Clinical Policy: Apremilast (Otezla)
Reference Number: CP.PHAR.245
Effective Date: 08.16
Last Review Date: 11.19
Line of Business: Medicaid

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. Failure of etanercept (*Enbrel® is preferred) and adalimumab (*Humira® is preferred), each used for ≥ 3 consecutive months, unless contraindicated or clinically significant adverse effects are experienced;
      *Prior authorization is required for etanercept and adalimumab
      5. 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. Failure of etanercept (Enbrel is preferred) and adalimumab (Humira is preferred), each used for ≥ 3 consecutive months, unless contraindicated or clinically significant adverse effects are experienced;  
*Prior authorization is required for etanercept and adalimumab*

6. 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 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.

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Dosing Regimen</th>
<th>Dose Limit/Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>acitretin (Soriatane®)</td>
<td>PsO 25 or 50 mg PO daily</td>
<td>50 mg/day</td>
</tr>
<tr>
<td>cyclosporine (Sandimmune®, Neoral®)</td>
<td>PsO 2.5 mg/kg/day PO divided BID</td>
<td>4 mg/kg/day</td>
</tr>
<tr>
<td>methotrexate (Rheumatrex®)</td>
<td>PsO 10 – 25 mg/week PO or 2.5 mg PO Q12 hr for 3 doses/week</td>
<td>30 mg/week</td>
</tr>
<tr>
<td>Enbrel® (etanercept)</td>
<td>PsO Initial dose: 50 mg SC twice weekly for 3 months Maintenance dose: 50 mg SC once weekly</td>
<td>50 mg/week</td>
</tr>
<tr>
<td></td>
<td>PsA 25 mg SC twice weekly or 50 mg SC once weekly</td>
<td></td>
</tr>
<tr>
<td>Humira® (adalimumab)</td>
<td>PsO Initial dose: 80 mg SC Maintenance dose: 40 mg SC every other week starting one week after initial dose</td>
<td>40 mg every other week</td>
</tr>
<tr>
<td></td>
<td>PsA 40 mg SC every other week</td>
<td></td>
</tr>
<tr>
<td>triamcinolone acetonide cream (Orabase® 0.1%)</td>
<td>BD* Apply topically to the isolated oral ulcer 3 to 4 times daily as needed for pain.</td>
<td>N/A</td>
</tr>
<tr>
<td>Drug Name</td>
<td>Dosing Regimen</td>
<td>Dose Limit/Maximum Dose</td>
</tr>
<tr>
<td>--------------------</td>
<td>-------------------------------------</td>
<td>-------------------------</td>
</tr>
<tr>
<td>prednisone</td>
<td><strong>BD</strong>*&lt;br&gt;Initial dose:&lt;br&gt;Week 1: 15 mg PO daily&lt;br&gt;Week 2 onwards: 10 mg PO daily tapered over 2-3 weeks&lt;br&gt;Maintenance dose (if recurrent): 5 mg PO daily</td>
<td>1 mg/kg/day</td>
</tr>
<tr>
<td>colchicine (Colcrys®)</td>
<td><strong>BD</strong>*&lt;br&gt;1.2 to 1.8 mg PO daily</td>
<td>1.8 mg/day</td>
</tr>
</tbody>
</table>

*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

<table>
<thead>
<tr>
<th>Indication</th>
<th>Dosing Regimen</th>
<th>Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>PsO, PsA, BD</td>
<td><strong>Initial dose:</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Day 1: 10 mg PO QAM</td>
<td>60 mg/day</td>
</tr>
<tr>
<td></td>
<td>Day 2: 10 mg PO QAM and 10 mg PO QPM</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Day 3: 10 mg PO QAM and 20 mg PO QPM</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Day 4: 20 mg PO QAM and 20 mg PO QPM</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Day 5: 20 mg PO QAM and 30 mg PO QPM</td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Maintenance dose:</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Day 6 and thereafter: 30 mg PO BID</td>
<td></td>
</tr>
</tbody>
</table>

VI. Product Availability

Tablets: 10 mg, 20 mg, 30 mg

VII. References


---

Reviews, Revisions, and Approvals

<table>
<thead>
<tr>
<th>Date</th>
<th>P&amp;T Approval Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>06.16</td>
<td>08.16</td>
</tr>
<tr>
<td>Reviews, Revisions, and Approvals</td>
<td>Date</td>
</tr>
<tr>
<td>--------------------------------------------------------------------------------------------------</td>
<td>------</td>
</tr>
<tr>
<td>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.</td>
<td></td>
</tr>
<tr>
<td>Converted to new template. Trial requirement modified to require the concomitant use of oral and topical or phototherapy.</td>
<td>08.17</td>
</tr>
<tr>
<td>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.</td>
<td>02.27.18</td>
</tr>
<tr>
<td>4Q 2018 annual review: allowed bypassing conventional DMARDs for axial PsA and required trial of NSAIDs; references reviewed and updated.</td>
<td>09.04.18</td>
</tr>
<tr>
<td>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.</td>
<td>03.05.19</td>
</tr>
<tr>
<td>No significant changes; removed HIM line of business and separated into policy HIM.PA.SP38.</td>
<td>06.03.19</td>
</tr>
<tr>
<td>Criteria added for new FDA indication: treatment of adult patients with oral ulcers associated with Behçet’s disease; references reviewed and updated.</td>
<td>09.03.19</td>
</tr>
</tbody>
</table>

**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.

©2016 Centene Corporation. All rights reserved. All materials are exclusively owned by Centene Corporation and are protected by United States copyright law and international copyright law. No part of this publication may be reproduced, copied, modified, distributed, displayed, stored in a retrieval system, transmitted in any form or by any means, or otherwise published without the prior written permission of Centene Corporation. You may not alter or remove any trademark, copyright or other notice contained herein. Centene® and Centene Corporation® are registered trademarks exclusively owned by Centene Corporation.