-blind, phase III trial to assess the safety and efficacy of sparsentan versus irbesartan (an ARB) in participants with primary IgAN with a urine protein excretion ≥1.0g/day despite maximised RAASi therapy for at least 12 weeks. Sparsentan was administered as per the SmPC dosing, while irbesartan was administered at a dose of 150mg o.d for 14 days, increasing to the maintenance dose of 300mg o.d. Treatments were administered for 110 weeks, followed by four weeks of SOC treatments, in which patients in both arms resumed treatments with

RAASi. The primary endpoint of PROTECT was the change from baseline in urine-to-protein ratio (UP/C) at week 36. Key secondary endpoints included the rate of change in the estimated glomerular filtration rate (eGFR) from baseline to week 110 (total slope) and the rate of change in eGFR from week six to week 110 (chronic slope).

At final analysis, sparsentan demonstrated a statistically significant improvement in UP/C at week 36 compared to irbesartan. Participants in the sparsentan arm achieved a 49.8% reduction in UP/C compared with baseline, versus a 15.1% reduction in the irbesartan arm compared with baseline. Two-year follow-up data showed favourable effects of sparsentan on the reduction in eGFR chronic slope and total slope compared with irbesartan.

Limitations of the PROTECT trial include: the inability to generalise the results to patients with a proteinuria level of <1.0 g/day; lack of comparative evidence to RAASi treatments other than irbesartan; the long-term effect of sparsentan on proteinuria is unknown; UP/C alone was not an accepted surrogate for long-term kidney damage by the EMA and therefore, a confirmatory secondary endpoint of eGFR slope over two years was used as a result; the efficacy of sparsentan in combination with SGLT2i is unknown as PROTECT did not allow treatment with SGLT2i during the double-blind period. The Applicant provided additional evidence on the use of sparsentan in combination with SGLT2i from the SPARTACUS trial. However, the certainty of the evidence is low due to study attrition, small sample size, and lack of a comparator arm.

2. Safety of sparsentan

In PROTECT, treatment-emergent adverse events (TEAEs) were reported in 187 (93%) of 202 participants in the sparsentan arm and 177 (88%) of 202 participants in the irbesartan arm by the final datacut (07 September 2023). Common TEAEs of dizziness (15% vs 6%), fatigue (8% vs 5%), hypotension (13% vs 4%), peripheral oedema (15% vs 12%), hyperkalaemia (16% vs 13%), hepatic-associated events (9% vs 6%) and increased lipase (6% vs 4%) were reported for sparsentan vs irbesartan. Acute kidney injury adverse drug reactions were reported in 12 (6%) participants in the sparsentan arm and five (2%) participants in the irbesartan arm. To reduce the risk of potential serious hepatotoxicity, the SmPC advises that serum aminotransferase levels and total bilirubin should be monitored prior to initiation of treatment with continued monitoring every three months. Sparsentan should be used with caution in patients with moderate hepatic impairment. Concomitant use of sparsentan with

endothelial receptor antagonists, ARBs, or renin inhibitors is contraindicated.

3. Cost effectiveness of sparsentan

The Applicant has compared the cost-effectiveness of sparsentan to SOC (i.e., RAASi therapy comprising ACEi [ramipril, lisinopril] and ARBs [irbesartan, losartan]) in the base case. The Applicant has assumed that irbesartan is representative of all RAASi treatments (ACEi and ARBs). The efficacy and safety data from the irbesartan arm in PROTECT was utilised for all the included ACEi and ARBs of RAASi. The inclusion of ramipril, lisinopril, and losartan only influenced SOC treatment costs, with equal usage assumed for all four RAASi treatments.

Methods

A cohort-level state transition Markov model considers patient outcomes based on their chronic kidney disease (CKD) stage and UP/C levels. The model splits UP/C levels into four Health States (UP/C <0.44g/g, UP/C 0.44-0.88g/g, UP/C 0.88-1.76g/g, and UP/C >1.76g/g). Within each UP/C Health State, modelled patients are distributed among Health States defined by CKD stage (CKD stage 1&2, CKD stage 3, and CKD stage 4). Once patients enter end stage renal disease (i.e., CKD stage 5), all patients are grouped together regardless of UP/C categories and are distributed between pre-renal replacement therapy (RRT), dialysis, and transplant.

During each model cycle, patients can transition to the Heath State representing Death from any earlier Health States. It was assumed that 80% of patients in both arms receive add-on dapagliflozin (SGLT2i). A relative dose intensity (RDI) of 98.8% (derived from the sparsentan arm of PROTECT) was assumed for sparsentan, RAASi, and dapagliflozin. A lifetime horizon with a 12-week cycle length was used.

A stopping rule is applied whereby patients who have a UP/C ≥1.76g/g and a <30% reduction in UP/C from baseline at week 36 are considered 'non-responders'. These 'non-responders' discontinue treatment with sparsentan, after which they receive SOC treatment with irbesartan. The Review Group note that this stopping rule was not applied in the PROTECT trial and is not recommended in the SmPC nor by clinical opinion (obtained by the Review Group) which indicated an infinite treatment duration for sparsentan or RAASi.

The main treatment effect in the model is improvement in UP/C Health State. In the Applicant's base case, transitions probabilities from CKD stages 1&2 and 3 are informed by

the PROTECT trial. Transition probabilities from CKD stage 4 are informed by a matched cohort of patients with IgAN from the UK National Registry of Rare Kidney Diseases (RaDaR) dataset. Health related quality of life (HRQoL) outcomes were exploratory within the PROTECT trial, and the utilities values obtained were higher than in prior submissions in a similar disease area and lack face validity. The Applicant used utility data for CKD stage derived from the literature. The Review Group identified a study by Zhou et al., which reported IgAN-specific utility values. However, the Review Group note limitations in the study design including that a vignette-based approach was used rather than EQ-5D which is preferrable. Therefore, the utilities from this study were explored in a scenario analysis. The model included drug acquisition and adverse event costs for sparsentan and RAASi and add-on SGLT2i costs. Other healthcare resources were aggregated as Health State-specific costs and included hospitalisations, outpatient appointments, primary care visits, emergency department visits, nephrologist visits, dialysis-related costs and transplant-related costs. A once-off end-of-life cost was applied to all patients entering the Death Heath State.

Results

An incremental analysis of the costs and benefits of sparsentan versus RAASi was presented by the Applicant. Results of the analysis are presented in Table 1.

Table 1: Applicant base case incremental cost-effectiveness results [a]

Treatments	Total costs (€)	Total QALYs	Incremental costs (€)	Incremental QALYs	ICER (€/QALY)
RAASi	513,881	10.45	-	-	-
Sparsentan	703,197	11.21	189,316	0.76	247,635

RAASi: Renin-angiotensin-aldosterone system inhibitor; **QALY**: Quality adjusted life year; **ICER**: Incremental cost-effectiveness ratio

[a] Corresponding probabilistic ICER using 1,000 iterations=€262,803/QALY. Figures in the table are rounded, and so calculations may not be directly replicable. Discount rate of 4% applied to costs and outcomes.

The NCPE Review Group identified several limitations in the Applicant's base case and have made changes in the NCPE-adjusted base case. These include: applying transition probabilities derived from the PROTECT trial for all cycles and all CKD stages; excluding patients with CKD stage 4 and UP/C <0.75g/g from treatment with sparsentan as per the SmPC recommendations and the PROTECT trial eligibility criteria; and removing the stopping rule for sparsentan. The NCPE adjusted base case is presented in Table 2.

Table 2: NCPE adjusted base case incremental cost-effectiveness results[a]

Treatments	Total costs (€)	Total QALYs	Incremental costs (€)	Incremental QALYs	ICER (€/QALY)
RAASi	383,615	11.55	-	-	-
Sparsentan	657,013	12.17	273,398	0.62	443,026

RAASi: Renin-angiotensin-aldosterone system inhibitor; **QALY**: Quality adjusted life year; **ICER**: Incremental cost-effectiveness ratio
[a] Corresponding probabilistic ICER using 1,000 iterations=€481,656/QALY. Figures in the table are rounded, and so calculations may not be directly replicable. Discount rate of 4% applied to costs and outcomes.

Sensitivity analysis

The probabilities of cost-effectiveness for sparsentan, versus RAASi, in the Applicant and NCPE-adjusted base cases was 0% at thresholds of €20,000 per quality-adjusted life year (QALY) and €45,000 per QALY. Deterministic one-way sensitivity analyses indicated that the most influential parameters in the model, for both the Applicant and the NCPE-base case, related to utilities and dialysis costs. The Review Group note that the probabilistic incremental cost-effectiveness ratios (ICERs) are somewhat higher than the deterministic ICERs, in particular for the NCPE adjusted base case. The Review Group consider that there is some additional uncertainty in the reliability of the deterministic ICER, in both the Applicant and the NCPE adjusted base case.

Budget impact of sparsentan

The price to wholesaler of sparsentan is €3,980.00 per pack (30 x 200mg or 30 x 400mg tablets). In the budget impact model (BIM), the Applicant assumed 80% of patients receiving sparsentan or RAASi would also receive add-on SGLT2i (dapagliflozin). The estimated cost of sparsentan plus dapagliflozin, per patient per year is €48,595 (VAT not applicable for oral drugs). The Applicant predicted that 359 patients will be treated with sparsentan in Year one rising to 382 patients in Year five; a total of 1,852 patients over five years. The estimated five-year cumulative gross drug budget impact for sparsentan is €19.97 million, and the five-year cumulative net drug budget impact is €19.72 million. Many of the BIM inputs are uncertain and there is considerable uncertainty associated with the budget impact estimates. The Applicant estimated, based on clinical opinion, that 22.5% of patients with primary IgAN will be unresponsive to standard RAASi and thus eligible for sparsentan. Estimates obtained from clinicians, by the Review Group, of the proportion of patients who could be eligible for sparsentan varied from 15% to 33.3%. The Review Group highlight uncertainty in the 80% estimate of patients receiving add-on SGLT2i. The Review Group note that sparsentan is a first-in-class treatment and therefore the market share estimates may

be underestimated. A scenario analysis in which the market share for sparsentan started at 20% in Year one and increased to 100% in Year five resulted in a five-year cumulative gross drug budget impact of €54.06 million and a five-year cumulative net drug budget impact of €53.38 million.

4. Patient Organisation Submission

No patient organisation submission was received during the course of the assessment.

5. Conclusion

The NCPE recommends that sparsentan (Filspari®) not be considered for reimbursement unless cost-effectiveness can be improved relative to existing treatment*.

*This recommendation should be considered while also having regard to the criteria specified in the Health (Pricing and Supply of Medical Goods) Act 2013.