Clinical Policy: Apremilast (Otezla)

Reference Number: CP.PHAR.245
Effective Date: 08.16
Last Review Date: 05.24
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)
- Adult patients with plaque psoriasis (PsO) who are candidates for phototherapy or systemic therapy
- Pediatric patients 6 years of age and older weighting at least 20 kg with moderate to severe 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 both of the following (a and b):
   a. 60 mg per day;
   b. 2 tablets per day.

Approval duration: 6 months

B. Plaque Psoriasis (must meet all)**:**
1. Diagnosis of PsO;
2. Member meets of the following (a or b):
   a. Age ≥ 18 years;
   b. Age 6 years to < 18 years, and both of the following (i and ii):
      i. PsO is moderate-to-severe as evidenced by involvement of one of the following (1 or 2):
         1) ≥ 3% of total body surface area;
         2) Hands, feet, scalp, face, or genital area;
      ii. Documentation that member weighs ≥ 20 kg;
3. Prescribed by or in consultation with a dermatologist or rheumatologist;
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 one of the following (a or b):
   a. Age ≥ 18 years (i and ii):
      i. 60 mg per day;
      ii. 2 tablets per day;
   b. Age 6 to < 18 years (i or ii):
      i. Weight ≥ 50 kg (1 and 2):
         1) 60 mg per day;
         2) 2 tablets per day;

ii. Weight ≥ 20 kg to < 50 kg (1 and 2):
1) 40 mg per day;
2) 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 both of the following (a and b):
   a. 60 mg per day;
   b. 2 tablets per day.

Approval duration: 6 months

D. Other diagnoses/indications (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.PMN.53 for Medicaid.

II. Continued Therapy

A. All Indications in Section I (must meet all)**:**
1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B);*
2. Member is responding positively to therapy;

3. For PsO: If member is between ages 6 to < 18 years, documentation that member weighs ≥ 20 kg;
4. For PsO and PsA: 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. If request is for a dose increase, new dose does not exceed one of the following (a or b):
   a. For BD and PsA (i and ii):
      i. 60 mg per day;
      ii. 2 tablets per day;
   b. For PsO (i or ii):
      i. Age ≥ 18 years (1 and 2):
         1) 60 mg per day;
         2) 2 tablets per day;
      ii. Age 6 to < 18 years (1 or 2):
         1) Weight ≥ 50 kg (a and b):
            a) 60 mg per day;
            b) 2 tablets per day;
         2) Weight ≥ 20 kg to < 50 kg (a and b):
            a) 40 mg per day;
            b) 2 tablets per day.

Approval duration: 12 months

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

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: 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 – 4 mg/kg/day PO divided BID	4 mg/kg/day
methotrexate (Trexall®, Otrexup™, Rasuvo®, RediTrex®, Rheumatrex®, Jylamvo®)	**Moderate-to-severe PsO** 10 to 25 mg/week IM, SC or 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

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
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		
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		

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
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.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
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
PsO	**Adults:** 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 **Pediatric:** *Weight ≥ 50 kg:* 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 *Weight 20 kg to < 50 kg:* 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 20 mg PO QPM Maintenance dose: Day 6 and thereafter: 20 mg PO BID	Adults: 60 mg/day Pediatric: *Weight ≥ 50 kg:* 60 mg/day *Weight 20 kg to < 50 kg:* 40 mg/day

VI. Product Availability

Tablets: 10 mg, 20 mg, 30 mg

VII. References

1. Otezla Prescribing Information. Summit, NJ: Celgene Corporation; April 2024. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/205437Orig1s013_Corrected_lbl.pdf. Accessed May 6, 2024.
2. Menter A, Strober BE, Kaplan DH, et al. Joint AAD-NPF guidelines of care for the management and treatment of psoriasis with biologics. *J Am Acad Dermatol* 2019;80:1029-72. doi:10.1016/j.aad.201811.057.
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.
4. Gossec L, Baraliakos X, Kerschbaumer A, et al. EULAR recommendations for the management of psoriatic arthritis with pharmacological therapies: 2019 update. Ann Rheum Dis. 2020;79:700–712. doi:10.1136/annrheumdis-2020-217159.
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.
8. Adil A, Goyal A, and Quint JM. Behcet Disease. 2022 December 1. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; January 2022. PMID: 29262080.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
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

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Template changes applied to other diagnoses/indications and continued therapy section.	10.10.22	
2Q 2023 annual review: no significant changes; references reviewed and updated.	02.10.23	05.23
2Q 2024 annual review: updated Appendix D with removal of PsA and PsO guideline supplemental information; references reviewed and updated.	01.23.24	05.24
RT4: for PsO, added newly approved pediatric extension to 6 years and older.	05.06.24	

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.