Clinical Policy: Apremilast (Otezla)

Reference Number: CP.PHAR.245
Effective Date: 08.16
Last Review Date: 05.22
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 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. 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 (2 tablets) 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. Member has moderate-to-severe disease, and one of the following (i, ii, or iii):
      i. Failure of a ≥ 3 consecutive month trial of methotrexate (MTX) at up to maximally indicated doses;
      ii. Member has intolerance or contraindication to MTX (*see Appendix D*), and failure of a ≥ 3 consecutive month trial of cyclosporine or acitretin at up to maximally indicated doses, unless clinically significant adverse effects are experienced or both are contraindicated;
      iii. Member has intolerance or contraindication to MTX, cyclosporine, and acitretin, and failure of phototherapy, unless contraindicated or clinically significant adverse effects are experienced;
   b. Member has mild disease, and both of the following (i and ii):
      i. Failure of a medium to ultra-high potency topical corticosteroid (*see Appendix B*) unless contraindicated or clinically significant adverse effects are experienced;
      ii. Failure of one of the following, unless clinically significant adverse effects are experienced or all are contraindicated: calcipotriene, calcitriol, or tazarotene;
5. If request is for concomitant use with biologic disease-modifying anti-rheumatic drug (DMARD) therapy (e.g., Humira®, Enbrel®, infliximab), member meets one of the following (a or b):
   a. Failure of a ≥ 3 consecutive month trial of MTX used in combination with the biologic DMARD at up to maximally indicated doses;
   b. Member has intolerance or contraindication to MTX (*see Appendix D*), and failure of a ≥ 3 consecutive month trial of cyclosporine or acitretin used in combination with the biologic DMARD at up to maximally indicated doses, unless clinically significant adverse effects are experienced or both are contraindicated;
6. Dose does not exceed 60 mg (2 tablets) per day.

Approval duration: 6 months

C. 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. If request is for concomitant use with biologic DMARD therapy (e.g., Humira, Enbrel, infliximab), member meets one of the following (a or b):
   a. Failure of a ≥ 3 consecutive month trial of MTX used in combination with the biologic DMARD at up to maximally indicated doses;
   b. Member has intolerance or contraindication to MTX (*see Appendix D*), and failure of a ≥ 3 consecutive month trial of cyclosporine or acitretin used in combination with the biologic DMARD at up to maximally indicated doses, unless clinically significant adverse effects are experienced or both are contraindicated
5. Dose does not exceed 60 mg (2 tablets) 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 concomitant use with biologic DMARD therapy (e.g., Humira, Enbrel, infliximab), member meets one of the following (a or b):
   a. Failure of a ≥ 3 consecutive month trial of MTX used in combination with the biologic DMARD at up to maximally indicated doses;
   b. Member has intolerance or contraindication to MTX (*see Appendix D*), and failure of a ≥ 3 consecutive month trial of cyclosporine or acitretin used in combination with the biologic DMARD at up to maximally indicated doses, unless clinically significant adverse effects are experienced or both are contraindicated
4. 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
DMARD: disease-modifying anti-rheumatic drug
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
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
acitretin (Soriatane®)	**Moderate-to-severe PsO** 25 or 50 mg PO daily	50 mg/day
cyclosporine (Sandimmune®, Neoral®)	**Moderate-to-severe PsO** 2.5 mg/kg/day PO divided BID	4 mg/kg/day
methotrexate (Rheumatrex®)	**Moderate-to-severe PsO** 10 – 25 mg/week PO or 2.5 mg PO Q12 hr for 3 doses/week	30 mg/week
calcipotriene	**Mild-to-moderate PsO** Apply topically as a thin layer to affected area(s) once daily in the morning or twice daily in the morning and evening for up to 8 weeks.	100 g/week
calcitriol (Vectical®)	**Mild-to-moderate PsO** Apply topically to the affected areas twice daily	200 g/week
tazarotene (Tazorac®)	**Mild-to-moderate PsO** Apply topically to the affected areas once daily in the evening	One application daily
Ultra-High Potency Topical Corticosteroids		
augmented betamethasone dipropionate 0.05% (Diprolene®, Alphatrex®) ointment, gel	Apply topically to the affected area(s) BID	Should not be used for longer than 2 consecutive weeks
clobetasol propionate 0.05% (Temovate®, Temovate E®) cream, ointment, gel, solution		
diflorasone diacetate 0.05% (Apexicon®) ointment		

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
halobetasol propionate 0.05% (Ultravate®) cream, ointment		
High Potency Topical Corticosteroids		
augmented betamethasone dipropionate 0.05% (Diprolone®, Diprolene® AF) cream, lotion	Apply topically to the affected area(s) BID	Should not be used for longer than 2 consecutive weeks
betamethasone dipropionate 0.05% ointment		
desoximetasone (Topicort®) 0.25%, 0.05% cream, ointment, gel		
diflorasone 0.05% (Apexicon E®) cream		
fluocinonide acetonide 0.05% cream, ointment, gel, solution		
triamcinolone acetonide 0.5% (Aristocort®, Kenalog®) cream, ointment		
Medium/Medium to High Potency Topical Corticosteroids		
betamethasone dipropionate 0.05% cream	Apply topically to the affected area(s) BID	Should not be used for longer than 2 consecutive weeks
desoximetasone 0.05% (Topicort®) cream, ointment, gel		
fluocinolone acetonide 0.025% (Synalar®) cream, ointment		
fluticasone propionate 0.05% (Cutivate®) cream		
mometasone furoate 0.1% (Elocon®) cream, lotion, ointment		
triamcinolone acetonide 0.1%, 0.25%,0.5% (Aristocort®, Kenalog®) cream, ointment		

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. In patients with inadequate response to oral small molecules, the guidelines recommend adding Otezla to the current oral small molecule therapy or switching to a biologic therapy. In patients with inadequate response to biologic monotherapy, the guidelines recommend switching to a different biologic agent over addition of MTX to the current biologic agent; there are no recommendations that address adding or switching to Otezla.
  - The 2019 European League Against Rheumatism guidelines recommend Otezla only in patients with mild disease who have inadequate response to a conventional DMARD and in whom neither biologic DMARDs nor targeted synthetic DMARDs (e.g., Janus kinase inhibitors) are appropriate.
- PsO: The 2019 American Academy of Dermatology and National Psoriasis Foundation guidelines recommend the combination of a biologic therapy with MTX over combination of a biologic therapy with Otezla, noting that there are limited data and the long-term safety and efficacy of the latter combination is unknown.
- 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; December 2021. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/205437s011lbl.pdf. Accessed January 26, 2022.
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3. Menter A, Gelfand JM, Connor C, et al. Joint AAD-NPF guidelines of care for the management of psoriasis with systemic nonbiologic therapies. *J Am Acad Dermatol* 2020;82:1445-86. https://doi.org/10.1016/j.jaad.2020.02.044
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5. 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
6. 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
7. 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
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	02.27.18	05.18

Reviews, Revisions, and Approvals	Date	P&T Approval Date
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.		
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
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
2Q 2021 annual review: added additional criteria related to diagnosis of moderate-to-severe PsO per 2019 AAD/NPF guidelines specifying at least 3% BSA involvement or involvement of areas that severely impact daily function; references reviewed and updated.	02.23.21	05.21
Added requirement of concomitant treatment with MTX and bDMARD if request is for concomitant treatment with Otezla and bDMARD; per August SDC, added Legacy WellCare line of business to policy (WCG.CP.PHAR.245 to be retired).	08.30.21	11.21
2Q 2022 annual review: for moderate-to-severe PsO, allowed phototherapy as alternative to systemic conventional DMARD if contraindicated or clinically significant adverse effects are experienced; RT4: added FDA use extension to mild PsO; references reviewed and updated.	01.26.22	05.22

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.

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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.

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