PRIOR AUTHORIZATION POLICY

POLICY: Inflammatory Conditions – Otezla Prior Authorization Policy
- Otezla® (apremilast tablets – Amgen)

REVIEW DATE: 06/07/2023

INSTRUCTIONS FOR USE

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CIGNA NATIONAL FORMULARY COVERAGE:

OVERVIEW

Otezla, an oral phosphodiesterase 4 (PDE4) inhibitor, is indicated for the following indications:[1]
- **Behcet's disease**, in adults with oral ulcers.
- **Plaque psoriasis**, in adults who are candidates for phototherapy or systemic therapy.
- **Psoriatic arthritis**, in adults with active disease.

Guidelines

Otezla is addressed in guidelines for treatment of inflammatory conditions.
- **Behcet's Disease:** Recommendations for the management of Behcet's disease from the European League Against Rheumatism (2018) mention Otezla as a treatment option for Behcet's disease with mucocutaneous involvement.[7] Other options include topical steroids, colchicine, azathioprine, thalidomide, interferon alpha, and tumor necrosis factor inhibitors (TNFis). TNFis are also listed among the therapeutic options for patients who present with eye involvement, refractory venous thrombosis, arterial involvement, refractory/severe gastrointestinal involvement, nervous system involvement, and/or joint involvement.
- **Plaque Psoriasis:** Joint guidelines from the American Academy of Dermatology and National Psoriasis Medical Board (2020) have been published

for management of psoriasis with systemic non-biologic therapies.[8] These guidelines list Otezla as a monotherapy treatment option for patients with moderate to severe plaque psoriasis. For treatment of moderate to severe psoriasis in adults, Otezla has a similar level of evidence and strength of recommendation as methotrexate. Additionally, data support use of methotrexate in combination with other systemic therapies for psoriasis,[4,8] whereas there is no strong evidence supporting combination use of Otezla with other systemic therapies or with phototherapy.[4]

- **Psoriatic Arthritis:** Guidelines from the American College of Rheumatology (2019) recommend TNFis over other biologics and Otezla for use in treatment-naïve patients with psoriatic arthritis and in those who were previously treated with an oral therapy.[6]

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of Otezla. 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 to be prescribed by or in consultation with a physician who specializes in the condition being treated. All approvals are for the duration noted below. In cases where the approval is authorized in months, 1 month is equal to 30 days.

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is(are) covered as medically necessary when the following criteria is(are) met for fda-approved indication(s) or other uses with supportive evidence (if applicable):

FDA-Approved Indications

1. **Behcet's Disease.** Approve for the duration noted if the patient meets ONE of the following criteria (A or B):
   - **A)** Initial Therapy. Approve for 4 months if the patient meets ALL of 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., an adalimumab product [Humira, biosimilars], an etanercept product [Enbrel, biosimilars], Cimzia [certolizumab pegol subcutaneous injection], Simponi [golimumab subcutaneous injection], Simponi Aria [golimumab intravenous infusion], or an infliximab product [Remicade, biosimilars]).
     - **iv.** The medication is prescribed by or in consultation with a rheumatologist or dermatologist.

B) Patient is Currently Receiving Otezla. Approve for 1 year if the patient meets ALL of the following (i, ii, and iii):

i. Patient has been established on therapy for at least 4 months; AND
Note: A patient who has received < 4 months of therapy or who is restarting therapy should be considered under criterion A (Initial Therapy).

ii. When assessed by at least one objective measure, patient experienced a beneficial clinical response from baseline (prior to initiating Otezla); AND
Note: Examples of objective measures are dependent upon organ involvement but may include best-corrected visual acuity (if ophthalmic manifestations); serum markers (e.g., C-reactive protein, erythrocyte sedimentation rate); ulcer depth, number, and/or lesion size.

iii. Compared with baseline (prior to initiating Otezla), patient experienced an improvement in at least one symptom, such as decreased pain, or improved visual acuity (if ophthalmic manifestations).

2. Plaque Psoriasis. Approve for the duration noted if the patient meets ONE of the following (A or B):

A) Initial Therapy. Approve for 4 months if the patient meets ALL of the following criteria (i, ii, and iii):

i. Patient is ≥18 years of age; AND

ii. Patient meets ONE of the following conditions (a or b):

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 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) Patient has a contraindication to 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 for 1 year if the patient meets ALL of the following (i, ii, and iii):

i. Patient has been established on therapy for at least 4 months; AND
Note: A patient who has received < 4 months of therapy or who is restarting therapy with with the requested drug should be considered under criterion A (Initial Therapy).

ii. Patient experienced a beneficial clinical response, defined as improvement from baseline (prior to initiating the requested drug) in at least one of the following: estimated body surface area, erythema, induration/thickness, and/or scale of areas affected by psoriasis; AND

iii. Compared with baseline (prior to receiving the requested drug), patient experienced an improvement in at least one symptom, such as decreased pain, itching, and/or burning.

3. **Psoriatic Arthritis.** Approve for the duration noted if the patient meets ONE of the following (A or B):
   A) Initial Therapy. Approve for 6 months 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 for 1 year if the patient meets BOTH of the following (i and ii):
      i. Patient has been established on the requested drug for at least 6 months; AND
      Note: A patient who has received < 6 months of therapy or who is restarting therapy is reviewed under criterion A (Initial Therapy).
      ii. Patient meets at least one of the following (a or b):
         a) When assessed by at least one objective measure, patient experienced a beneficial clinical response from baseline (prior to initiating Otezla); OR
         Note: Examples of standardized measures of disease activity include Disease Activity Index for Psoriatic Arthritis (DAPSA), Composite Psoriatic Disease Activity Index (CPDAI), Psoriatic Arthritis Disease Activity Score (PsA DAS), Grace Index, Leeds Enthesitis Score (LEI), Spondyloarthritis Consortuium of Canada (SPARCC) enthesitis score, Leeds Dactylitis Instrument Score, Minimal Disease Activity (MDA), Psoriatic Arthritis Impact of Disease (PsAID-12), and/or serum markers (e.g., C-reactive protein, erythrocyte sedimentation rate).
         b) Compared with baseline (prior to initiating Otezla), patient experienced an improvement in at least one symptom, such as less joint pain, morning stiffness, or fatigue; improved function or activities of daily living; decreased soft tissue swelling in joints or tendon sheaths.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

- **Otezla® (apremilast tablets – Amgen)**

is(are) considered experimental, investigational or unproven for ANY other use(s) including the following (this list may not be all inclusive; criteria will be updated as new published data are available):

1. **Ankylosing Spondylitis.** Current evidence does not support use of Otezla in ankylosing spondylitis. In a published, double-blind, placebo-controlled, Phase III study, patients (n = 490) were randomized in a 1:1:1 ratio to treatment with Otezla 30 mg twice daily, Otezla 20 mg twice daily, or placebo.[9] At Week 16, there was not a statistically significant change from baseline compared with placebo in the primary endpoint, which was the Assessment of the Spondyloarthritis international Society 20 (ASAS20) response.

2. **Concurrent Use with a Biologic or with a Targeted Synthetic Disease-Modifying Antirheumatic Drugs (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 tumor necrosis factor, interferon gamma, interleukin (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 adequately evaluated. Note: This does NOT exclude the use of conventional synthetic DMARDs (e.g., methotrexate, leflunomide, hydroxychloroquine, and sulfasalazine) in combination with Otezla.

3. **Rheumatoid Arthritis.** Current evidence does not support use of Otezla in rheumatoid arthritis. A multicenter, double-blind, Phase II study (n = 237) randomized patients in a 1:1:1 ratio to treatment with Otezla 20 mg twice daily, Otezla 30 mg twice daily, or placebo.[10] All patients were required to take a stable dose of methotrexate 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 twice daily 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 evaluation; however, no significant difference in response rate was observed at Week 16. The study was terminated early; data were not analyzed at Year 2 as originally planned.

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HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	No criteria changes.	05/11/2022
Annual Revision	No criteria changes.	06/07/2023

APPENDIX

	Mechanism of Action	Examples of Inflammatory Indications*
Biologics		
Adalimumab SC Products (Humira®, biosimilars)	Inhibition of TNF	AS, CD, JIA, PsO, PsA, RA, UC
Cimzia® (certolizumab pegol SC injection)	Inhibition of TNF	AS, CD, nr-axSpA, PsO, PsA, RA
Etanercept SC Products (Enbrel®, biosimilars)	Inhibition of TNF	AS, JIA, PsO, PsA
Infliximab IV Products (Remicade®, biosimilars)	Inhibition of TNF	AS, CD, PsO, PsA, RA, UC
Simponi®, Simponi® Aria™ (golimumab SC injection, golimumab IV infusion)	Inhibition of TNF	SC formulation: AS, PsA, RA, UC
		IV formulation: AS, PJIA, PsA, RA
Actemra® (tocilizumab IV infusion, tocilizumab SC injection)	Inhibition of IL-6	SC formulation: PJIA, RA, SJIA
		IV formulation: PJIA, RA, SJIA
Kevzara® (sarilumab SC injection)	Inhibition of IL-6	RA
Orencia® (abatacept IV infusion, abatacept SC injection)	T-cell costimulation modulator	SC formulation: JIA, PsA, RA
		IV formulation: JIA, PsA, RA
Rituximab IV Products (Rituxan®, biosimilars)	CD20-directed cytolytic antibody	RA
Kineret® (anakinra SC injection)	Inhibition of IL-1	JIA^, RA
Stelara® (ustekinumab SC injection, ustekinumab IV infusion)	Inhibition of IL-12/23	SC formulation: CD, PsO, PsA, UC
		IV formulation: CD, UC
Siliq™ (brodalumab SC injection)	Inhibition of IL-17	PsO
Cosentyx® (secukinumab SC injection)	Inhibition of IL-17A	AS, ERA, nr-axSpA, PsO, PsA
Taltz® (ixekizumab SC injection)	Inhibition of IL-17A	AS, nr-axSpA, PsO, PsA
Ilumya™ (tildrakizumab-asmn SC injection)	Inhibition of IL-23	PsO
Skyrizi® (risankizumab-rzaa SC injection)	Inhibition of IL-23	PsA, PsO
Tremfya™ (guselkumab SC injection)	Inhibition of IL-23	PsO
Entyvio™ (vedolizumab IV infusion)	Integrin receptor antagonist	CD, UC
Oral Therapies/Targeted Synthetic DMARDs		
Otezla® (apremilast tablets)	Inhibition of PDE4	PsO, PsA
Cibinqo™ (abrocitinib tablets)	Inhibition of JAK pathways	AD
Olumiant® (baricitinib tablets)	Inhibition of JAK pathways	RA
Rinvoq® (upadacitinib extended-release tablets)	Inhibition of JAK pathways	AD, CD, RA, PsA, UC
Xeljanz® (tofacitinib tablets)	Inhibition of JAK pathways	RA, PJIA, PsA, UC
Xeljanz® XR (tofacitinib extended-release tablets)	Inhibition of JAK pathways	RA, PsA, UC

* Not an all-inclusive list of indication (e.g., oncology indications and rare inflammatory conditions are not listed). Refer to the prescribing information for the respective agent for FDA-approved indications; SC – Subcutaneous; TNF – Tumor necrosis factor; AS – Ankylosing spondylitis; CD – Crohn's disease; JIA – Juvenile idiopathic arthritis; PsO – Plaque psoriasis; PsA – Psoriatic arthritis; RA – Rheumatoid arthritis; UC – Ulcerative colitis; nr-axSpA – Non-radiographic axial spondyloarthritis; IV – Intravenous, PJIA – Polyarticular juvenile idiopathic arthritis; IL – Interleukin; SJIA – Systemic juvenile idiopathic

arthritis; ^ Off-label use of Kineret in JIA supported in guidelines; ERA – Enthesitis-related arthritis; DMARDs – Disease-modifying antirheumatic drug; PDE4 – Phosphodiesterase 4; JAK – Janus kinase; AD – Atopic dermatitis.

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