NATIONAL KIDNEY FOUNDATION®

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February 18, 2026

The Honorable Dr. Martin A. Makary
Commissioner of Food and Drugs
U.S. Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993

cc: Dr. Tracy Beth Høeg, *Acting Director, Center for Drug Evaluation and Research (CDER), U.S. Food and Drug Administration*
Dr. Aliza Thompson, *Director of the Division of Cardiology and Nephrology, Center for Drug Evaluation and Research (CDER), U.S. Food and Drug Administration*

Re: Ensuring patient access to sparsentan for focal segmental glomerulosclerosis (FSGS)

Dear Commissioner Makary,

On behalf of the National Kidney Foundation (NKF) and the thousands of Americans living with FSGS, we write to express our support for FDA approval of sparsentan for the treatment of FSGS and urge the FDA to consider the patient voice in the approval decision.

FSGS is a devastating form of kidney disease that affects both children and adults and frequently progresses to kidney failure (ESRD). Importantly, there are currently no FDA-approved drugs specifically for the treatment of idiopathic/primary FSGS or APOL1-mediated FSGS. Presently, patients often rely on off-label immunosuppressive regimens with significant toxicity and inconsistent efficacy. Many patients ultimately progress to ESRD requiring either dialysis or transplant to survive. Even if transplant is achieved, people living with FSGS face disease recurrence.

Sparsentan is already FDA-approved for the treatment of IgA nephropathy (IgAN), reflecting prior agency determination of its safety and efficacy profile within a glomerular disease population. In FSGS, the benefit–risk calculus must appropriately account for the severity of disease, limited alternatives, and the patient community's willingness to accept uncertainty in exchange for the possibility of delaying kidney failure.

NKF and our clinical membership have reviewed the sparsentan data for FSGS in detail. At NKF's 2025 Spring Clinical Meeting, findings from the DUPLEX trial on sparsentan were presented.[1] The DUPLEX data demonstrated that patients achieved partial or complete remission of proteinuria earlier and more frequently with sparsentan compared to irbesartan.[2]In a disease characterized by persistent proteinuria and progressive loss of kidney function, reduction and remission of proteinuria are clinically meaningful outcomes that patients and clinicians prioritize. The demonstrated proteinuria effects are important in the context of a rare, heterogeneous disease with high unmet need. The

[1] Tumlin, J. (2025). Patients in DUPLEX Achieved Partial or Complete Remission of Proteinuria Earlier and More Often With Sparsentan vs Irbesartan: Implications for Slowing Progression to Kidney Failure in Focal Segmental Glomerulosclerosis. 2025 Spring Clinical Meetings, National Kidney Foundation. https://cme.kidney.org/spa/app/resource/r649-2025-spring-clinical-meetings/event/home/posters/abstracts?abstractId=7678

[2] Rheault MN, Alpers CE, Barratt J, et al. Sparsentan versus irbesartan in focal segmental glomerulosclerosis. N Engl J Med 2023;389:2436-2445.

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DUPLEX trial showed no significant difference in eGFR slope between sparsentan and irbesartan at 108 weeks in FSGS patients, despite sparsentan's superior proteinuria reduction. However, several nuanced findings suggest kidney protective effects that warrant consideration. In a prespecified sensitivity analysis excluding measurements after initiation or intensification of immunosuppressive treatments, the chronic eGFR slope (week 6-108) favored sparsentan with a difference of 2.1 ml/min/1.73 m²/year (95% CI 0.1 to 4.1), suggesting that differential use of immunosuppression in the irbesartan group may have diluted between-group differences. While not statistically significant, exploratory analyses showed consistent trends favoring sparsentan. The composite endpoint of ≥50% eGFR reduction, kidney failure, or renal death occurred in 11.4% of sparsentan patients vs. 16.6% of irbesartan patients.[3]

We also emphasize the importance of incorporating patient experience data into regulatory decision-making. The FSGS community has articulated the daily burden of uncontrolled proteinuria, relapse cycles, hospitalizations, dialysis, and transplant uncertainty.[4] In rare diseases such as FSGS, where large trials are challenging and timelines are long, FDA's Patient-Focused Drug Development framework plays a critical role in ensuring that regulatory decisions reflect what matters most to patients.

The kidney community has few therapeutic advances in FSGS despite decades of need. Timely regulatory action would represent meaningful progress for patients and families facing a lifelong, progressive disease without approved treatment options.

We appreciate FDA's commitment to rigorous, science-based, and patient-centered review and would welcome the opportunity to further discuss the FSGS unmet need landscape and the clinical implications of the DUPLEX findings.

Sincerely,

Joseph A Vassalotti, MD
Chief Medical Officer, National Kidney Foundation

[3] *Ibid.*

[4] National Kidney Foundation & NephCure Kidney International. (2021). The Voice of the Patient: Externally Led Patient-Focused Drug Development meeting on primary focal segmental glomerulosclerosis (FSGS) (Report date: September 10, 2021). https://www.kidney.org/sites/default/files/elpfdd_fsgs_vop_20210910.pdf