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Otsuka Receives FDA Accelerated Approval for VOYXACT® (sibeprenlimab-szsi) for the Reduction of Proteinuria in Adults with Primary Immunoglobulin A Nephropathy (IgAN) at Risk for Disease Progression

Otsuka Pharmaceutical, Co. Ltd. (Otsuka) and Otsuka Pharmaceutical Development & Commercialization, Inc. (OPDC) today announce the U.S. Food and Drug Administration (FDA) has granted accelerated approval of VOYXACT (sibeprenlimab-szsi) for the reduction of proteinuria in adults with primary immunoglobulin A nephropathy (IgAN) at risk for disease progression. VOYXACT is a self-administered, subcutaneous injection dosed every four weeks. VOYXACT was granted accelerated approval based on the VISIONARY Phase 3 interim analysis, where it achieved a significant placebo-adjusted treatment effect of 51% (P<0.0001) reduction in proteinuria at nine months (n=320) of treatment (50% VOYXACT vs 2% placebo). VOYXACT is the first and only therapy to block A-PRoliferation-Inducing-Ligand (APRIL).

- VOYXACT achieved a significant placebo-adjusted treatment effect of 51% (P<0.0001) reduction in proteinuria at 9 months of treatment (50% VOYXACT vs 2% placebo) in the VISIONARY Phase 3 interim analysis.
- In the study, the most common adverse reactions (reported in ≥10% of patients treated with VOYXACT and at a higher incidence than placebo) reported in patients treated with VOYXACT and placebo, respectively, were infections (49% versus 45%) and injection site reactions (24% versus 23%).
- VOYXACT blocks A-PRoliferation-Inducing-Ligand (APRIL), resulting in reduced levels of serum galactose-deficient IgA1 (Gd-IgA1). Gd-IgA1 is implicated in the pathogenesis of IgAN.
- Proteinuria reduction is a recognized surrogate marker correlating with delaying progression to kidney failure and has been used as a surrogate endpoint in IgAN clinical trials to support accelerated regulatory approvals.
- VOYXACT is a self-administered, subcutaneous injection dosed every 4 weeks.
- Despite the current standard of care, IgAN is a progressive, immune-mediated, chronic kidney disease that typically manifests in adults aged 20-40 years and can lead to end-stage kidney disease (ESKD) over the lifetime of most patients.

Proteinuria reduction is a recognized surrogate marker correlating with delaying progression to kidney failure and has been used as a surrogate endpoint in IgAN clinical trials to support accelerated regulatory approvals[1]. This indication is approved by the FDA under the accelerated approval pathway based on reduction of proteinuria. It has not been established whether VOYXACT slows kidney function decline over the long-term in patients with IgAN. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory clinical from the ongoing Phase 3 VISIONARY study evaluating whether VOYXACT slows disease progression as measured by estimated glomerular filtration rate (eGFR) decline at 24 months. The eGFR data are expected in early 2026 and are intended to support traditional FDA approval.

"The availability of VOYXACT represents a novel targeted approach to help manage this complex disease for patients living with IgAN," said John Kraus, M.D., Ph.D., executive vice president and chief medical officer, Otsuka. "With its targeted mechanism, strong efficacy, safety profile, and once-every-four-weeks dosing, VOYXACT offers a new option for IgAN patients. We recognize the urgent need for new treatment options for IgAN and are thankful for the patients and healthcare professionals who continue to participate in our clinical trial program."

VOYXACT works by blocking APRIL, which plays a key role in the 4-hit process of IgAN pathogenesis and is an important initiating and sustaining factor in IgAN progression by promoting the production of pathogenic galactose-deficient IgA1 (Gd-IgA1)[2,3,4,5]. Inhibition of APRIL results in reduced levels of serum galactose-deficient IgA1 (Gd-IgA1), which is implicated in the pathogenesis of IgAN.

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3. Chang S, Li XK. The Role of Immune Modulation in Pathogenesis of IgA Nephropathy (nih.gov)
4. Cheung CK, Barratt J, Liew A, Zhang H, Tesar V, Lafayette R. The role of BAFF and April in IGA nephropathy: Pathogenic mechanisms and targeted therapies. Frontiers in nephrology. February 1, 2024.
5. Mathur M, Barratt J, Chacko B, et al. A Phase 2 Trial of Sibeprenlimab in Immunoglobulin A Nephropathy Patients. NEJM. 2023 https://www.nejm.org/doi/full/10.1056/NEJMoa2305635