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OTEZLA® (apremilast) - First Oral Therapy Approved by the U.S. Food and Drug Administration for the Treatment of Adults with Active Psoriatic Arthritis

In phase III studies, OTEZLA demonstrated clinically significant improvements across multiple manifestations of psoriatic arthritis and a consistent safety profile.

Routine laboratory monitoring for patients taking OTEZLA is not required.

OTEZLA is an oral therapy that modulates inflammation through intracellular inhibition of PDE4.

SUMMIT, N.J.--(BUSINESS WIRE)-- Celgene Corporation (NASDAQ: CELG) today announced that the U.S. Food and Drug Administration (FDA) has approved OTEZLA® (apremilast), the Company's oral, selective inhibitor of phosphodiesterase 4 (PDE4), for the treatment of adult patients with active psoriatic arthritis. A chronic disorder, psoriatic arthritis is characterized by pain, stiffness, swelling and tenderness of the joints, inflammation of specific ligaments and tendons, and a decrease in physical functioning. OTEZLA is the only FDA-approved oral treatment for psoriatic arthritis.

"The approval of oral OTEZLA is significant for patients living with psoriatic arthritis, which is a debilitating, painful disease that has a significant effect on a patient's day-to-day activities," said Dr. Alvin Wells, M.D., Ph.D., Director, Rheumatology and Immunotherapy Center, Franklin, WI, U.S. "OTEZLA offers physicians and patients a meaningful new treatment option, with the potential to benefit psoriatic arthritis patients irrespective of prior treatment."

"OTEZLA works differently from other therapies approved for psoriatic arthritis through the intracellular inhibition of PDE4," said Philip Mease, MD, Director of the Rheumatology Clinical Research Division of Swedish Medical Center and Clinical Professor, University of Washington. "The approval of an oral therapy with a novel mechanism of action for patients with psoriatic arthritis offers a different approach to patient care."

The approval was based on safety and efficacy results from three multi-center, randomized, double-blind, placebo-controlled trials - PALACE 1, 2 and 3 - conducted in adult patients with active psoriatic arthritis who were inadequately controlled by disease-modifying anti-rheumatic drugs (DMARDs) and/or biologics. More than 75 percent of patients were previously treated with DMARDs only and 22 percent of patients were previously treated with biologics.

OTEZLA treatment with or without (±) concomitant DMARDs, compared with placebo ± concomitant DMARDs, resulted in greater improvement in the signs and symptoms of psoriatic arthritis, as demonstrated by the proportion of patients with an ACR 20 response at week 16. In PALACE-1, 38 percent of patients treated with OTEZLA® (apremilast) 30 mg twice daily achieved an ACR 20 response at week 16 versus 19 percent of patients on placebo. Consistent results were observed in PALACE-2 and PALACE-3. Improvement in ACR 50 and ACR 70 responses were observed at week 16 across the three studies.

A characteristic of psoriatic arthritis is tenderness and swelling in and around the joints. At week 16, patients treated with OTEZLA achieved a reduction in tender and swollen joint counts compared with placebo. OTEZLA treatment resulted in improvement for each of the seven ACR components measured, compared with placebo, at week 16. Improvements were also seen in disease-related physical functioning.

Treatment with OTEZLA resulted in improvement in dactylitis (inflammation of fingers and toes) and enthesitis (inflammation at sites where tendons or ligaments insert into bone) in patients with these pre-existing symptoms. Enthesitis and dactylitis are specific disease manifestations related to psoriatic arthritis.

In OTEZLA clinical trials, the majority of the most common adverse reactions occurred within the first two weeks of treatment and tended to resolve over time with continued dosing. Adverse reactions reported in at least two percent of patients on OTEZLA 30 mg twice daily and at least one percent greater than that observed in patients on placebo for up to 16 weeks were diarrhea, nausea, headache, upper respiratory tract infection, vomiting, nasopharyngitis, and upper abdominal pain. The proportion of patients who discontinued treatment due to any adverse reaction was 4.6 percent for patients taking OTEZLA 30 mg twice daily and 1.2 percent for patients taking placebo. The most common adverse reactions leading to discontinuation among patients treated up to 16 weeks with OTEZLA 30 mg twice daily were nausea (1.8 percent), diarrhea (1.8 percent) and headache (1.2 percent).
OTEZLA® (apremilast) is contraindicated in patients with a known hypersensitivity to OTEZLA or to any of the excipients in the formulation.

Important Safety Information

Contraindications

OTEZLA® (apremilast) is contraindicated in patients with a known hypersensitivity to apremilast or to any of the excipients in the formulation.

Warnings and Precautions

Depression

Treatment with OTEZLA is associated with an increase in adverse reactions of depression. During clinical trials, 1.0% (10/998) of patients treated with OTEZLA reported depression or depressed mood compared to 0.8% (4/495) treated with placebo; 0.3% (4/1441) of patients treated with OTEZLA discontinued treatment due to depression or depressed mood compared with none among placebo-treated patients. In the PALACE studies, 10 percent of patients taking OTEZLA, compared with 3.3 percent of patients taking placebo, reported weight loss of five to ten percent. It is recommended that patients taking OTEZLA have their weight checked regularly.

During the placebo-controlled phase of the clinical trials, the rate of major adverse cardiac events, serious infections, including opportunistic infections, and malignancies, was comparable between placebo and OTEZLA groups. The product labeling does not require routine laboratory monitoring for patients taking OTEZLA.

“Patients and physicians have expressed their desire for a safe and effective therapy for psoriatic arthritis that has the potential to simplify patient management. Celgene is excited to be expanding our transformational science into the therapeutic realm of Inflammation and Immunology, with a new approach for patients with psoriatic arthritis,” said Scott Smith, Global Head, Inflammation and Immunology, Celgene Corporation. “The FDA approval of OTEZLA is good news for patients and healthcare professionals who are looking for a different way to manage this disease.”

OTEZLA® (apremilast) is expected to be available in the U.S. in March 2014 and will be dispensed through a comprehensive network of specialty pharmacies. For more information about OTEZLA distribution and the exclusive treatment support services (including reimbursement assistance and 24/7 nurse support), doctors and patients can contact Otezla SupportPlus™ at 1-844-4OTEZLA (1-844-468-3952) or visit www.OTEZLA.com for more information.

About PALACE Program

PALACE 1, 2 and 3 are the pivotal phase III multi-center, double-blind, placebo-controlled, parallel-group studies with two active-treatment groups. Across these studies, approximately 1,500 patients were randomized 1:1:1 to receive either OTEZLA 20 mg twice daily, OTEZLA 30 mg twice daily, or identically-appearing placebo, for 16 weeks. At week 16, some placebo-treated patients were randomized to one of the two OTEZLA groups, while others remained on placebo through week 24. After week 24, patients began a subsequent long term, open-label, active treatment phase. The PALACE 1, 2 and 3 studies included a wide spectrum of patients with active psoriatic arthritis, including those who had been previously treated with oral DMARDs, and/or biologics, with some patients who had previously failed a tumor necrosis factor (TNF) blocker.

The primary endpoint of the PALACE 1, 2 and 3 studies was the modified American College of Rheumatology criteria for 20 percent improvement (ACR20) at week 16. Secondary endpoints included other measures of signs and symptoms of psoriatic arthritis, physical functioning, and patient-reported outcomes.

Taken together, the PALACE program is the largest psoriatic arthritis program to date intended for regulatory submission.

About OTEZLA

OTEZLA is an oral small-molecule inhibitor of phosphodiesterase 4 (PDE4) specific for cyclic adenosine monophosphate (cAMP). PDE4 inhibition results in increased intracellular cAMP levels.
Carefully weigh the risks and benefits of treatment with OTEZLA for patients with a history of depression and/or suicidal thoughts/behavior, and of continued treatment with OTEZLA for patients with these symptoms. Patients, caregivers, and families should be advised of the need to be alert for the emergence or worsening of depression, suicidal thoughts or other mood changes, and they should contact their healthcare provider.

**Weight Decrease**

Body weight loss of 5-10% was reported in 10% of patients taking OTEZLA and in 3.3% of patients taking placebo. Monitor body weight regularly; evaluate unexplained or clinically significant weight loss, and consider discontinuation of OTEZLA.

**Drug Interactions**

Apremilast exposure is decreased when OTEZLA is co-administered with strong CYP450 inducers, such as rifampin, which may result in loss of efficacy of OTEZLA. Concomitant use of OTEZLA with CYP450 enzyme inducers (e.g., rifampin, phenobarbital, carbamazepine, phenytoin) is not recommended.

**Adverse Reactions**

Adverse reactions reported in at least 2% of patients taking OTEZLA, that occurred at a frequency at least 1% higher than that observed in patients taking placebo, for up to 16 weeks (after the initial 5-day titration), were (OTEZLA%, placebo%): diarrhea (7.7, 1.6); nausea (8.9, 3.1); headache (5.9, 2.2); upper respiratory tract infection (3.9, 1.8); vomiting (3.2, 0.4); nasopharyngitis (2.6, 1.6); upper abdominal pain (2.0, 0.2).

**Use in Specific Populations**

**Pregnancy and Nursing Mothers**

OTEZLA is Pregnancy Category C; it has not been studied in pregnant women. Use during pregnancy only if the potential benefit justifies the potential risk to the fetus. It is not known whether apremilast or its metabolites are present in human milk. Caution should be exercised when OTEZLA is administered to a nursing woman.

**Renal Impairment**

OTEZLA dosage should be reduced in patients with severe renal impairment (creatinine clearance less than 30 mL/min); for details, see Dosage and Administration, Section 2, in the Full Prescribing Information

Please click here for Full Prescribing Information.

**About Psoriatic Arthritis**

Psoriatic arthritis is a painful, chronic inflammatory disease characterized by pain, stiffness, swelling and tenderness of the joints, inflammation of specific ligaments and tendons, and decrease in physical functioning. It is estimated that nearly 38 million people worldwide have psoriatic arthritis. Psoriatic arthritis can impact day-to-day activities and has been reported to increase work disability. Common signs and symptoms of psoriatic arthritis include pain, stiffness, and swelling in joints. To learn more about psoriatic arthritis, go to www.discoverpsa.com. To learn more about the role of PDE4 in inflammatory diseases, go to www.discoverpde4.com.

**About Celgene**

Celgene Corporation, headquartered in Summit, New Jersey, is an integrated global pharmaceutical company engaged primarily in the discovery, development and commercialization of innovative therapies for the treatment of cancer and inflammatory diseases through gene and protein regulation. For more information, please visit www.celgene.com.

**Forward-Looking Statements**

This press release contains forward-looking statements, which are generally statements that are not historical facts. Forward-looking statements can be identified by the words "expects," "anticipates," "believes," "intends," "estimates," "plans," "will," "outlook" and similar expressions. Forward-looking statements are based on management's current plans, estimates, assumptions and projections, and speak only as of the date they are made. We undertake no obligation to update any forward-looking statement in light of new information or future events, except as otherwise required by law. Forward-looking statements involve inherent risks and uncertainties, most of which are difficult to predict and are generally beyond our control. Actual results or outcomes may differ materially from those implied by the forward-looking statements as a result of the impact of a
number of factors, many of which are discussed in more detail in our Annual Report on Form 10-K and other reports filed with the Securities and Exchange Commission.

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