Filspari™ (sparsentan) – New orphan drug approval

- On February 17, 2023, Travere Therapeutics announced the FDA approval of Filspari (sparsentan), to reduce proteinuria in adults with primary immunoglobulin A nephropathy (IgAN) at risk of rapid disease progression, generally a urine protein-to-creatinine ratio (UPCR) ≥ 1.5 g/g.
    - This indication is approved under accelerated approval based on a reduction of proteinuria. It has not been established whether Filspari slows kidney function decline in patients with IgAN. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory clinical trial.
- IgAN, also called Berger's disease, is a rare progressive kidney disease characterized by the buildup of immunoglobulin A (IgA) in the kidneys. The deposits of IgA cause a breakdown of the normal filtering mechanisms in the kidney, leading to blood in the urine, protein in the urine, and a progressive loss of kidney function.
    - IgAN affects up to 150,000 people in the U.S.
- Filspari is an endothelin type A and angiotensin II receptor antagonist. Endothelin and angiotensin II are thought to contribute to the pathogenesis of IgAN.
- The efficacy of Filspari was established in PROTECT, a randomized, double-blind, active-controlled study in 281 adults with biopsy-proven IgAN, on a maximized stable dose of renin-angiotensin system (RAS) inhibitor treatment that was at least 50% of maximum labeled dose. Patients were randomized to either Filspari or irbesartan (an angiotensin II receptor blocker). Rescue immunosuppressive treatment could be initiated during the trial. The primary endpoint was the relative change from baseline in UPCR at week 36.
    - The mean reduction in proteinuria from baseline was 45% for Filspari vs. 15% for irbesartan ($p < 0.0001$).
- Filspari carries a boxed warning for hepatotoxicity and embryo-fetal toxicity.
    - For all patients, Filspari is available only through a restricted program under a REMS called the Filspari REMS because of the risk of hepatotoxicity and embryo-fetal toxicity.
    - Information about the REMS is available at www.filsparirems.com.
- Filspari is contraindicated in patients who are pregnant and should not be coadministered with angiotensin receptor blockers, endothelin receptor antagonists, or aliskiren.
- Additional warnings and precautions for Filspari include hypotension, acute kidney injury, hyperkalemia, and fluid retention.
- The most common adverse reactions (≥ 5%) with Filspari use were peripheral edema, hypotension (including orthostatic hypotension), dizziness, hyperkalemia, and anemia.
- The recommended initial dose of Filspari is 200 mg orally once daily. After 14 days, the dose should be increased to 400 mg once daily, as tolerated.

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- Travere Therapeutics plans to launch Filspari beginning the week of February 27, 2023. Filspari will be available as a 200 mg and 400 mg tablet.