MEDICAL MUTUAL®

Drug Policy

Policy:	Otezla (apremilast)	Annual Review Date: 08/24/2023 Last Revised Date: 08/24/2023

OVERVIEW

Otezla is an inhibitor of phosphodiesterase 4 (PDE4), and is indicated for the treatment of adult patients with active psoriatic arthritis or plaque psoriasis or adults with oral ulcers due to Behcet's disease. PDE4 regulates immune and inflammatory processes through control of intracellular cAMP levels and downstream protein kinase A pathways. The production of a number of key inflammatory cytokines is affected by PDE4 including interferon (IFN)γ, tumor necrosis factor (TNF)α, interleukin (IL)-12, and IL-23, thus shaping the immune response. Otezla is a targeted synthetic disease-modifying anti-rheumatic drug (DMARD) that specifically targets intracellular PDE4 and, therefore, has an inhibitory effect on multiple cytokines involved in the inflammatory process. To reduce the risk of GI symptoms, a titration to the recommended dose of 30mg twice daily is recommended.

Warnings/Precautions for Otezla include depression, weight decrease, and drug interactions with strong cytochrome P450 inducers. Of note, Otezla does not have Warnings regarding serious infection and malignancy, which are listed for the biologic DMARDs approved for PsA, nor does Otezla have warnings for organ toxicity and laboratory monitoring that are noted with methotrexate (MTX) and leflunomide.

POLICY STATEMENT

This policy involves the use of Otezla. Prior authorization is recommended for pharmacy benefit coverage of Otezla. Approval is recommended for those who meet the conditions of coverage in the **Criteria and Initial/Extended Approval** for the diagnosis provided. **Conditions Not Recommended for Approval** are listed following the recommended authorization criteria. Requests for uses not listed in this policy will be reviewed for evidence of efficacy and for medical necessity on a case-by-case basis.

Because of the specialized skills required for evaluation and diagnosis of patients treated with Otezla as well as the monitoring required for adverse events and long-term efficacy, initial approval requires Otezla be prescribed by or in consultation with a physician who specializes in the condition being treated. All approvals for initial therapy are provided for the initial approval duration noted below; if reauthorization is allowed, a response to therapy is required for continuation of therapy unless otherwise noted below. **Otezla is subject to the Inflammatory Conditions Care Value Program under pharmacy benefits.**

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Otezla is recommended in those who meet the following criteria:

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1. Behcet's Disease. Approve if the patient meets ONE of the following criteria (A or B):
- **A)** Initial Therapy. Approve if the patient meets ALL the following (i, ii, iii and iv):
  - **i.** Patient is ≥ 18 years of age; AND
  - **ii.** Patient has oral ulcers or other mucocutaneous involvement; AND
  - **iii.** Patient has tried at least ONE other systemic therapy; AND
    Note: Examples of systemic therapies include colchicine, systemic corticosteroids, azathioprine, thalidomide, interferon alpha, tumor necrosis factor inhibitors (e.g., adalimumab [e.g., Humira, biosimilars], etanercept [e.g., Enbrel, biosimilars], certolizumab pegol [Cimzia], golimumab [Simponi/Aria], or infliximab products [e.g., Remicade, biosimilars]).
  - **iv.** The medication is prescribed by or in consultation with a rheumatologist or dermatologist.
- **B)** Patient is Currently Receiving Otezla. Approve if the patient meets the following criteria (i and ii):
  - **i.** Patient has been established on the requested drug for at least 4 months; AND
    Note: A patients who has received < 4 months of therapy or who is restarting therapy with Otezla should be considered under criterion A (Initial Therapy).
  - **ii.** The patient has had a clinical response as determined by the prescriber

Initial Approval/ Extended Approval.
A) *Initial Approval:* 4 months (120 days)
B) *Extended Approval:* 1 year (365 days)

2. Plaque Psoriasis. Approve if the patient meets ONE of the following (A or B):
- **A)** Initial Therapy. Approve if the patient meets ALL the following criteria (i, ii, and iii):
  - **i.** Patient is ≥18 years of age; AND
  - **ii.** Patient meets ONE of the following conditions (a, b, c or d):
    - **a)** Patient has tried at least one traditional systemic agent for psoriasis for at least 3 months, unless intolerant; OR
      Note: Examples of traditional systemic agents for psoriasis include methotrexate, cyclosporine, acitretin tablets, or psoralen plus ultraviolet A light (PUVA). An exception to the requirement for a trial of one traditional systemic agent for psoriasis can be made if the patient has already had a 3-month trial or previous intolerance to at least one biologic. Refer to Appendix A for examples of biologics used for plaque psoriasis. A patient who has already tried a biologic for psoriasis is not required to "step back" and try a traditional systemic agent for psoriasis.
    - **b)** The patient has tried ONE biologic disease-modifying antirheumatic drug (DMARD) for at least 3 months; OR
    - **c)** The patient experienced an intolerance to a trial of at least one oral therapy for plaque psoriasis; OR
    - **d)** The patient has a contraindication to one oral agent for psoriasis, such as methotrexate, as determined by the prescriber; AND
  - **iii.** The medication is prescribed by or in consultation with a dermatologist.
- **B)** Patient is Currently Receiving Otezla. Approve if the patient meets ALL the following (i and ii):
  - **i.** The patient has been established on the requested drug at least 4 months; AND
    Note: A patient who has received < 4 months of therapy is who is restarting therapy with the requested drug should be considered under criterion A (Initial Therapy); AND

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ii. The patient has had a clinical response as determined by the prescriber.

Initial Approval/ Extended Approval.
A) *Initial Approval:* 4 months (120 days)
B) *Extended Approval:* 1 year (365 days)

3. **Psoriatic Arthritis.** Approve if the patient meets ONE of the following (A or B):
   A) Initial Therapy. Approve if the patient meets BOTH of following (i and ii):
      i. Patient is ≥ 18 years of age; AND
      ii. The medication is prescribed by or in consultation with a rheumatologist or a dermatologist.
   B) Patient is Currently Receiving Otezla. Approve if the patient meets ALL the following (i and ii):
      i. The patient has been established on the requested drug at least 4 months; AND
      Note: A patient who has received < 4 months of therapy is who is restarting therapy with the requested drug should be considered under criterion A (Initial Therapy); AND
      ii. The patient has had a clinical response as determined by the prescriber.

Initial Approval/ Extended Approval.
A) *Initial Approval:* 6 months (180 days)
B) *Extended Approval:* 1 year (365 days)
:

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Otezla has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval).

1. **Ankylosing Spondylitis (AS):** Current evidence does not support use of Otezla in AS. In a published double-blind, placebo-controlled Phase II study, patients (n = 38) were randomized in a 1:1 ratio to treatment with Otezla 30 mg BID or placebo.[13] At Week 12, there was not a statistically significant change from baseline compared with placebo in multiple endpoints, including the Bath Ankylosing Spondylitis Disease Activity Index, Functional Index, Global Score, or Metrology Index (BASDAI, BASFI, BAS-G, or BASMI), the Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F), or night pain scores.

2. **Concurrent Use with a Biologic or with a Targeted Synthetic DMARD:** Otezla is a small molecule that specifically targets intracellular PDE4 and has an inhibitory effect on multiple cytokines involved in the inflammatory process, including TNF, IFNγ, IL-12, and IL-23.[2-3] Co-administration of Otezla with a biologic or another targeted synthetic DMARD (see APPENDIX for examples) has the risk of added immunosuppression and has not been evaluated. Note: This does NOT exclude the use of conventional synthetic DMARDs (e.g., MTX, leflunomide, hydroxychloroquine, and sulfasalazine) in combination with Otezla.

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3. **Rheumatoid Arthritis (RA):** Current evidence does not support use of Otezla in RA. A multicenter, double-blind, Phase II study (n = 237) randomized patients in a 1:1:1 ratio to treatment with Otezla 20 mg BID, Otezla 30 mg BID, or placebo.[14] All patients were required to take a stable dose of MTX throughout the study. At Week 16, a similar proportion of patients in all treatment groups achieved an American College of Rheumatology (ACR) 20 response (28%, 34%, and 35%, respectively). At Week 16, patients who were non-responders, defined as patients with a swollen joint count and tender joint count that had not improved by at least 20%, were required to enter early escape (patients who were receiving placebo were transitioned to Otezla 20 mg BID and patients receiving Otezla continued on the assigned therapy for an additional year). At Week 24, all patients who received placebo were similarly transitioned to Otezla. At Weeks 24 and 52, both doses of Otezla were associated with generally similar changes versus placebo, including ACR 20, ACR 50, and ACR 70. A subset of patients underwent magnetic resonance imaging (MRI) evaluation; however, no significant difference in response rates was observed at Week 16. The study was terminated early; data were not analyzed at Year 2 as originally planned.

4. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

Documentation Requirements:

The Company reserves the right to request additional documentation as part of its coverage determination process. The Company may deny reimbursement when it has determined that the drug provided or services performed were not medically necessary, investigational or experimental, not within the scope of benefits afforded to the member and/or a pattern of billing or other practice has been found to be either inappropriate or excessive. Additional documentation supporting medical necessity for the services provided must be made available upon request to the Company. Documentation requested may include patient records, test results and/or credentials of the provider ordering or performing a service. The Company also reserves the right to modify, revise, change, apply and interpret this policy at its sole discretion, and the exercise of this discretion shall be final and binding.

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Appendix A

Biologic or Targeted Synthetic DMARD	Mechanism of Action	Indications
Cimzia® (certolizumab pegol for SC injection)	Inhibition of TNF	AS, ASpA ,CD, PPs, PsA, RA
Enbrel® (etanercept for SC injection)	Inhibition of TNF	AS, PPs, PsA, RA
Erelzi™ (etanercept-szzs for SC injection)	Inhibition of TNF	AS, PPs, PsA, RA
Humira® (adalimumab for SC injection)	Inhibition of TNF	AS, CD, HS, PPs, RA, UC, UV
Amjevita™ (adalimumab-atto for SC injection)	Inhibition of TNF	AS, CD, PPs, RA, UC
Cyltezo® (adalimumab-adbm for SC injection)	Inhibition of TNF	AS, CD, PPs, RA, UC
Simponi® (golimumab for SC injection)	Inhibition of TNF	AS, PsA, RA, UC
Simponi® Aria™ (golimumab for IV infusion)	Inhibition of TNF	AS, PsA, RA, UC
Remicade® (infliximab for IV infusion)	Inhibition of TNF	AS, CD, PPs, PsA, RA, UC
Inflectra™ (infliximab-dyyb for IV infusion)	Inhibition of TNF	AS, CD, PPs, PsA, RA, UC
Renflexis® (infliximab-abda for IV infusion)	Inhibition of TNF	AS, CD, PPs, PsA, RA, UC
Actemra® (tocilizumab for IV infusion)	Inhibition of IL-6	CRS, GCA, RA
Actemra® (tocilizumab for SC injection)	Inhibition of IL-6	CRS, GCA, RA
Kevzara® (sarilumab for SC injection)	Inhibition of IL-6	RA
Orencia® (abatacept for IV infusion)	T-cell costimulation modulator	PsA, RA
Orencia® (abatacept for SC injection)	T-cell costimulation modulator	PsA, RA
Rituxan® (rituximab for IV infusion)	CD20-directed cytolytic antibody	Various
Kineret® (anakinra for subcutaneous SC injection)	Inhibition of IL-1	NOMID, RA
Stelara® (ustekinumab for SC injection)	Inhibition of IL-12/23	CD, PPs, PsA, UC
Stelara® (ustekinumab for IV infusion)	Inhibition of IL-12/23	CD, PPs, PsA, UC
Siliq™ (brodalumab SC injection)	Inhibition of IL-17	PPs
Cosentyx™ (secukinumab for SC injection)	Inhibition of IL-17A	AS, PPs, PsA
Taltz® (ixekizumab for SC injection)	Inhibition of IL-17A	AS, PPs, PsA
Ilumya™ (tildrakizumab-asmn for SC injection)	Inhibition of IL-23	PPs

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Tremfya® (guselkumab for SC injection)	Inhibition of IL-23	PPs
Otezla® (apremilast tablets)	Inhibition of PDE4	BD, PPs, PsA
Olumiant® (baricitinib tablets)	Inhibition of the JAK pathways	RA
Xeljanz®, Xeljanz XR (tofacitinib tablets, tofacitinib ER tabs)	Inhibition of the JAK pathways	PsA, RA, UC

Agents and associated indications are for reference only.

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AS = Ankylosing Spondylitis, ASpA = Axial Spondyloarthritis, BD = Behcet Disease, CD = Crohn's Disease, CRS = Cytokine Release Syndrome, GCA = Giant Cell Arteritis, GVHD = Graft-Versus-Host Disease, HS = Hidradenitis Suppurativa, NOMID = Neonatal-onset Multisystem Inflammatory Disease, PPs = Plaque Psoriasis, PsA = Psoriatic Arthritis, RA = Rheumatoid Arthritis, SpA = Spondyloarthritis, UC = Ulcerative Colitis, UV = Uveitis

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