



Lilly's Taltz® (ixekizumab) is the First IL-17A Antagonist to Receive U.S. FDA Approval for the Treatment of Non-Radiographic Axial Spondyloarthritis (nr-axSpA)

June 1, 2020

- Taltz is now approved to treat patients across the full axSpA spectrum, including ankylosing spondylitis (AS), also known as radiographic axSpA, and nr-axSpA -

INDIANAPOLIS, June 1, 2020 /PRNewswire/ -- Eli Lilly and Company (NYSE: LLY) announced today the U.S. Food and Drug Administration (FDA) has approved a supplemental Biologics License Application (sBLA) for Taltz® (ixekizumab) injection 80 mg/mL for the treatment of active non-radiographic axial spondyloarthritis (nr-axSpA) in patients with objective signs of inflammation. Another first-in-class milestone for the treatment, today's approval makes Taltz the first IL-17A antagonist to be approved by the FDA for nr-axSpA.

Axial spondyloarthritis (axSpA), which includes both AS and nr-axSpA, is a disease predominantly affecting the sacroiliac joints and the spine, resulting in chronic inflammatory back pain and fatigue.^{1,2,3} It is estimated that 2.3 million people in the U.S. have axSpA, and approximately half of those individuals live with nr-axSpA.^{2,4} For patients with AS, the disease is characterized by the presence of structural damage of the sacroiliac joints that appears on an X-ray, while patients with nr-axSpA do not have clearly detectable structural damage radiographically.⁵ These two patient subsets share a similar burden of disease and similar clinical features, but approved biologic treatment options for patients with nr-axSpA are much more limited and patients are often underdiagnosed.^{5,6}

"We recognize that many patients living with this condition suffer from chronic inflammatory back pain and other symptoms of inflammation for years before being diagnosed, and we're excited about the possibility of these patients finding relief with Taltz," said Patrik Jonsson, senior vice president and president of Lilly Bio-Medicines. "This approval reflects Lilly's continued growth and commitment to supporting rheumatologists and people with autoimmune conditions, including nr-axSpA."

This approval is based on the results from the Phase 3 COAST-X trial, which evaluated improvement in signs and symptoms of nr-axSpA as measured by the proportion of patients who achieved Assessment of Spondyloarthritis International Society 40 (ASAS40) response criteria compared to placebo. ASAS40 measures disease signs and symptoms such as pain, inflammation and function.

The safety profile of Taltz in patients with nr-axSpA was consistent with previous experience with Taltz in other approved indications. Taltz should not be used in patients with a previous serious hypersensitivity reaction, such as anaphylaxis, to ixekizumab or to any of the excipients. Taltz may increase the risk of infection. Other warnings and precautions for Taltz include pre-treatment evaluation for tuberculosis, hypersensitivity, inflammatory bowel disease, and immunizations. See Important Safety Information below.

"There are limited treatment options that can address both AS and nr-axSpA symptoms, and people living with these conditions are often underdiagnosed and undertreated," said Cassie Shafer, chief executive officer of the Spondylitis Association of America. "This approval represents an important milestone in providing relief to patients where there has been a significant unmet need."

This approval reaffirms the long track record that Taltz has in providing efficacy for patients in multiple indications. This is the fifth approval for Taltz, which was first approved by the FDA in March 2016 for the treatment of moderate to severe plaque psoriasis (PsO) in adult patients who are candidates for systemic therapy or phototherapy. The FDA also approved Taltz for the treatment of adults with active psoriatic arthritis (PsA) in December 2017, for the treatment of adults with active AS in August 2019 and for moderate to severe plaque PsO in pediatric patients 6 years of age and older who are candidates for systemic therapy or phototherapy in March 2020.

In COAST-X, the safety and efficacy of Taltz was demonstrated in a Phase 3, multicenter, randomized, double-blind, placebo-controlled 52-week study of adult patients with active nr-axSpA with objective signs of inflammation. The primary endpoint of the study was the proportion of patients achieving ASAS40 at Week 52. The proportion of Taltz patients (n=96) achieving the primary endpoint was superior to placebo (n=105), with 30 percent of patients treated with Taltz 80 mg every four weeks achieving ASAS40 response compared to 13 percent of patients treated with placebo at Week 52 (P=0.0045). A major secondary endpoint was ASAS40 response at Week 16 with 35 percent of Taltz patients compared to 19 percent of placebo patients achieving that endpoint (P<0.01).

"In the COAST-X study, Taltz provided relief to nr-axSpA patients living with debilitating symptoms such as chronic back pain and fatigue," said Atul Deodhar, M.D., professor of medicine, Oregon Health & Science University and clinical investigator for the COAST pivotal trial program. "The study results indicate that Taltz is safe and effective in patients suffering from this condition. Today's FDA approval provides patients with a much-needed treatment option targeting IL-17A to improve the signs and symptoms of nr-axSpA."

Other major secondary endpoints of the study included Ankylosing Spondylitis Disease Activity Score (ASDAS), Bath Ankylosing Spondylitis Disease Activity (BASDAI), the proportion of patients achieving low disease activity (ASDAS <2.1) and the 36-Item Short Form Health Survey (SF-36) Physical Component Summary (PCS) Score.

An estimated 137,000 patients have been treated with Taltz worldwide since launch, with approximately 80,000 of those in the U.S., giving rheumatologists confidence in making informed prescribing decisions for patients with PsO, PsA, AS and nr-axSpA.⁷

Lilly will work with insurers, health systems and providers to ensure patients are able to access this treatment. We recognize that COVID-19 may be impacting the ability for people to afford their medications, and the Taltz Together™ program helps ensure patients pay the lowest amount possible and can have Taltz delivered straight to their homes. Patients, physicians, pharmacists or other healthcare professionals with questions about Taltz

should contact The Lilly Answers Center at **1-800-LillyRx (1-800-545-5979)** or visit www.lilly.com. If you'd like to learn more about insurance support, call at **1-844-TALTZ-NOW (1-844-825-8966)** or visit www.taltz.com/patient-support.

INDICATIONS AND USAGE FOR TALTZ

Taltz is approved for the treatment of adult patients with active non-radiographic axial spondyloarthritis with objective signs of inflammation, active psoriatic arthritis, or active ankylosing spondylitis, and for the treatment of patients 6 years of age and older with moderate-to-severe plaque psoriasis who are candidates for systemic therapy or phototherapy.

IMPORTANT SAFETY INFORMATION FOR TALTZ

CONTRAINDICATIONS

Taltz is contraindicated in patients with a previous serious hypersensitivity reaction, such as anaphylaxis, to ixekizumab or to any of the excipients.

WARNINGS AND PRECAUTIONS

Infections

Taltz may increase the risk of infection. In clinical trials of adult patients with plaque psoriasis, the Taltz group had a higher rate of infections than the placebo group (27% vs 23%). A similar increase in risk of infection was seen in placebo-controlled trials of adult patients with psoriatic arthritis, ankylosing spondylitis, non-radiographic axial spondyloarthritis, and pediatric patients with plaque psoriasis. Serious infections have occurred. Instruct patients to seek medical advice if signs or symptoms of clinically important chronic or acute infection occur. If a serious infection develops, discontinue Taltz until the infection resolves.

Pre-Treatment Evaluation for Tuberculosis

Evaluate patients for tuberculosis (TB) infection prior to initiating treatment with Taltz. Do not administer to patients with active TB infection. Initiate treatment of latent TB prior to administering Taltz. Closely monitor patients receiving Taltz for signs and symptoms of active TB during and after treatment.

Hypersensitivity

Serious hypersensitivity reactions, including angioedema and urticaria (each $\leq 0.1\%$), occurred in the Taltz group in clinical trials. Anaphylaxis, including cases leading to hospitalization, has been reported in post-marketing use with Taltz. If a serious hypersensitivity reaction occurs, discontinue Taltz immediately and initiate appropriate therapy.

Inflammatory Bowel Disease

Patients treated with Taltz may be at an increased risk of inflammatory bowel disease. In clinical trials, Crohn's disease and ulcerative colitis, including exacerbations, occurred at a greater frequency in the Taltz group than the placebo group. During Taltz treatment, monitor patients for onset or exacerbations of inflammatory bowel disease and if IBD occurs, discontinue Taltz and initiate appropriate medical management.

Immunizations

Prior to initiating therapy with Taltz, consider completion of all age-appropriate immunizations according to current immunization guidelines. Avoid use of live vaccines in patients treated with Taltz.

ADVERSE REACTIONS

Most common adverse reactions ($\geq 1\%$) associated with Taltz treatment are injection site reactions, upper respiratory tract infections, nausea, and tinea infections. Overall, the safety profiles observed in adult patients with psoriatic arthritis, ankylosing spondylitis, non-radiographic axial spondyloarthritis, and pediatric patients with plaque psoriasis were consistent with the safety profile in adult patients with plaque psoriasis, with the exception of influenza and conjunctivitis in psoriatic arthritis and conjunctivitis, influenza, and urticaria in pediatric psoriasis.

Please see full [Prescribing Information](#) and [Medication Guide](#) for Taltz. See [Instructions for Use](#) included with the device.

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About Taltz®

Taltz is a monoclonal antibody that selectively binds with interleukin 17A (IL-17A) cytokine and inhibits its interaction with the IL-17 receptor.⁸ IL-17A is a naturally occurring cytokine that is involved in normal inflammatory and immune responses. Taltz inhibits the release of pro-inflammatory cytokines and chemokines.⁷

About the COAST-X Study

COAST-X is a multicenter, randomized, double-blind, placebo-controlled 52-week study evaluating the efficacy and safety of Taltz for the treatment of active non-radiographic axial spondyloarthritis (nr-axSpA) in patients with objective signs of inflammation. Patients were required to have an established diagnosis of nr-axSpA and active disease defined by a Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) Numeric Rating Scale (NRS) score ≥ 4 and total back pain ≥ 4 at screening and baseline, and were required to have objective signs of inflammation by presence of sacroiliitis on MRI or presence of elevated CRP.

About the Taltz Program in axSpA

The COAST-X study is part of a clinical development program that aims to evaluate the efficacy and safety of Taltz across various population subsets of patients with axSpA. The COAST program includes three registration studies each of one year duration: COAST-V in patients with ankylosing spondylitis (AS)/radiographic axSpA who are biologic-naïve; COAST-W in patients with AS/radiographic axSpA who previously had an inadequate response or were intolerant to tumor necrosis factor (TNF) inhibitors; and COAST-X in biologic-naïve nr-axSpA patients with objective signs of inflammation. Patients may enroll into a long-term extension study (COAST-Y) after completion of any of these registration studies to receive Taltz treatment for up to an additional two years.

About Lilly in Immunology

Lilly is bringing our heritage of championing groundbreaking, novel science to immunology and is driven to change what's possible for people living with autoimmune diseases. There are still significant unmet needs, as well as personal and societal costs, for people living with a variety of autoimmune diseases and our goal is to minimize the burden of disease. Lilly is investing in leading-edge clinical approaches across its immunology portfolio in hopes of transforming the autoimmune disease treatment experience. We've built a deep pipeline and are focused on advancing cutting

edge science to find new treatments that offer meaningful improvements to support the people and the communities we serve.

About Eli Lilly and Company

Lilly is a global health care leader that unites caring with discovery to create medicines that make life better for people around the world. We were founded more than a century ago by a man committed to creating high-quality medicines that meet real needs, and today we remain true to that mission in all our work. Across the globe, Lilly employees work to discover and bring life-changing medicines to those who need them, improve the understanding and management of disease, and give back to communities through philanthropy and volunteerism. To learn more about Lilly, please visit us at lilly.com and lilly.com/news. P-LLY

This press release contains forward-looking statements (as that term is defined in the Private Securities Litigation Reform Act of 1995) about Taltz (ixekizumab) as a treatment for patients with non-radiographic axial spondyloarthritis and reflects Lilly's current belief. However, as with any pharmaceutical product, there are substantial risks and uncertainties in the process of development and commercialization. Among other things, there can be no guarantee that Taltz will receive additional regulatory approvals or be commercially successful. For further discussion of these and other risks and uncertainties, see Lilly's most recent Form 10-K and Form 10-Q filings with the United States Securities and Exchange Commission. Except as required by law, Lilly undertakes no duty to update forward-looking statements to reflect events after the date of this release.

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¹ Reveille JD, et al. Prevalence of axial spondylarthritis in the United States: Estimates from a cross-sectional survey. *Arthritis Care Res.* 2012;64(6):905-910.

² Strand V, et al. Prevalence of axial spondyloarthritis in United States rheumatology practices: Assessment of SpondyloArthritis International Society criteria versus rheumatology expert clinical diagnosis. *Arthritis Care Res.* 2013;65(8):1299-306.

³ Kiltz U, et al. Do patients with non-radiographic axial spondylarthritis differ from patients with ankylosing spondylitis? *Arthritis Care Res.* 2012;64(9):1415-22.

⁴ U.S. Census Bureau, Population Estimates Program (PEP) <https://www.census.gov/quickfacts/fact/table/US#> accessed on April 30, 2020.

⁵ Deodhar A, et al. The concept of axial spondyloarthritis: joint statement of the spondyloarthritis research and treatment network and the Assessment of SpondyloArthritis International Society in response to the US Food and Drug Administration's comments and concerns. *Arth Rheum.* 2014;66(10):2649-2656.

⁶ De Miguel Mendieta E, et al. *Ann Rhuem Dis.* 2018;77:1156. Abstract AB0857.

⁷ Data on File. Lilly USA, LLC. DOF-IX-US-0240.

⁸ Taltz Prescribing Information, 2020.

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