

PRIOR AUTHORIZATION POLICY

POLICY: Inflammatory Conditions – Otezla Prior Authorization Policy

- Otezla® (apremilast tablets – Amgen)

REVIEW DATE: 05/12/2021; selected revision 12/01/2021

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 moderate to severe disease in patients who are candidates for phototherapy or systemic therapy.
- **Psoriatic arthritis** in adults.

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 recommendations 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.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

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

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., 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 for 1 year if the patient meets ALL of the following (i, ii, and iii):
 - 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. When assessed by at least one objective measure, patient experienced a beneficial clinical response from baseline (prior to initiating the requested drug); 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 receiving the requested drug), 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 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 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 with the requested drug 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 the requested drug); 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 Consortium 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 receiving the requested drug), 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

Coverage of Otezla is not recommended in the following situations:

1. **Ankylosing Spondylitis.** Current evidence does not support use of Otezla in ankylosing spondylitis. 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 twice daily or placebo.⁹ 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, the Functional Assessment of Chronic Illness Therapy-Fatigue, or night pain scores.
 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.
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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.
4. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

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HISTORY

Type of Revision	Summary of Changes	Review Date
Early Annual Revision	<p>Plaque Psoriasis: Examples of traditional systemic agents were moved to a Note (previously listed as examples within the criteria). Examples of biologics for plaque psoriasis were moved to be included in the Appendix (previously listed in a Note in the criteria section). For the exception applying to patients with a contraindication to methotrexate, wording was updated to more generally allow this determination by the prescriber (criteria previously specified this was according to the prescribing physician).</p> <p>Psoriatic Arthritis: The criterion that requires a 3-month trial or intolerance to a conventional synthetic disease-modifying antirheumatic drug was removed from the policy.</p>	04/29/2020
Annual Revision	No criteria changes.	05/12/2021
Selected Revision	<p>Behcet's Disease: Requirements were added for a patient who is currently taking, that there has been at least one objective and at least one subjective response to therapy. For continuation, approvals were changed to be 1 year in duration. Previously, response was more general and according to the prescriber, and approvals were for 3 years.</p> <p>Plaque Psoriasis: Requirements were added for a patient who is currently taking, that there is has at least one objective and at least one subjective response to therapy. For continuation, approvals were changed to be 1 year in duration. Previously, response was more general and according to the prescriber, and approvals were for 3 years.</p> <p>Psoriatic Arthritis: Initial approval duration was changed to 6 months (previously was 4 months). For a patient currently receiving this drug, it was clarified that this applies to a patient who is taking for ≥ 6 months. A requirement was added for a patient who is currently receiving to have at least one objective or subjective response to therapy. For continuation, approvals were changed to be 1 year in duration. Previously, response was more general and according to the prescriber, and approvals were for 3 years.</p>	12/01/2021

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, nr-axSpA, PsO, PsA
Taltz® (ixekizumab SC injection)	Inhibition of IL-17A	AS, nr-axSpA, PsO, PsA
Ilumya™ (tildrakizumab-asnm SC injection)	Inhibition of IL-23	PsO
Skyrizi™ (risankizumab-rzaa SC injection)	Inhibition of IL-23	PsO
Tremfya™ (guselkumab SC injection)	Inhibition of IL-23	PsO
Entyvio™ (vedolizumab IV infusion)	Integrin receptor antagonist	CD, UC
Targeted Synthetic DMARDs		
Otezla® (apremilast tablets)	Inhibition of PDE4	PsO, PsA
Olumiant® (baricitinib tablets)	Inhibition of JAK pathways	RA
Rinvoq® (upadacitinib extended-release tablets)	Inhibition of JAK pathways	RA
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 indications (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; IL – Interleukin; [^] Off-label use of Kineret in systemic JIA supported in guidelines; DMARD – Disease-modifying antirheumatic drug; PDE4 – Phosphodiesterase 4; JAK – Janus kinase.