PRIOR AUTHORIZATION POLICY

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

REVIEW DATE: 05/08/2024; selected revision 09/11/2024

INSTRUCTIONS FOR USE

THE FOLLOWING COVERAGE POLICY APPLIES TO HEALTH BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. CERTAIN CIGNA COMPANIES AND/OR LINES OF BUSINESS ONLY PROVIDE UTILIZATION REVIEW SERVICES TO CLIENTS AND DO NOT MAKE COVERAGE DETERMINATIONS. REFERENCES TO STANDARD BENEFIT PLAN LANGUAGE AND COVERAGE DETERMINATIONS DO NOT APPLY TO THOSE CLIENTS. COVERAGE POLICIES ARE INTENDED TO PROVIDE GUIDANCE IN INTERPRETING CERTAIN STANDARD BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. PLEASE NOTE, THE TERMS OF A CUSTOMER'S PARTICULAR BENEFIT PLAN DOCUMENT [GROUP SERVICE AGREEMENT, EVIDENCE OF COVERAGE, CERTIFICATE OF COVERAGE, SUMMARY PLAN DESCRIPTION (SPD) OR SIMILAR PLAN DOCUMENT] MAY DIFFER SIGNIFICANTLY FROM THE STANDARD BENEFIT PLANS UPON WHICH THESE COVERAGE POLICIES ARE BASED. FOR EXAMPLE, A CUSTOMER'S BENEFIT PLAN DOCUMENT MAY CONTAIN A SPECIFIC EXCLUSION RELATED TO A TOPIC ADDRESSED IN A COVERAGE POLICY. IN THE EVENT OF A CONFLICT, A CUSTOMER'S BENEFIT PLAN DOCUMENT ALWAYS SUPERSEDES THE INFORMATION IN THE COVERAGE POLICIES. IN THE ABSENCE OF A CONTROLLING FEDERAL OR STATE COVERAGE MANDATE, BENEFITS ARE ULTIMATELY DETERMINED BY THE TERMS OF THE APPLICABLE BENEFIT PLAN DOCUMENT. COVERAGE DETERMINATIONS IN EACH SPECIFIC INSTANCE REQUIRE CONSIDERATION OF 1) THE TERMS OF THE APPLICABLE BENEFIT PLAN DOCUMENT IN EFFECT ON THE DATE OF SERVICE; 2) ANY APPLICABLE LAWS/REGULATIONS; 3) ANY RELEVANT COLLATERAL SOURCE MATERIALS INCLUDING COVERAGE POLICIES AND; 4) THE SPECIFIC FACTS OF THE PARTICULAR SITUATION. EACH COVERAGE REQUEST SHOULD BE REVIEWED ON ITS OWN MERITS. MEDICAL DIRECTORS ARE EXPECTED TO EXERCISE CLINICAL JUDGMENT AND HAVE DISCRETION IN MAKING INDIVIDUAL COVERAGE DETERMINATIONS. COVERAGE POLICIES RELATE EXCLUSIVELY TO THE ADMINISTRATION OF HEALTH BENEFIT PLANS. COVERAGE POLICIES ARE NOT RECOMMENDATIONS FOR TREATMENT AND SHOULD NEVER BE USED AS TREATMENT GUIDELINES. IN CERTAIN MARKETS, DELEGATED VENDOR GUIDELINES MAY BE USED TO SUPPORT MEDICAL NECESSITY AND OTHER COVERAGE DETERMINATIONS.

CIGNA NATIONAL FORMULARY COVERAGE:

OVERVIEW

Otezla, an oral phosphodiesterase 4 (PDE4) inhibitor, is indicated for the following uses:[1]
- **Behcet's disease**, in adults with oral ulcers.
- **Plaque psoriasis**, in adults who are candidates for phototherapy or systemic therapy.
- **Plaque psoriasis**, in pediatric patients ≥ 6 years of age and ≥ 20 kg with moderate to severe disease 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] Pediatric guidelines were published by the American Academy of Dermatology and the National Psoriasis Foundation (NPF) [2020]. These guidelines list traditional systemic therapies (e.g., methotrexate, cyclosporine, acitretin) and biologics as options for treatment of moderate to severe plaque psoriasis. There was insufficient data in pediatric patients to make recommendations for Otezla.
- **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. All approvals are for the duration noted below. In cases where the approval is authorized in months, 1 month is equal to 30 days. 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.

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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 (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 (i, ii, and iii):

i. Patient is ≥ 6 years of age; AND

ii. Patient meets ONE of the following (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, or acitretin tablets. A 3-month trial of psoralen plus ultraviolet A light (PUVA) also counts. 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 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 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 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

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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 Oral Small Molecule Drug.** This medication should not be administered in combination with another biologic or with a targeted synthetic oral small molecule drug used for an inflammatory condition (see Appendix for examples). Combination therapy is generally not recommended due to a potentially higher rate of adverse events and lack of controlled clinical data supporting additive efficacy.
   Note: This does NOT exclude the use of conventional synthetic DMARDs (e.g., methotrexate, leflunomide, hydroxychloroquine, or sulfasalazine) in combination with this medication.

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.

REFERENCES

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HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	No criteria changes.	06/07/2023
Early Annual Revision	**Plaque Psoriasis**: Expanded age requirement from ≥ 18 to ≥ 6 years of age.	05/08/2024
Selected Revision	**Plaque Psoriasis:** In the Note, psoralen plus ultraviolet A light (PUVA) was removed from the examples of traditional systemic therapies. An additional Note was added that a 3-month trial of PUVA counts as a traditional systemic therapy. **Conditions Not Covered** **:** Concurrent use with a Biologic or with a Targeted Synthetic Oral Small Molecule Drug was changed to as listed (previously oral small molecule drug was listed as Disease-Modifying Antirheumatic Drug).	09/11/2024

APPENDIX

	Mechanism of Action	Examples of 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, RA
Infliximab IV Products (Remicade®, biosimilars)	Inhibition of TNF	AS, CD, PsO, PsA, RA, UC
Zymfentra® (infliximab-dyyb SC injection)	Inhibition of TNF	CD, 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
Tocilizumab Products (Actemra® IV, biosimilar; Actemra SC, biosimilar)	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
Omvoh® (mirikizumab IV infusion, SC injection)	Inhibition of IL-23	UC
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; secukinumab IV infusion)	Inhibition of IL-17A	SC formulation: AS, ERA, nr-axSpA, PsO, PsA
		IV formulation: AS, nr-axSpA, PsA
Taltz® (ixekizumab SC injection)	Inhibition of IL-17A	AS, nr-axSpA, PsO, PsA

Bimzelx® (bimekizumab-bkzx SC injection)	Inhibition of IL-17A/17F	PsO
Ilumya® (tildrakizumab-asmn SC injection)	Inhibition of IL-23	PsO
Skyrizi® (risankizumab-rzaa SC injection, risankizumab-rzaa IV infusion)	Inhibition of IL-23	SC formulation: CD, PSA, PsO, UC
		IV formulation: CD, UC
Tremfya® (guselkumab SC injection, guselkumab IV infusion)	Inhibition of IL-23	SC formulation: PsA, PsO, UC
		IV formulation: UC
Entyvio® (vedolizumab IV infusion, vedolizumab SC injection)	Integrin receptor antagonist	CD, UC

APPENDIX (CONTINUED)

	Mechanism of Action	Examples of Indications*
Oral Therapies/Targeted Synthetic Oral Small Molecule Drugs		
Otezla® (apremilast tablets)	Inhibition of PDE4	PsO, PsA
Cibinqo™ (abrocitinib tablets)	Inhibition of JAK pathways	AD
Olumiant® (baricitinib tablets)	Inhibition of JAK pathways	RA, AA
Litfulo® (ritlecitinib capsules)	Inhibition of JAK pathways	AA
Leqselvi® (deuruxolitinib tablets)	Inhibition of JAK pathways	AA
Rinvoq® (upadacitinib extended-release tablets)	Inhibition of JAK pathways	AD, AS, nr-axSpA, RA, PsA, UC
Rinvoq® LQ (upadacitinib oral solution)	Inhibition of JAK pathways	PsA, PJIA
Sotyktu® (deucravacitinib tablets)	Inhibition of TYK2	PsO
Xeljanz® (tofacitinib tablets/oral solution)	Inhibition of JAK pathways	RA, PJIA, PsA, UC
Xeljanz® XR (tofacitinib extended-release tablets)	Inhibition of JAK pathways	RA, PsA, UC
Zeposia® (ozanimod tablets)	Sphingosine 1 phosphate receptor modulator	UC
Velsipity® (etrasimod tablets)	Sphingosine 1 phosphate receptor modulator	UC

* Not an all-inclusive list of indications. 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; DMARD – Disease-modifying antirheumatic drug; PDE4 – Phosphodiesterase 4; JAK – Janus kinase; AD – Atopic dermatitis; AA – Alopecia areata; TYK2 – Tyrosine kinase 2.