

**Company**

Aurinia Pharmaceuticals Inc.

**Drug or Device Name**

LUPKYNIS®

**Category**

Pharmaceutical

**Compound/Technical Name**

Voclosporin

**Trade Name**

LUPKYNIS®

**Date of Approval**

01/22/2021

**Therapeutic Categories**

Immunological Agents

**Indications**

LUPKYNIS is a calcineurin-inhibitor immunosuppressant indicated in combination with a background immunosuppressive therapy regimen for the treatment of adult patients with active lupus nephritis (LN).

**Background**

Lupus nephritis (LN) is a serious and life-threatening manifestation of systemic lupus erythematosus (SLE), a chronic and complex autoimmune disease. About 200,000-300,000 people live with SLE in the U.S. and approximately half of these individuals will develop LN during their lifetime. If poorly controlled, LN can lead to permanent and irreversible kidney damage resulting in kidney failure. Patients with SLE are predominantly female and the burden of the disease falls disproportionately on patients of color; African Americans, Latinos, and Asian Americans are 2-3 times more likely to develop LN than Caucasians. Black and Hispanic individuals with SLE tend to develop LN earlier and have poorer outcomes compared to Caucasian individuals. Within fifteen years of LN diagnosis, up to 15% of people with LN progress to kidney failure, which requires dialysis or a kidney transplant. Patients diagnosed with LN have three times higher risk of death than patients with SLE and no renal involvement. For decades, physicians and patients have been challenged by a lack of safe and effective treatment options dedicated to LN. Until recently, the standard of care for LN primarily depended on immunosuppression with mycophenolate mofetil and steroids. This approach has been only modestly effective and burdens patients with numerous toxicities.

**Development**

The origins of voclosporin date back to the mid-nineties and were originally imagined as an improvement to the drug cyclosporine – at that time, the standard of care for organ transplant patients. There had been no significant improvements on cyclosporine (which was approved in 1983) until voclosporin. Voclosporin, a novel calcineurin inhibitor, has a key modification on one amino acid that allows it to bind to calcineurin more effectively. This modification also changes the metabolism of voclosporin, allowing for an improved side effect profile and is the only calcineurin inhibitor to be used without therapeutic drug monitoring. As the research team worked on voclosporin for organ transplants, it became apparent that voclosporin could be useful for treating other autoimmune diseases. Researchers focused on LN, due to voclosporin's ability to inhibit T-cell activation and cytokine production, while promoting podocyte stability and minimizing podocyte damage in the kidney. (Podocytes are specialized epithelial cells of the glomerulus that play a vital role in the creation and filtering of urine.) In 2017, Aurinia initiated the global Phase 3 clinical trial AURORA 1, which included 357 subjects with biopsy-confirmed LN in 27 countries. Subjects received either voclosporin or placebo twice daily, alongside standard therapy. Positive results were announced late in 2019, demonstrating that voclosporin helps to control LN and protect the kidneys from further damage without the use of high-dose steroids. At one year, voclosporin plus standard of care was more than twice as effective at achieving a complete renal response versus standard care alone. Clinically and statistically significant improvements were seen in all pre-planned secondary endpoints, including time to renal response, partial response, and improvements in subjects' urinary protein-to-creatinine ratios compared to standard care. The FDA approved LUPKYNIS (voclosporin) in January 2021.

## **Innovation**

The FDA approval of LUPKYNIS marked a turning point for the LN community who had been challenged for decades with preventing irreversible kidney damage, clinical trial failures and need for kidney transplant associated with the condition. The standardized mortality rate for individuals with LN and end stage renal disease is 64x higher than the general population. For many years, LN treatment options were not tailored to the condition, were only modestly effective and were highly toxic, especially to young women. LUPKYNIS is not only the first FDA-approved LN treatment intended to be taken orally; but its use reduces the dose of steroids needed and acts quickly to reduce kidney harm. In clinical trials, people who took voclosporin as part of their treatment plan were more than twice as likely to have their LN under control at 1 year of treatment than those only taking the current standard of care. Additionally, studies of Phase 3 subjects who remained on voclosporin treatment for an additional 24 months (the AURORA 2 trial) demonstrated that the treatment continued to be safe, well-tolerated and preserve kidney function. Unique to LUPKYNIS is the proprietary, patented eGFR pharmacodynamic dosing protocol featured on the FDA approved label, which allows for tailored dose adjustments to address individual patient needs. LUPKYNIS fills a major unmet need for the lupus community, especially for historically underserved patients of color. Tens of thousands of people will be diagnosed with lupus in the coming years, and LUPKYNIS now serves as a vital treatment for the nearly half of these patients who will develop LN. The availability of a fast acting, effective, and less toxic LN treatment elevates the standard of care for patients and will ultimately help protect the lives and livelihoods of patients who may have previously progressed to total kidney failure.

## **Pubmed**

PMID: 33788181 - Voclosporin: First Approval PMID: 30420324 - A randomized, controlled double-blind study comparing the efficacy and safety of dose-ranging voclosporin with placebo in achieving remission in patients with active lupus nephritis. PMID: 33971155 - Efficacy and safety of voclosporin versus placebo for lupus nephritis (AURORA 1): a double-blind, randomized, multicentre, placebo-

controlled, phase 3 trial PMID: 24504808: The incidence and prevalence of systemic lupus erythematosus, 2002-2004: The Georgia Lupus Registry PMID: 24504809 Population-based incidence and prevalence of systemic lupus erythematosus: the Michigan Lupus Epidemiology and Surveillance program PMID: 28891252 The Incidence and Prevalence of Systemic Lupus Erythematosus in New York County (Manhattan), New York: The Manhattan Lupus Surveillance Program PMID: 28891237 The Incidence and Prevalence of Systemic Lupus Erythematosus in San Francisco County, California: The California Lupus Surveillance Project PMID: 33474834 Prevalence of Systemic Lupus Erythematosus in the United States: Estimates From a Meta-Analysis of the Centers for Disease Control and Prevention National Lupus Registries PMID: 22851469 Joint European League Against Rheumatism and European Renal Association-European Dialysis and Transplant Association (EULAR/ERA-EDTA) recommendations for the management of adult and paediatric lupus nephritis PMID: 26342222 Joint European League Against Rheumatism and European Renal Association-European Dialysis and Transplant Association (EULAR/ERA-EDTA) recommendations for the management of adult and paediatric lupus nephritis PMID: 23203603 Epidemiology and sociodemographics of systemic lupus erythematosus and lupus nephritis among US adults with Medicaid coverage, 2000-2004 PMID: 12079714 Demographic differences in the development of lupus nephritis: a retrospective analysis PMID: 12004788 Systemic lupus erythematosus in three ethnic groups. XII. Risk factors for lupus nephritis after diagnosis PMID: 26342222 The frequency and outcome of lupus nephritis: results from an international inception cohort study PMID: 31115180 Racial and Ethnic Differences in the Prevalence and Time to Onset of Manifestations of Systemic Lupus Erythematosus: The California Lupus Surveillance Project PMID: 23754671 Effect of renal disease on the standardized mortality ratio and life expectancy of patients with systemic lupus erythematosus FOR ADDITIONAL REFERENCE: <https://LUPKYNISpro.com/safety/#isi> <https://bit.ly/3MYZrYk>

## Attachments

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