Otezla (apremilast) Prior Authorization with Quantity Limit Program Summary

This program applies to MN Medicaid.

This program is implemented with auto-grandfathering.

For Medicaid, the Non-Preferred Drug Supplement applies.

The BCBS MN Step Therapy Supplement also applies to this program for Medicaid.

Program specific denial language for prerequisite step therapy component does not apply. Instead, supplemental program denial language will apply.

FDA APPROVED INDICATIONS AND DOSAGE[1]

Agent	FDA Labeled Indication	Dosing
Otezla® (apremilast) tablets	Treatment of adult patients with active psoriatic arthritis	Initial dose titration: Day 1: 10 mg morning (am) Day 2: 10 mg am and 10 mg evening (pm) Day 3: 10 mg am and 20 mg pm Day 4: 20 mg am and 20 mg pm Day 5: 20 mg am and 30 mg pm Day 6 and thereafter: 30 mg twice daily Maintenance dose: 30 mg twice daily
	Treatment of patients with moderate to severe plaque psoriasis who are candidates for phototherapy or systemic therapy	
	Treatment of adult patients with oral ulcers associated with Behcet's disease	

CLINICAL RATIONALE

Psoriasis (PS)

Psoriasis (PS) is a chronic inflammatory skin condition that is often associated with systemic manifestations, especially arthritis. Diagnosis is usually clinical, based on the presence of typical erythematous scaly patches, papules, and plaques that are often pruritic and sometimes painful. Treatment goals for psoriasis include improvement of skin, nail, and joint lesions plus enhanced quality of life. [2]

The American Academy of Family Physicians (AAFP) categorizes psoriasis severity into mild to moderate (less than 5% of body surface area [BSA]) and moderate to severe (5% or more of BSA). The AAFP psoriasis treatment guidelines recommend basing treatment on disease severity:[2]

- Mild to moderate (less than 5% of BSA and sparing the genitals, hands, feet, and face):
  - Candidate for intermittent therapy: topical corticosteroids, vitamin D analogs (calcipotriene and calcitriol), or tazarotene (Tazorac)
  - Candidate for continuous therapy: calcineurin inhibitors (tacrolimus and pimecrolimus)
- Severe (5% or more of BSA or involving the genitals, hands, feet, and face):

    - Less than 20% of BSA affected: vitamin D analogs (calcipotriene and calcitriol) with or without phototherapy. These agents have a slower onset of action but a longer disease-free interval than topical corticosteroids
    - 20% or more of BSA affected: systemic therapy with MTX, cyclosporine, acitretin, or biologics. Biologics are recommended for those with concomitant PsA
- Less commonly used topical therapies include non-medicated moisturizers, salicylic acid, coal tar, and anthralin

The American Academy of Dermatology (AAD) and National Psoriasis Foundation (NPF) categorize psoriasis severity as limited or mild (less than 3% of BSA), moderate (3% to 10% of BSA), or severe (great than 10% of BSA). The AAD/NPF guidelines also note that psoriasis can be considered severe irrespective of BSA when is occurs in select locations (e.g., hands, feet, scalp, face, or genital area) or when it causes intractable pruritus.[5] The AAD psoriasis treatment guidelines recommend the following:[3,4]

- Limited disease (less than 5% of BSA):
    - Topical corticosteroids are first line as either monotherapy or in conjunction with non-steroidal topical agents
    - Vitamin D analogs, calcipotriene, calcipotriol, and calcitriol, are other first line agents and are often used in combination with topical corticosteroids
    - Tazarotene is a corticosteroid sparing agent and can be used in combination with topical corticosteroids to produce a synergistic effect and longer durations of treatment benefit and remission
    - Phototherapy is another first line option for limited disease, and allows for selective targeting of localized lesions and resistant areas such as the scalp and skin folds, leaving surrounding, non-lesional skin unaffected
    - Calcineurin inhibitors (tacrolimus and pimecrolimus) may also be considered first line for intertriginous, inverse, face, and genital psoriasis
    - Systemic agents are considered second line and only for short term use
- Moderate to severe disease without PsA (more than 5% of BSA or psoriasis in vulnerable areas [e.g., face, genitals, hands, and feet] that adversely affects quality of life):
    - UV-therapy is considered first line as monotherapy or in combination with acitretin or MTX
    - If UV-therapy is unavailable first line therapies include MTX, cyclosporine, acitretin, and biologics
    - Second line systemic agents include leflunomide, sulfasalazine, and tacrolimus
- Biologics are routinely used when one or more traditional systemic agents fail to produce adequate response, but are considered first line in patients with moderate to severe psoriasis with concomitant severe PsA

The National Psoriasis Foundation (NPF) medical board recommend a treat-to-target approach to therapy for psoriasis that include the following:[6]

- The preferred assessment instrument for determining disease severity is BSA
- Target response after treatment initiation should be BSA ≤1% after 3 months
- Acceptable response is either a BSA ≤3% or a BSA improvement ≥75% from baseline at 3 months after treatment initiation

Psoriatic Arthritis (PsA)

Psoriatic arthritis (PsA) is a chronic inflammatory musculoskeletal disease associated with psoriasis, most commonly presenting with peripheral arthritis, dactylitis, enthesitis, and spondylitis. Treatment involves the use of a variety of interventions, including many agents used for the treatment of other inflammatory arthritis, particularly spondyloarthritis and RA, and other management strategies of the cutaneous manifestations of psoriasis.[7]

The American Academy of Dermatology (AAD) recommends initiating MTX in most patients with moderate to severe PsA. After 12 to 16 weeks of MTX therapy with appropriate dose escalation,

the AAD recommends adding or switching to a TNF inhibitor if there is minimal improvement on MTX monotherapy.[3]

The American College of Rheumatology (ACR) and the National Psoriasis Foundation (NPF) guidelines for PsA recommend a treat-to-target approach in therapy, regardless of disease activity, and the following:[7]

- Active PsA is defined as symptoms at an unacceptably bothersome level as reported by the patient and health care provider to be due to PsA based on the presence of one of the following:
    - Actively inflamed joints
    - Dactylitis
    - Enthesitis
    - Axial disease
    - Active skin and/or nail involvement
    - Extraarticular manifestations such as uveitis or inflammatory bowel disease
- Disease severity includes level of disease activity at a given time point and the presence/absence of poor prognostic factors and long-term damage
- Severe PsA disease includes the presence of 1 or more of the following:
    - Erosive disease
    - Elevated markers of inflammation (ESR, CRP) attributable to PsA
    - Long-term damage that interferes with function (i.e., joint deformities)
    - Highly active disease that causes a major impairment in quality of life
    - Active PsA at many sites including dactylitis, enthesitis
    - Function limiting PsA at a few sites
    - Rapidly progressive disease
- Symptomatic treatments include nonsteroidal anti-inflammatory drugs (NSAIDs), glucocorticoids, local glucocorticoid injections
- Treatment recommendations for active disease:
    - Treatment naïve patients first line options include oral small molecules (OSM), TNF biologics, IL-17 inhibitor, and IL-12/23 inhibitor
        - OSM (i.e., methotrexate[MTX], sulfasalazine, cyclosporine, leflunomide, apremilast) should be considered if the patient does not have severe PsA, does not have severe psoriasis, prefers oral therapy, has concern over starting a biologic, or has contraindications to TNF inhibitor
        - Biologics (i.e., TNF biologic, IL-17 inhibitor, IL-12/23 inhibitor) are recommended as a first line option in patients with severe PsA and/or severe psoriasis
    - Previous treatment with OSM and continued active disease:
        - Switch to a different OSM (except apremilast) in patients without severe PsA or severe PS, contraindications to TNF biologics, prefers oral therapy OR add on apremilast to current OSM therapy
        - May add another OSM (except apremilast) to current OSM therapy for patients that have exhibited partial response to current OSM in patients without severe PsA or severe PS, contraindications to TNF biologics, or prefers oral therapy
        - Biologic (i.e., TNF biologic, IL-17 inhibitor, IL-12/23 inhibitor) monotherapy
    - Previous treatment with a biologic (i.e., TNF biologic, IL-17 inhibitor, IL-12/23 inhibitor) and continued active disease:
        - Switch to another biologic (i.e., TNF biologic, IL-17 inhibitor, IL-12/23 inhibitor, abatacept, or tofacitinib) monotherapy or add MTX to the current TNF biologic

Behcet's Disease (BD)[8]

Behcet's disease (BD) is a type of vasculitis that involves numerous organ systems, such as the skin, mucosa, joints, eyes, veins, arteries, nervous system, and gastrointestinal system. BD runs a relapsing and remitting course and a multidisciplinary approach is necessary for optimal

care. The goal of treatment is to suppress inflammatory exacerbations and recurrences to prevent irreversible organ damage.

Chronic oral ulceration can cause scaring requiring vigorous treatment to prevent oropharyngeal narrowing. The European League Against Rheumatism recommends topical measures, such as steroids, for the treatment of oral and genital ulcers. Colchicine is recommended for the prevention of recurrent mucocutaneous lesions. Patients with lesions that continue to recur despite colchicine may use immunomodulatory or immunosuppressive agents, such as azathioprine, tumor necrosis factor (TNF) inhibitors, or apremilast.

Efficacy[1]
The efficacy of Otezla for the treatment of oral ulcers associated with BD was established in a multicenter, randomized, placebo-controlled trial. Patients were required to have active oral ulcers at the time of enrollment, have had at least 3 occurrences of oral ulcers within the previous 12 months, and have received treatment with at least one non-biologic therapy. All subjects had a history of recurrent oral ulcers that were currently active. Otezla had a greater reduction in the number of oral ulcers and patient reported ulcer pain when compared to placebo.

Safety[1]
Otezla is contraindicated in patients with a known hypersensitivity to apremilast or to any of the excipients in the formulation.

REFERENCES

1. Otezla Prescribing Information. Celgene Corporation. July 2019.
2. Weigle, Nancy, MD, et al. Psoriasis. American Academy of Family Physicians. May 2013. 87 (9): 626-633.
3. Menter A, Korman NJ, Elmets CA, et al. Guidelines of care for the management of psoriasis and psoriatic arthritis. J Am Acad Dermatol. 2011;65(1):137–174.
4. Menter A, 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. Journal of the American Academy of Dermatology. 2008; 58:826–850. doi: 10.1016/j.jaad.2008.02.039.
5. Menter, Alan et al. (2019). Joint AAD-NPF guidelines of care for the management and treatment of psoriasis with biologics. Journal of the American Academy of Dermatology. doi: https://doi.org/10.1016/j.jaad.2018.11.057.
6. Armstrong AW, Siegel MP, Bagel J, et al. From the medical board of the National Psoriasis Foundation: treatment targets for plaque psoriasis. Journal of the American Academy of Dermatology. 2017;76(2):290-298. doi: 10.1016/j.jaad.2016.10.017.
7. Singh, J. A., et al. (2019). 2018 American College of Rheumatology/National Psoriasis Foundation Guideline for the Treatment of Psoriatic Arthritis. Arthritis Care Res, 71: 2-29. doi:10.1002/acr.23789.
8. Hatemi G, Christensen R, Bang D, et al. 2018 update of the EULAR recommendations for the management of Behçet's syndrome. Ann Rheum Dis 2018; 77:808.

Otezla (apremilast) Prior Authorization with Quantity Limit

TARGET AGENT
Otezla® (apremilast)

Brand (generic)	GPI	Quantity Limit	Multisource Code
Otezla (apremilast)			
10 mg, 20 mg & 30 mg tablet starter pack (4 week)	6670001500B720	1 starter kit (55 tablets)/180 days	M, N, O, or Y
30mg tablets	66700015000330	60 tablets/30 days	M, N, O, or Y

PRIOR AUTHORIZATION CRITERIA FOR APPROVAL
Initial Evaluation
Target Agent will be approved when the ALL of the following are met**:**

1. ONE of the following:
   a. Information has been provided that indicates the patient has been treated with the requested agent (starting on samples is not approvable) within the past 90 days
   OR
   b. The prescriber states the patient has been treated with the requested agent (starting on samples is not approvable) within the past 90 days AND is at risk if therapy is changed
   OR
   c. BOTH of the following:
      i. The patient has an FDA labeled indication or an indication supported in DrugDex with 1 or 2a level of evidence or AHFS for the requested agent
      AND
      ii. ONE of the following:
         A. The patient has a diagnosis of active psoriatic arthritis (PsA) AND ONE of the following:
            1. The patient has tried and had an inadequate response to ONE conventional agent (i.e., cyclosporine, hydroxychloroquine, leflunomide, methotrexate, sulfasalazine) used in the treatment of PsA for at least 3-months
            OR
            2. The patient has an intolerance, FDA labeled contraindication, or hypersensitivity to ALL of the following conventional agents (i.e., cyclosporine, leflunomide, methotrexate, sulfasalazine) used in the treatment of PsA
            OR
            3. The patient's medication history indicates use of another biologic immunomodulator agent that is FDA labeled or supported in DrugDex with 1 or 2a level of evidence or AHFS for the treatment of PsA

         OR

         B. The patient has a diagnosis of moderate to severe plaque psoriasis (PS) AND ONE of the following:
            1. The patient has tried and had an inadequate response to ONE conventional agent (i.e., acitretin, anthralin, calcipotriene, calcitriol, coal tar products, cyclosporine, methotrexate, pimecrolimus, PUVA [phototherapy], tacrolimus, tazarotene, topical corticosteroids) used in the treatment of PS for at least 3-months
            OR

2. The patient has an intolerance, FDA labeled contraindication, or hypersensitivity to ALL conventional agents used in the treatment of PS
OR
3. The patient's medication history indicates use of another biologic immunomodulator agent that is FDA labeled or supported in DrugDex with 1 or 2a level of evidence or AHFS for the treatment of PS

OR

C. The patient has a diagnosis of Behcet's disease (BD) AND ALL of the following:
1. The patient has active oral ulcers associated with BD
AND
2. The patient has had at least 3 occurrences of oral ulcers in the last 12-months
AND
3. ONE of the following:
a. The patient has tried and had an inadequate response to ONE conventional agent (i.e., topical oral corticosteroids [i.e., triamcinolone dental paste], colchicine, azathioprine) used in the treatment of BD
OR
b. The patient has an intolerance, FDA labeled contraindication, or hypersensitivity to ALL conventional agents used in the treatment of BD
OR
c. The patient's medication history indicates use of another biologic immunomodulator agent that is FDA labeled or supported in DrugDex with 1 or 2a level of evidence or AHFS for the treatment of BD

OR

D. The patient has another FDA labeled indication or an indication supported in DrugDex with 1 or 2a level of evidence or AHFS for the requested agent not mentioned previously

AND

2. The patient will NOT be using the requested agent in combination with another biologic immunomodulator agent
AND
3. The prescriber is a specialist in the area of the patient's diagnosis (e.g., dermatologist, rheumatologist) or the prescriber has consulted with a specialist in the area of the patient's diagnosis
AND
4. The patient does NOT have any FDA labeled contraindications to the requested agent
AND
5. ONE of the following:
a. The requested quantity (dose) does NOT exceed the program quantity limit
OR
b. ALL of the following:
i. The requested quantity (dose) is greater than the program quantity limit
AND
ii. The requested quantity (dose) does NOT exceed the maximum FDA labeled dose for the requested indication
AND
iii. The requested quantity (dose) cannot be achieved with a lower quantity of a higher strength that does not exceed the program quantity limit

OR

c. ALL of the following:
    i. The requested quantity (dose) is greater than the program quantity limit
    AND
    ii. The requested quantity (dose) is greater than the maximum FDA labeled dose for the requested indication
    AND
    iii. The prescriber has provided information in support of therapy with a higher dose for the requested indication (e.g., clinical trials, phase III studies, guidelines required)

Length of approval: 12 months

Renewal Evaluation

Target Agent will be approved when ALL of the following are met:

1. The patient has been previously approved for the requested agent through the plan's Prior Authorization process
   AND
2. The patient has had clinical benefit with the requested agent
   AND
3. The patient will NOT be using the requested agent in combination with another biologic immunomodulator agent
   AND
4. The prescriber is a specialist in the area of the patient's diagnosis (e.g., dermatologist, rheumatologist) or has consulted with a specialist in the area of the patient's diagnosis
   AND
5. The patient does NOT have any FDA labeled contraindications to the requested agent
   AND
6. ONE of the following:
    a. The requested quantity (dose) does NOT exceed the program quantity limit
    OR
    b. ALL of the following:
        i. The requested quantity (dose) is greater than the program quantity limit
        AND
        ii. The requested quantity (dose) does NOT exceed the maximum FDA labeled dose for the requested indication
        AND
        iii. The requested quantity (dose) cannot be achieved with a lower quantity of a higher strength that does not exceed the program quantity limit
    OR
    c. ALL of the following:
        i. The requested quantity (dose) is greater than the program quantity limit
        AND
        ii. The requested quantity (dose) is greater than the maximum FDA labeled dose for the requested indication
        AND
        iii. The prescriber has provided information in support of therapy with a higher dose for the requested indication (e.g., clinical trials, phase III studies, guidelines required)

Length of approval: 12 months

Step Therapy Supplement Program Summary

This program applies to Medicaid.

Please note, this does not include or apply to quantity limit questions.

STEP THERAPY SUPPLEMENT
OBJECTIVE
The intent of the Step Therapy Supplement is to provide additional questions, to ensure compliance to MN Statute 62Q.184. These questions will apply if the step therapy component within a Prior Authorization or Step Therapy program is not able to be approved.

CONDITIONS FOR APPROVAL
The requested agent will be approved when ONE of the following are met:

1. The patient is currently being treated with the requested agent as indicated by ALL of the following:
    a. A statement by the prescriber that the patient is currently taking the requested agent
    AND
    b. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on requested agent
    AND
    c. The prescriber states that a change in therapy is expected to be ineffective or cause harm

    OR
2. BOTH of the following
    a. The patient's medication history includes the required prerequisite/preferred agent(s) or a drug in the same pharmacological class with the same mechanism of action as indicated by ONE of the following:
        i. Evidence of a paid claim(s) within the past 999 days
        OR
        ii. The prescriber has stated that the patient has tried the required prerequisite/preferred agent(s) in the past 999 days

    AND
    b. ONE of the following:
        i. The required prerequisite/preferred agent(s) was discontinued due to lack of effectiveness or an adverse event
        OR
        ii. The prescriber has submitted an evidence-based and peer-reviewed clinical practice guideline supporting the use of the requested agent over the prerequisite/preferred agent(s)

    OR
3. The prescriber has provided documentation that the required prerequisite/preferred agent(s) cannot be used due to a documented medical condition or comorbid condition that is likely to cause an adverse reaction, decrease ability of the patient to achieve or maintain reasonable functional ability in performing daily activities or cause physical or mental harm

Length of Approval: As per program specific criteria

Non-Preferred Drug Supplement Program Summary

This program applies to Medicaid.

NON-PREFERRED DRUG SUPPLEMENT
OBJECTIVE
The intent of the Non-Preferred Drug Supplement is to provide additional questions, to ensure compliance to the MN Uniform Preferred Drug List. These questions will apply to specified Prior Authorization programs that do not already contain these requirements.

CONDITIONS FOR APPROVAL
The requested agent will be approved when ONE of the following are met:

1. The requested agent is a preferred agent in the Minnesota Medicaid Preferred Drug List (PDL)
   OR
2. The request is for a non-preferred agent in the Minnesota Medicaid Preferred Drug List (PDL) and ONE of the following:
   a. The patient is currently being treated with the requested agent and is experiencing a positive therapeutic outcome AND the prescriber provides documentation that switching the member to a preferred drug is expected to cause harm to the member or that the preferred drug would be ineffective
      OR
   b. The patient has tried and had an inadequate response to two preferred chemically unique agents within the same drug class in the Minnesota Medicaid Preferred Drug List (PDL) as indicated by BOTH of the following:
      i. ONE of the following:
         1. Evidence of a paid claim(s) within the past 999 days
            OR
         2. The prescriber has stated that the patient has tried the required prerequisite/preferred agent(s) in the past 999 days

      AND
      ii. ONE of the following:
         1. The required prerequisite/preferred agent(s) was discontinued due to lack of effectiveness or an adverse event
            OR
         2. The prescriber has submitted an evidence-based and peer-reviewed clinical practice guideline supporting the use of the requested agent over the prerequisite/preferred agent(s)

      OR
   c. The patient has a documented intolerance, FDA labeled contraindication, or hypersensitivity to the preferred agents within the same drug class in the Minnesota Medicaid Preferred Drug List (PDL) that is not expected to occur with the requested agent
      OR
   d. The prescriber has provided documentation that the required prerequisite/preferred agent(s) cannot be used due to a documented medical condition or comorbid condition that is likely to cause an adverse reaction, decrease ability of the patient to achieve or maintain reasonable functional ability in performing daily activities or cause physical or mental harm
      OR

e. The prescriber has submitted documentation supporting the use of the non-preferred agent over the preferred agent(s)

Length of Approval: As per program specific criteria

Minnesota Medicaid Preferred Drug List (PDL):
https://mn.gov/dhs/partners-and-providers/policies-procedures/minnesota-health-care-programs/provider/types/