BlueCross BlueShield of Arizona
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PHARMACY COVERAGE GUIDELINES	**ORIGINAL EFFECTIVE DATE: 6/19/14**
SECTION: DRUGS	**LAST REVIEW DATE: 9/20/18**
	LAST CRITERIA REVISION DATE: 9/20/18
	ARCHIVE DATE:

OTEZLA® (apremilast) oral tablet

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Pharmacy Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.

This Pharmacy Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide BCBSAZ complete medical rationale when requesting any exceptions to these guidelines.

The section identified as "Description" defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as "Criteria" defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Pharmacy Coverage Guidelines are subject to change as new information becomes available.

For purposes of this Pharmacy Coverage Guideline, the terms "experimental" and "investigational" are considered to be interchangeable.

This Pharmacy Coverage Guideline does not apply to FEP or other states' Blues Plans.

Information about medications that require precertification is available at www.azblue.com/pharmacy.

Some large (100+) benefit plan groups may customize certain benefits, including adding or deleting precertification requirements.

All applicable benefit plan provisions apply, e.g., waiting periods, limitations, exclusions, waivers and benefit maximums.

Precertification for medication(s) or product(s) indicated in this guideline requires completion of the request form in its entirety with the chart notes as documentation. All requested data must be provided. Once completed the form must be signed by the prescribing provider and faxed back to BCBSAZ Pharmacy Management at (602) 864-3126 or emailed to Pharmacyprecert@azblue.com. **Incomplete forms or forms without the chart notes will be returned.**

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Criteria:

- **Criteria for initial therapy:** Otezla is considered ***medically necessary*** and will be approved with medical record documentation of **ALL** of the following:

  1. Prescriber is a Rheumatologist

  2. Individual is 18 years of age or older

  3. A confirmed diagnosis is **ONE** of the following:
     - Active psoriatic arthritis where the disease remains active despite use of maximally tolerated anti-inflammatory dose of an NSAID

     - Moderate to severe plaque psoriasis **AND** all of the following:
       - Lesions involving 5% BSA or affects hands, feet, face, or genitals
       - Individual is on topical treatment
         - Topical treatment includes: corticosteroid, calcipotriene, calcitrol, betamethasone with calcipotriene
       - Individual is unable to tolerate, or failed phototherapy, or phototherapy is not an option due extent of disease, or it is not available
         - Types of phototherapy include: psoralens (methoxasalen, trioxasalen) with UVA light (PUVA), UVB with coal tar or dithranol, UVB (standard or narrow-band), laser

  4. Individual has failure, or intolerance to **ONE** preferred oral therapy or contraindication to **ALL** three of the preferred products
     - Active psoriatic arthritis: One preferred DMARD: leflunomide, methotrexate, sulfasalazine

     - Moderate to severe plaque psoriasis: One preferred psoriasis drug: acitretin, cyclosporine, methotrexate

  Initial approval duration: 4 months

- **Criteria for continuation of coverage (renewal request):** Otezla is considered ***medically necessary*** and will be approved with documentation of **ALL** of the following:

  1. The condition has not worsened while on therapy
     - Progression or worsening in psoriatic arthritis:
       - Seen as worsening in number of swollen, tender joints, pain, or stiffness
       - Less than a 20% improvement in number of swollen, tender joints, pain, or stiffness using the American College of Rheumatology (ACR)

     - Progression or worsening in plaque psoriasis:
       - Seen as failed to maintain clear or minimal disease or failed to achieve at least a 50% improvement in Psoriasis Area and Severity Index (PASI)
       - PASI calculation: http://www.pasitraining.com/

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2. Individual has been adherent with the medication

3. Individual has not developed any contraindications or other significant level 4 adverse drug effects that may exclude continued use, such as:
   - Unexplained clinically significant weight loss
   - Depression

4. There are no significant interacting drugs

Renewal duration: 12 months

Description:

Otezla (apremilast) is indicated for the **treatment of adult patients with active psoriatic arthritis and moderate to severe plaque psoriasis who are candidates for phototherapy or systemic therapy**. It is an oral small-molecule inhibitor of phosphodiesterase 4 (PDE4) specific for cyclic adenosine monophosphate (cAMP). PDE4 inhibition results in increased intracellular cAMP levels. The specific mechanism(s) by which apremilast exerts its therapeutic action in psoriatic arthritis and psoriasis patients is not well defined.

Phosphodiesterase (PDE) is an enzyme that is responsible for the intracellular degradation of cAMP and cyclic guanosine monophosphate (cGMP). cAMP is a key intracellular second messenger used in signal transduction in many biologic processes. There are several PDE families. PDE4 is found in most immune cells including lymphocyte subsets, granulocytes and monocytes/macrophages. Inhibition of PDE4 activity leads to elevated levels of intracellular cAMP which down-regulates the response of pro-inflammatory mediators such as tumor necrosis factor TNF and various interleukins.

Psoriasis is a chronic skin condition characterized by patches of abnormal skin that are red, itchy, and scaly. The patches vary in severity, size, and location. There are five main types of psoriasis: plaque (accounts for up to 90% of cases), guttate, inverse, pustular, and erythrodermic.

Plaque psoriasis appears as raised, red patches covered with a silvery white scaly buildup of dead skin cells. They are often localized to the elbows, knees, scalp, and back and the plaques may be itchy or painful. Treatment of psoriasis, including plaque psoriasis, includes phototherapy, topical medications, systemic therapy, and biologic medications for moderate to severe disease.

Mild to moderate disease, defined as affecting less than 5% of the body surface area and sparing the genitals, hands, feet, and face, can be treated with topical therapies such as corticosteroids, vitamin D analogs (calcipotriene or calcitriol), anthralin, the retinoid Tazorac (tazarotene), and calcineurin inhibitors (tacrolimus or pimecrolimus).

Severe psoriasis that involves more than 10% of the body surface area or involves crucial body areas such as the hands, feet, face, or genitals can be treated with phototherapy in combination with oral systemic therapies that may include methotrexate, cyclosporine, acitretin, and biologic therapies such as TNF-inhibitors. Phototherapy includes excimer laser, ultraviolet A combined with psoralen (methoxsalen), and ultraviolet B.

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Psoriatic arthritis (PsA) is a chronic inflammatory disease; left untreated, a proportion of patients may develop persistent inflammation with deforming progressive joint damage leading to severe physical limitation and disability. PsA is more common in individuals with psoriasis. PsA is characterized by stiffness, pain, swelling, and tenderness of the joints as well as the surrounding ligaments and tendons. Extra-articular manifestations are also seen such as dactylitis and enthesopathy. Unlike rheumatoid arthritis, PsA is usually rheumatoid factor negative. PsA affects men and women equally and typically presents at the age of 30-50 years of age.

Treatment of PsA consists of use of Nonsteroidal Anti-Inflammatory Drugs (NSAIDs) to help with symptomatic relief, but they do not alter the disease course or prevent disease progression. Intra-articular corticosteroid injections can also be used for symptomatic relief. Systemic corticosteroids may be used for individuals with persistent skin flares.

Disease Modifying Anti-Rheumatic Drugs (DMARDs) are the mainstay of treatment for patients suffering from PsA. Traditional oral agents include leflunomide, methotrexate, and sulfasalazine. They have demonstrated variable efficacy in treating the rheumatologic and dermatologic manifestations of PsA.

Biologic agents, particularly TNF blockers/inhibitors are the most effective class of therapeutic agents for treating PsA. They have demonstrated substantial responses for many, but not all, patients. TNF inhibitors include Humira (adalimumab), Cimzia (certolizumab), Enbrel (etanercept), Simponi (golimumab), and Remicade (infliximab). Stelara (ustekinumab), an IL-12/23 inhibitor, and Cosentyx (secukinumab), an IL-17A antagonist, also show efficacy in the treatment of PsA. The biologic agents work by mechanisms different from those of conventional systemic agents and may be effective alternatives or add-on therapies to patients who have unsatisfactory responses to the older drugs.

A recent review on the pharmacologic management of psoriatic arthritis recommended NSAIDs as first-line therapy to manage joint and musculoskeletal symptoms, a DMARD for individuals with active disease defined as one or more tender and inflamed joint and/or tender enthesis point (the site of a tendon, ligament, joint capsule, or fascia to bone) and/or dactylitic digit (inflammation of finger or toe) and/or inflammatory back pain. With regard to selection of which DMARD, the review stated that although there are few data, it recommends Methotrexate as first choice DMARD, unless other patient characteristics suggest a different DMARD should be agent. Use of local injections of corticosteroids is considered as adjunctive therapy, with systemic corticosteroids used cautiously in selective cases and using the lowest effective dose. In general, individuals with an inadequate response to at least one DMARD should be considered for therapy with a TNF inhibitor. In patients with an inadequate response to the initial TNF inhibitor, a switch to another TNF inhibitor should be considered.

Definitions:

Disease Modifying Anti-Rheumatic Drugs (DMARDs):
- Cyclosporine
- Leflunomide
- Methotrexate
- Sulfasalazine

Generic oral psoriasis medications:
- Acitretin
- Cyclosporine

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- Methotrexate

Resources:

"Small Molecules and Biologics Chart AP94", BCBSAZ Administrative Procedure Guideline when preferred TNF medications are otherwise contraindicated or not labeled for the indication being prescribed

Otezla AMCP Dossier 4-10-2014 Revised 06/2015, patient counseling revised 12/2014

Otezla. Package Insert. Revised by manufacturer 3/2014, accessed 6/4/14; revised 9/2014, accessed 10/17/14; revised 12/2014, accessed 8/31/15; revised 12/2015, accessed 7/22/16.

Menter A, Gottlieb A, Feldman SR, et al.: Guidelines of care for the management of psoriasis and psoriatic arthritis. Section 1 Overview of psoriasis and guidelines of care for the treatment of psoriasis with biologics. J Am Acad Dermatol 2008; 58; 826-50

Gossec L, Smolen JS, Gaujoux-Viala C, et al.: European League Against Rheumatism recommendations for the management of psoriatic arthritis with pharmacological therapies. Ann Rheum Dis 2012;71:4-12

Hsu S, Papp KA, Lebwohl MG, et al.: Consensus Guidelines for the Management of Plaque Psoriasis. Arch Dermatol 2012; 148(1): 95-102

Papp K, Gulliver W, Lynde C, et al.: Canadian Guidelines for the Management of Plaque Psoriasis: Overview. J Cutan Med Surg 2011; 15(4 July/Aug): 210-219

Menter A, Korman NJ, Elmets CA, et al.: Guidelines of care for the management of psoriasis and psoriatic arthritis. Section 6 Guidelines of care for the treatment of psoriasis and psoriatic arthritis: cased-based presentations and evidence-based conclusions. J Am Acad Dermatol 2011; 65: 137-174

Gottlieb A, Korman NJ, Gordon KB, et al.: Guidelines of care for the management of psoriasis and psoriatic arthritis. Section 2 Psoriatic arthritis: Overview and guidelines of care for treatment with emphasis on the biologics. J Am Acad Dermatol 2008; 58: 851-864

Coates LC, Kavanaugh AK, Mease PJ, et al.: Group for Research and Assessment of Psoriasis and Psoriatic Arthritis 2015 Treatment Recommendations for Psoriatic Arthritis. Arthritis and Rheumatology 2016; 68 (5 May): 1060-1071

Schmitt J and Wozel G. The Psoriasis Area and Severity Index Is the Adequate Criterion to Define Severity in Chronic Plaque-Type Psoriasis. Dermatology 2005; 210:194-199.

Mrowietz U, Kragballe K, Reich K, et al.: Definition of treatment goals for moderate to severe psoriasis: a European consensus. Arch Dermatol Res 2011; 303:1-10

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UpToDate: Treatment of psoriatic arthritis. Current through Jul 2017. https://www-uptodate-com.mwu.idm.oclc.org/contents/treatment-of-psoriatic-arthritis?source=search_result&search=psoriatic%20arthritis%20treatment&selectedTitle=1~150#H20469265

UpToDate: Treatment of psoriasis. Current through Jul 2017. https://www-uptodate-com.mwu.idm.oclc.org/contents/treatment-of-psoriasis?source=search_result&search=plaque%20psoriasis&selectedTitle=1~77#H45

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Fax completed prior authorization request form to 602-864-3126 or email to pharmacyprecert@azblue.com.
Call 866-325-1794 to check the status of a request.
All requested data must be provided. **Incomplete forms or forms without the chart notes will be returned.**
Pharmacy Coverage Guidelines are available at www.azblue.com/pharmacy.

Pharmacy Prior Authorization Request Form

Do not copy for future use. Forms are updated frequently.
REQUIRED: Office notes, labs, and medical testing relevant to the request that show medical justification are required.

Member Information

Member Name (first & last):	Date of Birth:	Gender:	BCBSAZ ID#:
Address:	City:	State:	Zip Code:

Prescribing Provider Information

Provider Name (first & last):	Specialty:	NPI#:	DEA#:
Office Address:	City:	State:	Zip Code:
Office Contact:	Office Phone:	Office Fax:	

Dispensing Pharmacy Information

Pharmacy Name:	Pharmacy Phone:	Pharmacy Fax:

Requested Medication Information

Medication Name:	Strength:	Dosage Form:
Directions for Use:	Quantity: / Refills:	Duration of Therapy/Use:

☐ Check if requesting **brand** only ☐ Check if requesting **generic**

☐ Check if requesting continuation of therapy (prior authorization approved by BCBSAZ expired)

Turn-Around Time For Review

☐ Standard ☐ Urgent. Sign here: _____ ☐ Exigent (requires prescriber to include a written statement)

Clinical Information

1. **What is the diagnosis? Please specify below.**

   ICD-10 Code: _____ **Diagnosis Description:** _____

2. ☐ Yes ☐ No **Was this medication started on a recent hospital discharge or emergency room visit?**

3. ☐ Yes ☐ No **There is absence of ALL contraindications.**

4. **What medication(s) has the individual tried and failed for this diagnosis? Please specify below.**
Important note: Samples provided by the provider are not accepted as continuation of therapy or as an adequate trial and failure.

Medication Name, Strength, Frequency	Dates started and stopped or Approximate Duration	Describe response, reason for failure, or allergy

5. **Are there any supporting labs or test results? Please specify below.**

Date	Test	Value

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Pharmacy Prior Authorization Request Form

6. Is there any additional information the prescribing provider feels is important to this review? Please specify below.
For example, explain the negative impact on medical condition, safety issue, reason formulary agent is not suitable to a specific medical condition, expected adverse clinical outcome from use of formulary agent, or reason different dosage form or dose is needed.

Signature affirms that information given on this form is true and accurate and reflects office notes

Prescribing Provider's Signature: Date:

Please note: Some medications may require completion of a drug-specific request form.

Incomplete forms or forms without the chart notes will be returned.

Office notes, labs, and medical testing relevant to the request that show medical justification are required.