Clinical Policy: Apremilast (Otezla)

Reference Number: CP.PHAR.245
Effective Date: 08.16
Last Review Date: 05.20
Line of Business: Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Apremilast (Otezla®) is an inhibitor of phosphodiesterase 4 (PDE4).

FDA Approved Indication(s)

Otezla is indicated for the treatment of:

- Adult patients with active psoriatic arthritis (PsA)
- Patients with moderate to severe plaque psoriasis (PsO) who are candidates for phototherapy or systemic therapy
- Adult patients with oral ulcers associated with Behçet's disease (BD)

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Otezla is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Psoriatic Arthritis (must meet all)**:**

1. Diagnosis of PsA;
2. Prescribed by or in consultation with a dermatologist or rheumatologist;
3. Age ≥ 18 years;
4. Dose does not exceed 60 mg per day.

Approval duration: 6 months

B. Plaque Psoriasis (must meet all)**:**

1. Diagnosis of PsO;
2. Prescribed by or in consultation with a dermatologist or rheumatologist;
3. Age ≥ 18 years;
4. Member meets one of the following (a or b):
   a. Failure of a ≥ 3 consecutive month trial of MTX at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
   b. If intolerance or contraindication to MTX (*see Appendix D*), failure of a ≥ 3 consecutive month trial of cyclosporine or acitretin at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;

5. Dose does not exceed 60 mg per day.

Approval duration: 6 months

C. Behçet's Disease (must meet all)**:**

1. Diagnosis of oral ulcers in members with BD;
2. Prescribed by or in consultation with a dermatologist or rheumatologist;
3. Age ≥ 18 years;
4. Failure of a topical corticosteroid (e.g., triamcinolone acetonide cream) at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
5. Failure of an oral corticosteroid (e.g., prednisone) at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
6. Failure of colchicine at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
7. Dose does not exceed 60 mg per day.

Approval duration: 6 months

D. Other diagnoses/indications

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.PMN.53 for Medicaid.

II. Continued Therapy

A. All Indications in Section I (must meet all)**:**

1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
2. Member is responding positively to therapy;
3. If request is for a dose increase, new dose does not exceed 60 mg (2 tablets) per day.

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

BD: Behçet's disease

FDA: Food and Drug Administration

MTX: methotrexate
PDE4: phosphodiesterase 4
PsO: plaque psoriasis
PsA: psoriatic arthritis

Appendix B: Therapeutic Alternatives
This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
acitretin (Soriatane®)	**PsO** 25 or 50 mg PO daily	50 mg/day
cyclosporine (Sandimmune®, Neoral®)	**PsO** 2.5 mg/kg/day PO divided BID	4 mg/kg/day
methotrexate (Rheumatrex®)	**PsO** 10 – 25 mg/week PO or 2.5 mg PO Q12 hr for 3 doses/week	30 mg/week
triamcinolone acetonide cream (Orabase® 0.1%)	**BD*** Apply topically to the isolated oral ulcer 3 to 4 times daily as needed for pain.	N/A
prednisone	**BD*** Initial dose: Week 1: 15 mg PO daily Week 2 onwards: 10 mg PO daily tapered over 2-3 weeks Maintenance dose (if recurrent): 5 mg PO daily	1 mg/kg/day
colchicine (Colcrys®)	**BD*** 1.2 to 1.8 mg PO daily	1.8 mg/day

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.
**Off-label*

Appendix C: Contraindications/Boxed Warnings
- Contraindication(s): known hypersensitivity to apremilast or to any of the excipients in the formulation
- Boxed warning(s): none reported

Appendix D: General Information
- Failure of a trial of conventional DMARDs:
  - Child-bearing age is not considered a contraindication for use of MTX. Each drug has risks in pregnancy. An educated patient and family planning would allow use of MTX in patients who have no intention of immediate pregnancy.
  - Social use of alcohol is not considered a contraindication for use of MTX. MTX may only be contraindicated if patients choose to drink over 14 units of alcohol per week. However, excessive alcohol drinking can lead to worsening of the condition, so

patients who are serious about clinical response to therapy should refrain from excessive alcohol consumption.

- PsA: According to the 2018 American College of Rheumatology and National Psoriasis Foundation guidelines, TNF inhibitors or oral small molecules (e.g., methotrexate, sulfasalazine, cyclosporine, leflunomide, apremilast) are preferred over other biologics (e.g., interleukin-17 inhibitors or interleukin-12/23 inhibitors) for treatment-naïve disease. TNF inhibitors are also generally recommended over oral small molecules as first-line therapy unless disease is not severe, member prefers oral agents, or TNF inhibitor therapy is contraindicated.
- Otezla is the first and only FDA-approved treatment for oral ulcers associated with Behçet's disease. However, patients included in the pivotal study had prior treatment with at least one non-biologic Behçet's disease therapy, such as, but not limited to, topical corticosteroids, or systemic treatment.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
PsO, PsA, BD	Initial dose: Day 1: 10 mg PO QAM Day 2: 10 mg PO QAM and 10 mg PO QPM Day 3: 10 mg PO QAM and 20 mg PO QPM Day 4: 20 mg PO QAM and 20 mg PO QPM Day 5: 20 mg PO QAM and 30 mg PO QPM Maintenance dose: Day 6 and thereafter: 30 mg PO BID	60 mg/day

VI. Product Availability

Tablets: 10 mg, 20 mg, 30 mg

VII. References

1. Otezla Prescribing Information. Summit, NJ: Celgene Corporation; July 2019. Available at http://www.otezla.com/. Accessed February 28, 2020.
2. Menter A, Gottlieb A, Feldman SR, Van Voorhees AS, Leonardi CL, Gordon KB, et al. American Academy of Dermatology. 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 May; 58(5):826-50.
3. Gossec L, Smolen JS, Ramiro S, et al European League Against Rheumatism (EULAR) recommendations for the management of psoriatic arthritis with pharmacological therapies: 2015 update Annals of the Rheumatic Diseases Published Online First: 07 December 2015. doi: 10.1136/annrheumdis-2015-208337.
4. Singh JA, Guyatt G, Ogdie A, et al. 2018 American College of Rheumatology/National Psoriasis Foundation Guideline for the treatment of psoriatic arthritis. American College of Rheumatology. 2019; 71(1):5-32. doi: 10.1002/art.40726
5. Hatemi G, Mahr A, Takeno M, et al. Improvements and correlations in oral ulcers, disease activity, and QOL in behçet's syndrome patients treated with apremilast: a phase 3

randomized, double-blind, placebo-controlled study. Rheumatology, Volume 58, Issue Supplement_2, March 2019, kez062.023, https://doi.org/10.1093/rheumatology/kez062.02
6. Hatemi G, Christensen R, Bang D, et al. 2018 update of the EULAR recommendations for the management of Behçet's syndrome Annals of the Rheumatic Diseases 2018;77:808-818.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy split from CP.PHAR.85.Psoriasis Treatment. Added prescriber specialty, max dose and contraindications per PI. Added requirement for trial and failure of PDL Enbrel and Humira, unless contraindicated; Removed question related to concurrent use with another biologic-not in contraindications section per PI. Modified prior treatment trial for PSA to require trial of MTX and added requirement for the following agents as an alternative if MTX cannot be used: leflunomide, cyclosporine, sulfasalazine, azathioprine. Plaque Psoriasis: removed duration of trial for topical and phototherapy; added requirement for trial and failure of one oral systemic agent (e.g., MTX, cyclosporine or acitretin), unless contraindicated to such therapies; re-auth: modified specific efficacy criteria related to Psoriasis Area and Severity Index (PASI)-75 to general efficacy statement. Re-auth: combined into "All Indications", added max dose and reasons to discontinue per PI.	06.16	08.16
Converted to new template. Trial requirement modified to require the concomitant use of oral and topical or phototherapy.	08.17	08.17
2Q 2018 annual review: policies combined for HIM and Medicaid lines of business; HIM: removed azathioprine as an option for trial and failure for PsA, removed specific diagnosis requirements for PsO, removed trial and failure of phototherapy and topical therapy for PsO, added requirement for trial and failure of cyclosporine or acitretin if methotrexate use is not tolerated or contraindicated; Medicaid: removed requirement that Otezla will not be used concurrently with a biologic agent; references reviewed and updated.	02.27.18	05.18
4Q 2018 annual review: allowed bypassing conventional DMARDs for axial PsA and required trial of NSAIDs; references reviewed and updated.	09.04.18	11.18
2Q 2019 annual review: removed trial and failure requirement of conventional DMARDs (e.g., MTX)/NSAIDs for PsA per ACR/NPF 2018 guidelines; references reviewed and updated.	03.05.19	05.19
No significant changes; removed HIM line of business and separated into policy HIM.PA.SP38.	06.03.19	
Criteria added for new FDA indication: treatment of adult patients with oral ulcers associated with Behçet's disease; references reviewed and updated.	09.03.19	11.19

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Updated preferred redirections based on SDC recommendation and prior clinical guidance: for PsA and PsO, removed trial of etanercept and adalimumab.	12.16.19	
2Q 2020 annual review: no significant changes; references reviewed and updated.	02.28.20	05.20

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.