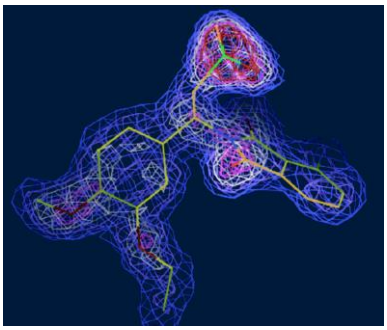
Otezla® (apremilast) 30mg tablets

WHAT IS OTEZLA?

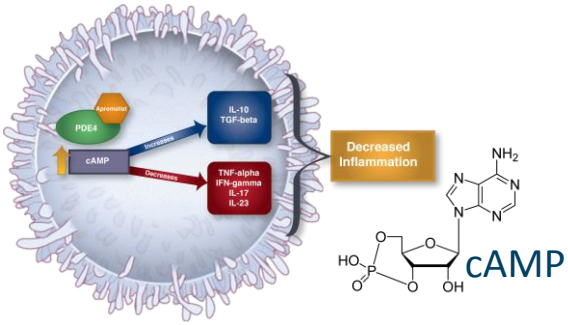
OTEZLA® (apremilast) is the first oral therapy approved by the U.S. Food and Drug Administration (FDA) for the treatment of adult patients with active psoriatic arthritis. A chronic disorder, psoriatic arthritis is characterized by pain, stiffness, swelling and tenderness of the joints, inflammation of specific ligaments and tendons, and a decrease in physical functioning.



WHAT IS INFLAMMATION?

Acute inflammation is a normal, protective response against harmful stimuli such as injury and infection. Chronic inflammation, by contrast, is long-term, may often go unnoticed and occurs when the immune system becomes improperly regulated. In patients with psoriatic arthritis, this deregulation results in a chronic imbalance in the production of pro- and anti-inflammatory cytokines (molecules that increase and decrease inflammation, respectively).

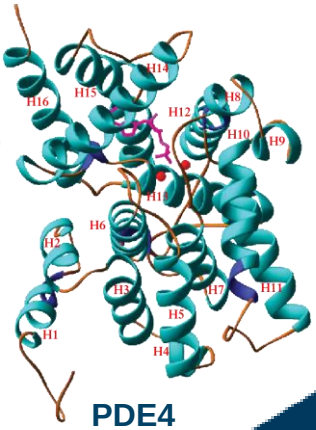
WHAT IS THE ROLE OF PDE4 IN INFLAMMATION?



In immune cells, the phosphodiesterase 4 (PDE4) enzyme leads to inflammation by reducing levels of a tiny chemical messenger called cyclic AMP (cAMP). The degradation of cAMP results in high levels of pro-inflammatory cytokines and low levels of anti-inflammatory cytokines.

HOW DOES OTEZLA WORK?

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.



PDE4

WHAT DATA SUPPORT THE USE OF OTEZLA IN PSORIATIC ARTHRITIS?

The approval was based on the largest psoriatic arthritis clinical trial program to date intended for regulatory submission. Three multi-center, randomized, double-blind, placebo-controlled trials – PALACE 1, 2 and 3 – were conducted in 1,493 adult patients with active psoriatic arthritis who were inadequately controlled by disease-modifying anti-rheumatic drugs (DMARDs) and/or biologics.

In PALACE-1, 38 percent of patients treated with OTEZLA 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.

Treatment with OTEZLA resulted in improvements 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).

IN WHAT OTHER DISEASES IS OTEZLA BEING STUDIED?

OTEZLA is being tested in clinical trials for patients with a wide variety of debilitating inflammatory diseases who have limited treatment options and high unmet medical needs. A New Drug Application (NDA) was submitted to the U.S. FDA for psoriasis in Q4 2013. Clinical trials are ongoing in ankylosing spondylitis and Behçet's disease.

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.

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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 and 0.3% (4/1441) of patients treated with OTEZLA discontinued treatment due to depression or depressed mood compared with none in placebo treated patients (0/495). Depression was reported as serious in 0.2% (3/1441) of patients exposed to OTEZLA, compared to none in placebo treated patients (0/495). Suicidal ideation and behavior were observed in 0.2% (3/1441) of patients on OTEZLA, compared to none on placebo (0/495). Two patients who received placebo committed suicide compared to none on OTEZLA.

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 (https://www.celgene.com/content/uploads/2014/03/1528_0011.pdf) for Full Prescribing Information.