NOW APPROVED

THE FIRST AND ONLY ORAL THERAPY APPROVED ACROSS ALL SEVERITIES OF ADULT PLAQUE PSORIASIS [1]

#1 **Otezla is the #1 prescribed brand for psoriasis patients starting systemic therapy [2,*]**

*Based on IQVIA licensed data: Jan 2018 – Jul 2021 Longitudinal Prescription (LRx) Data and Medical Claims (Dx) Data, reflecting estimates of real-world activity. Study information maintained by Amgen. LRx Data covers retail, traditional/specialty mail order, and long-term claims. Dx data captures US physicians. Patient classified as systemic-naïve if not previously on systemic therapy for the past 12 months, had any claim for a branded systemic, and had at least one psoriasis diagnosis.

INDICATION

Otezla® (apremilast) is indicated for the treatment of adult patients with plaque psoriasis who are candidates for phototherapy or systemic therapy.

IMPORTANT SAFETY INFORMATION

Contraindications

- Otezla is contraindicated in patients with a known hypersensitivity to apremilast or to any of the excipients in the formulation

Please see additional Important Safety Information throughout and accompanying Brief Summary of full Prescribing Information.

Otezla® (apremilast) 30mg tablets

OTEZLA IS THE FIRST AND ONLY ORAL THERAPY WITH DATA IN THE LABEL FOR MILD TO MODERATE PLAQUE PSORIASIS [1]

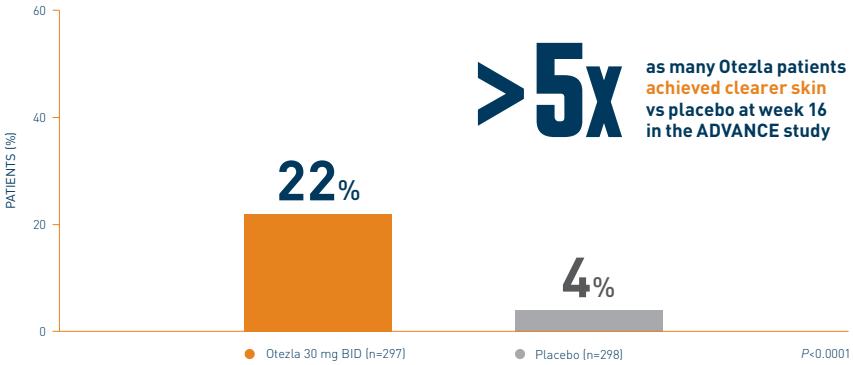
NOW APPROVED

Otezla is the first and only systemic treatment approved for mild to moderate plaque psoriasis [1]

Significantly more patients achieved clear or almost clear skin with Otezla [1]

ADVANCE: Otezla demonstrated significantly greater achievement of sPGA response vs placebo at week 16

Primary endpoint; ITT population [1,2]



The only systemic plaque psoriasis treatment with no label-required initial lab testing or ongoing lab monitoring. [1]

BID, twice daily; ITT, intent to treat; sPGA, Static Physician Global Assessment.

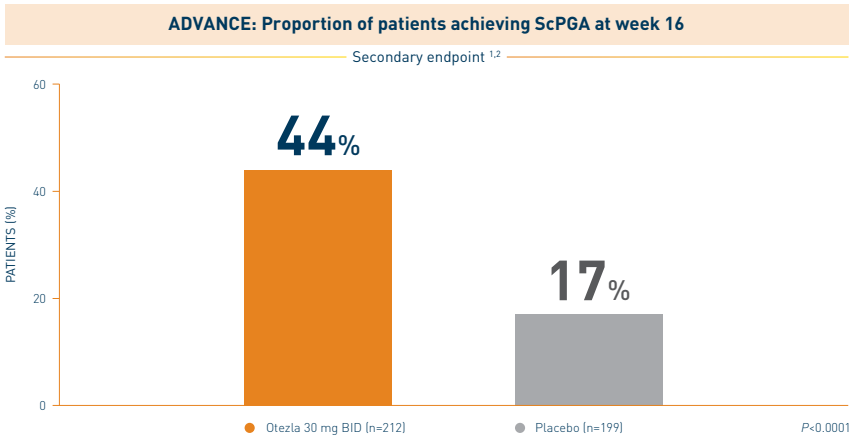
IMPORTANT SAFETY INFORMATION (cont'd)

Warnings and Precautions

- Hypersensitivity: Hypersensitivity reactions, including angioedema and anaphylaxis, have been reported during postmarketing surveillance. If signs or symptoms of serious hypersensitivity reactions occur, discontinue Otezla and institute appropriate therapy
- Diarrhea, Nausea, and Vomiting: Cases of severe diarrhea, nausea, and vomiting were associated with the use of Otezla. Most events occurred within the first few weeks of treatment. In some cases, patients were hospitalized. Patients 65 years of age or older and patients taking medications that can lead to volume depletion or hypotension may be at a higher risk of complications from severe diarrhea, nausea, or vomiting. Monitor patients who are more susceptible to complications of diarrhea or vomiting; advise patients to contact their healthcare provider. Consider Otezla dose reduction or suspension if patients develop severe diarrhea, nausea, or vomiting
- Depression: Carefully weigh the risks and benefits of treatment with Otezla for patients with a history of depression and/or suicidal thoughts/behavior, or in patients who develop such symptoms while on Otezla. 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 if such changes occur
  - Treatment with Otezla is associated with an increase in depression. During clinical trials in patients with moderate to severe plaque psoriasis, 1.3% (12/920) of patients reported depression compared to 0.4% (2/506) on placebo. Depression was reported as serious in 0.1% (1/1308) of patients exposed to Otezla, compared to none in placebo-treated patients (0/506). Suicidal behavior was observed in 0.1% (1/1308) of patients on Otezla, compared to 0.2% (1/506) on placebo. One patient treated with Otezla attempted suicide; one patient on placebo committed suicide

Please see additional Important Safety Information throughout.

Otezla also demonstrated significant improvement in scalp response, a difficult-to-treat area [1-3,*]



*ScPGA score of clear [0] or almost clear [1] with at least a 2-point reduction from baseline.

Study design: ADVANCE was a multicenter, randomized, placebo-controlled, double-blind study of biologic-naïve adults with mild to moderate plaque psoriasis. Patients were randomized 1:1 to receive Otezla or placebo for a 16-week double-blind phase, followed by a 16-week extension phase (continued Otezla or switched to Otezla) and a 4-week observational phase. [1,2]

- **Selected inclusion criteria:** Biologic-naïve adults with chronic mild to moderate plaque psoriasis (sPGA score 2-3, BSA 2%-15%, PASI score 2-15) whose psoriasis was inadequately controlled with or who were intolerant to ≥1 topical psoriasis therapy [1,2]

Adverse events in mild to moderate plaque psoriasis patients were consistent with the established Otezla safety profile for moderate to severe plaque psoriasis [1]

The **most commonly reported adverse events** that occurred in ≥5% of patients in either treatment group (Otezla%, placebo%) were diarrhea (16.4, 5.1), headache (13.1, 5.1), nausea (12.8, 4.4), nasopharyngitis (7.4, 2.7), and upper respiratory tract infection (5.7, 5.1) [2]

Now you can treat mild to moderate plaque psoriasis differently. Scan for more data.

BSA, body surface area; PASI, Psoriasis Area and Severity Index; ScPGA, Scalp Physician Global Assessment.

IMPORTANT SAFETY INFORMATION (cont'd)

Warnings and Precautions (cont'd)

- Weight Decrease: Monitor body weight regularly; evaluate unexplained or clinically significant weight loss, and consider discontinuation of Otezla. Body weight loss of 5-10% occurred in 12% (96/784) of patients with moderate to severe plaque psoriasis treated with Otezla and in 5% (19/382) of patients treated with placebo. Body weight loss of ≥10% occurred in 2% (16/784) of patients treated with Otezla compared to 1% (3/382) of patients treated with placebo
- Drug Interactions: Apremilast exposure was decreased when Otezla was co-administered with rifampin, a strong CYP450 enzyme inducer; loss of Otezla efficacy may occur. Concomitant use of Otezla with CYP450 enzyme inducers (e.g., rifampin, phenobarbital, carbamazepine, phenytoin) is not recommended

Adverse Reactions

- The most common adverse reactions (≥5%) are diarrhea, nausea, upper respiratory tract infection, and headache, including tension headache. Overall, the safety profile of Otezla in patients with mild to moderate plaque psoriasis was consistent with the safety profile previously established in adult patients with moderate to severe plaque psoriasis

Use in Specific Populations

- Otezla has not been studied in pregnant women. Advise pregnant women of the potential risk of fetal loss

Please see accompanying Brief Summary of full Prescribing Information.

References: 1. Otezla [package insert]. Thousand Oaks, CA: Amgen Inc. **2.** Stein Gold L, Papp K, Pariser D, et al. *J Am Acad Dermatol.* 2021. doi:10.1016/j.jaad.2021.07.040 **3.** Aldredge LM, Higham RC. Manifestations and management of difficult-to-treat psoriasis. *JDNA.* 2018;10(4):189-197.

AMGEN®

12/21 USA-407-81821

Otezla® (apremilast) 30mg tablets

Brief Summary of Prescribing Information

OTEZLA® (apremilast) tablets, for oral use

PLEASE SEE PACKAGE INSERT FOR FULL PRESCRIBING INFORMATION

INDICATION AND USAGE

OTEZLA is indicated for the treatment of adult patients with plaque psoriasis who are candidates for phototherapy or systemic therapy.

CONTRAINDICATIONS

OTEZLA is contraindicated in patients with a known hypersensitivity to apremilast or to any of the excipients in the formulation *[see Adverse Reactions (6.1)]*.

WARNINGS AND PRECAUTIONS

Hypersensitivity

Hypersensitivity reactions, including angioedema and anaphylaxis, have been reported during postmarketing surveillance. Avoid the use of OTEZLA in patients with known hypersensitivity to apremilast or to any of the excipients in the formulation. If signs or symptoms of serious hypersensitivity reactions occur, discontinue Otezla and institute appropriate therapy.

Diarrhea, Nausea, and Vomiting

There have been reports of severe diarrhea, nausea, and vomiting associated with the use of OTEZLA. Most events occurred within the first few weeks of treatment. In some cases, patients were hospitalized. Patients 65 years of age or older and patients taking medications that can lead to volume depletion or hypotension may be at a higher risk of complications from severe diarrhea, nausea, or vomiting. Monitor patients who are more susceptible to complications of diarrhea or vomiting. Patients who reduced dosage or discontinued OTEZLA generally improved quickly. Consider OTEZLA dose reduction or suspension if patients develop severe diarrhea, nausea, or vomiting.

Depression

Treatment with OTEZLA is associated with an increase in adverse reactions of depression. Before using OTEZLA in patients with a history of depression and/or suicidal thoughts or behavior prescribers should carefully weigh the risks and benefits of treatment with OTEZLA in such patients. Patients, their 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 if such changes occur to contact their healthcare provider. Prescribers should carefully evaluate the risks and benefits of continuing treatment with OTEZLA if such events occur.

During the 0 to 16 week placebo-controlled period of the 3 controlled clinical trials, 1.3% (12/920) of subjects treated with OTEZLA reported depression compared to 0.4% (2/506) treated with placebo. During the clinical trials, 0.1% (1/1308) of subjects treated with OTEZLA discontinued treatment due to depression compared with none in placebo-treated subjects (0/506). Depression was reported as serious in 0.1% (1/1308) of subjects exposed to OTEZLA, compared to none in placebo-treated subjects (0/506). Instances of suicidal behavior have been observed in 0.1% (1/1308) of subjects while receiving OTEZLA, compared to 0.2% (1/506) in placebo-treated subjects. In the clinical trials, one subject treated with OTEZLA attempted suicide while one who received placebo committed suicide.

During the 0 to 16-week placebo-controlled period of the mild to moderate plaque psoriasis clinical trial, the incidence of subjects reporting depression was similar to what was observed in the moderate to severe plaque psoriasis trials.

Weight Decrease

During the controlled period of the trials in psoriasis, weight decrease between 5%-10% of body weight occurred in 12% (96/784) of subjects treated with OTEZLA compared to 5% (19/382) treated with placebo. Weight decrease of ≥10% of body weight occurred in 2% (16/784) of subjects treated with OTEZLA 30 mg twice daily compared to 1% (3/382) subjects treated with placebo.

During the placebo-controlled period of the mild to moderate plaque psoriasis clinical trial, weight decrease was similar to what was observed in the moderate to severe plaque psoriasis trials.

Patients treated with OTEZLA should have their weight monitored regularly. If unexplained or clinically significant weight loss occurs, weight loss should be evaluated, and discontinuation of OTEZLA should be considered *[see Adverse Reactions (6.1)]*.

Drug Interactions

Co-administration of strong cytochrome P450 enzyme inducer, rifampin, resulted in a reduction of systemic exposure of apremilast, which may result in a loss of efficacy of OTEZLA. Therefore, the use of cytochrome P450 enzyme inducers (e.g., rifampin, phenobarbital, carbamazepine, phenytoin) with OTEZLA is not recommended *[see Drug Interactions (7.1) and Clinical Pharmacology (12.3)]*.

ADVERSE REACTIONS

Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in clinical practice.

Moderate to Severe Plaque Psoriasis Clinical Trials

The safety of OTEZLA was assessed in 1426 subjects in 3 randomized, double-blind, placebo-controlled trials in adult subjects with moderate to severe plaque psoriasis who were candidates for phototherapy or systemic therapy. Subjects were randomized to receive OTEZLA 30 mg twice daily or placebo twice daily. Titration was used over the first 5 days *[see Dosage and Administration (2.1)]*. Subjects ranged in age from 18 to 83 years, with an overall median age of 46 years.

Diarrhea, nausea, and upper respiratory tract infection were the most commonly reported adverse reactions. The most common adverse reactions leading to discontinuation for subjects taking OTEZLA were nausea (1.6%), diarrhea (1.0%), and headache (0.8%). The proportion of subjects with psoriasis who discontinued treatment due to any adverse reaction was 6.1% for subjects treated with OTEZLA 30 mgtwice daily and 4.1% for placebo-treated subjects.

Adverse Reactions Reported in ≥1% of Subjects on OTEZLA and With Greater Frequency Than in Subjects on Placebo; up to Day 112 (Week 16)

Adverse Reactions	Placebo (N=506) n (%)	OTEZLA 30 mg BID[b] (N=920) n (%)
Diarrhea	32 (6)	160 (17)
Nausea	35 (7)	155 (17)
Upper respiratory tract infection	31 (6)	84 (9)
Tension headache	21 (4)	75 (8)
Headache	19 (4)	55 (6)
Abdominal pain[a]	11 (2)	39 (4)
Vomiting	8 (2)	35 (4)
Fatigue	9 (2)	29 (3)
Dyspepsia	6 (1)	29 (3)
Decreased appetite	5 (1)	26 (3)
Insomnia	4 (1)	21 (2)
Back pain	4 (1)	20 (2)
Migraine	5 (1)	19 (2)
Frequent bowel movements	1 (0)	17 (2)
Depression	2 (0)	12 (1)
Bronchitis	2 (0)	12 (1)
Tooth abscess	0 (0)	10 (1)
Folliculitis	0 (0)	9 (1)
Sinus headache	0 (0)	9 (1)

[a] Two subjects treated with OTEZLA experienced serious adverse reaction of abdominal pain.

[b] BID = twice daily.

Severe worsening of psoriasis (rebound) occurred in 0.3% (4/1184) subjects following discontinuation of treatment with OTEZLA.

OTEZLA was evaluated in a Phase 3, multicenter, randomized, placebo-controlled study (PSOR-3) in adults with moderate to severe psoriasis of the scalp *[see Clinical Studies (14.2)]*. A total of 302 subjects were randomized to receive OTEZLA 30 mg twice daily or placebo twice daily. The most commonly reported adverse reactions that occurred at a higher rate in the OTEZLA group than in the placebo group were: diarrhea (31% vs. 11%), nausea (22% vs. 6%), headache (12% vs. 5%), and vomiting (6% vs. 2%). The proportion of subjects who discontinued treatment because of any adverse reaction during the 16 -week placebo-controlled period of the study was 6% for subjects who received OTEZLA 30 mg twice daily and 3% for subjects who received placebo. Gastrointestinal adverse reactions that led to discontinuation of treatment were diarrhea (3% vs 0%), nausea (1.5% vs 1%), and vomiting (1.5% vs 0 %) in the OTEZLA group compared to placebo.

Mild to Moderate Plaque Psoriasis Clinical Trial

OTEZLA was evaluated in a Phase 3, multicenter, randomized, placebo-controlled trial (PSOR-4) in adult subjects with mild to moderate plaque psoriasis *[see Clinical Studies (14.3)]*. A total of 595 subjects were randomized to receive OTEZLA 30 mg twice daily (297 subjects) or placebo twice daily (298 subjects) during the placebo-controlled phase of the trial. The trial also included an open-label extension phase during which all subjects received OTEZLA 30 mg twice daily. Overall, the safety profile observed in the OTEZLA group during the placebo-controlled phase was consistent with the safety profile previously established in adult subjects with moderate to severe plaque psoriasis.

DRUG INTERACTIONS

Strong CYP450 Inducers

Apremilast exposure is decreased when OTEZLA is co-administered with strong CYP450 inducers (such as rifampin) and may result in loss of efficacy *[see Warnings and Precautions (5.5)] and Clinical Pharmacology (12.3)]*.

USE IN SPECIFIC POPULATIONS

Pregnancy

Pregnancy Exposure Registry

There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to OTEZLA during pregnancy. Information about the registry can be obtained by calling 1-877-311-8972 or visiting https://mothertobaby.org/ongoing-study/otezla/.

Risk Summary

Available pharmacovigilance data with OTEZLA use in pregnant women have not established a drug-associated risk of major birth defects, miscarriage or adverse maternal or fetal outcomes, but these data are extremely limited. Advise pregnant women of the potential risk of fetal loss. Consider pregnancy planning and prevention for females of reproductive potential.

Lactation

Risk Summary

There are no data on the presence of apremilast or its metabolites in human milk, the effects of apremilast on the breastfed infant, or the effects of the drug on milk production. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for OTEZLA and any potential adverse effects on the breastfed child from OTEZLA or from the underlying maternal condition.

Pediatric Use

The safety and effectiveness of OTEZLA in pediatric patients less than 18 years of age have not been established.

Geriatric Use

Of the 1257 subjects who enrolled in two placebo-controlled psoriasis trials (PSOR 1 and PSOR 2), a total of 108 psoriasis subjects were 65 years of age and older, including 9 subjects who were 75 years of age and older. No overall differences were observed in the efficacy and safety in elderly subjects ≥65 years of age and younger adult subjects <65 years of age in the clinical trials.

Renal Impairment

Apremilast pharmacokinetics were characterized in subjects with mild, moderate, and severe renal impairment as defined by a creatinine clearance of 60-89, 30-59, and less than 30 mL per minute, respectively, by the Cockcroft–Gault equation. While no dosage adjustment is needed in patients with mild or moderate renal impairment, the dosage of OTEZLA should be reduced to 30 mg once daily in patients with severe renal impairment *[see Dosage and Administration (2.2) and Clinical Pharmacology (12.3)]*.

Hepatic Impairment

Apremilast pharmacokinetics were characterized in subjects with moderate (Child Pugh B) and severe (Child Pugh C) hepatic impairment. No dosage adjustment is necessary in these patients.

The risk information provided here is not comprehensive. The FDA-approved product labeling can be found at www.otezlapro.com or contact Amgen Medical Information at 1-800-772-6436.

Manufactured for:

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