Clinical Policy Title:	apremilast
Policy Number:	RxA.741
Drug(s) Applied:	Otezla®
Original Policy Date:	04/18/2022
Last Review Date:	04/18/2022
Line of Business Policy Applies to:	All lines of business

Background

Otezla®, an inhibitor of phosphodiesterase 4 (PDE4), 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).

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
apremilast (Otezla®)	PsO, PsA, BD	Initial dose: Day 1: 10 mg orally in morning Day 2: 10 mg orally in morning and 10 mg orally in evening Day 3: 10 mg orally in morning and 20 mg orally in evening Day 4: 20 mg orally in morning and 20 mg orally in evening Day 5: 20 mg orally in morning and 30 mg orally in evening Maintenance dose: Day 6 and thereafter: 30 mg orally twice daily Renal Impairment: CrCl less than 30 mL/minute: Do not exceed 30 mg orally once daily. For initiation of therapy, administer 10 mg orally in the morning for Days 1, 2, and 3. Give 20 mg orally in the morning for Days 4 and 5, and then give 30 mg orally once daily in the morning on Day 6 and thereafter.	60 mg/day

Dosage Forms

- Tablets: 10 mg, 20 mg, 30 mg

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria. The provision of provider samples does not guarantee coverage under the terms of the pharmacy benefit administered by RxAdvance. All criteria for initial approval must be met in order to obtain coverage.

I. Initial Approval Criteria

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

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

Approval Duration
Commercial: 12 months
Medicaid: 12 months

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

1. Diagnosis of PsO;
2. Age ≥ 18 years;
3. Prescribed by or in consultation with a dermatologist or rheumatologist;
4. Trial and failure of ≥ 3 months of at least one (1) conventional systemic therapy {methotrexate (MTX), cyclosporin, acitretin}, or phototherapy {psoralen plus ultraviolet A light (PUVA) at up to maximally indicated doses unless contraindicated or clinically significant adverse effects are experienced;
   *Exception: If one biologic DMARD that is FDA-approved for plaque psoriasis has been previously tried, then trial of a conventional systemic agent or phototherapy is not required;
5. Dose does not exceed 60 mg/day.

Approval Duration
Commercial: 12 months
Medicaid: 12 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 a rheumatologist;
3. Age ≥ 18 years;
4. Trial and failure of at least one (1) of the therapy (e.g. colchicine, systemic corticosteroids, azathioprine, thalidomide) at maximally indicated doses unless contraindicated or significantly adverse effects are experienced;
5. Dose does not exceed 60 mg per day.

Approval duration
Commercial: 12 months
Medicaid: 12 months

II. Continued Therapy Approval

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

1. Member is currently receiving medication that has been authorized by RxAdvance or the member has met initial approval criteria listed in this policy;
2. Member is responding positively to therapy;
3. If request is for a dose increase, new dose does not exceed 60 mg/day.

Approval Duration
Commercial: 12 months
Medicaid: 12 months

III. Appendices

APPENDIX A: Abbreviation/Acronym Key
DMARDs: Disease-Modifying Antirheumatic Drugs
MTX: Methotrexate
PsO: Plaque Psoriasis
PsA: Psoriatic Arthritis
BD: Behçet's Disease
FDA: Food and Drug Administration
TNF: Tumor Necrosis Factor
PUVA: psoralen plus ultraviolet A light

APPENDIX B: Therapeutic Alternatives
Below are suggested therapeutic alternatives based on clinical guidance. Please check drug formulary for preferred agents and utilization management requirements.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
acitretin	**PsO:** 25 or 50 mg orally once daily	50 mg/day
cyclosporine (Sandimmune®, Neoral®)	**PsO:** 1 – 4 mg/kg/day orally divided twice daily	PsO: 4 mg/kg/day
methotrexate	**PsO:** 10 – 25 mg/week orally or 2.5 mg orally every 12 hr for 3 doses/week	30 mg/week
Corticosteroids	**BD (off-label):** triamcinolone acetonide cream (Orabase® 0.1%) Apply topically to the isolated oral ulcer 3 to 4 times daily as needed for pain. prednisone Initial dose: Week 1: 15 mg orally daily; week 2 onwards: 10 mg orally daily tapered over 2-3 weeks Maintenance dose (if recurrent): 5 mg orally daily	Various
colchicine (Colcrys®)	**BD*:** 1.2 to 1.8 mg orally daily	1.8 mg/day
Biologic DMARDs		

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Humira®	**PsO**: Initial dose: 80 mg Maintenance dose: 40 mg subcutaneous every other week starting one week after initial dose **PsA**: 40 mg subcutaneously every other week	40 mg every other week
Cosentyx®	**PsA:** With loading dose: 150 mg subcutaneous at week 0, 1, 2, 3, and 4, followed by 150 mg subcutaneous every 4 weeks Without loading dose: 150 mg subcutaneous every 4 weeks If a patient continues to have active psoriatic arthritis, consider a dosage of 300 mg every 4 weeks. Pediatric Patients 2 years and older: Recommended dosage is administered by subcutaneous injection at weeks 0,1 ,2,3, and 4 and every 4 weeks after: For patients weighing ≥ 15 kg and < 50 kg the dose is 75 mg. For patients weighing ≥ 50 kg the dose is 150 mg. **PsO:** Adults:300 mg subcutaneous at weeks 0, 1, 2, 3, and 4, followed by 300 mg subcutaneous every 4 weeks. (for some patients, a dose of 150 mg may be acceptable) Pediatric Patients 6 years of age and older Weight < 50 kg : 75 mg at weeks 0,1,2,4 and 4 followed by dosing every 4 weeks Weight ≥ 50 kg: 150 mg at weeks 0,1,2,3 and 4 followed by dosing every 4 weeks.	PsA: 300 mg every 4 weeks PsO: Adults:300 mg every 4 weeks Pediatrics: Weight < 50 kg: 75 mg every 4 weeks Weight ≥ 50 kg: 150 mg every 4 weeks
infliximab (Remicade®) Renflexis, Inflectra®, Avsola®	**PsA PsO:** Initial dose: 5 mg/kg intravenous at weeks 0, 2 and 6 Maintenance dose: 5 mg/kg intravenous every 8 weeks	PsA PsO: 5 mg/kg every 8 weeks
Simponi Aria®	**PsA:** Initial dose: 2 mg/kg IV at weeks 0 and 4 Maintenance dose: 2 mg/kg intravenous every 8 weeks	PsA: 2 mg/kg every 8 weeks
Xeljanz® / Xeljanz® oral Solution, Xeljanz® XR	Xeljanz®: **PsA**: 5 mg orally twice daily PsA: use in combination with nonbiologic disease-modifying antirheumatic drugs Xeljanz® XR: **PsA**: 11 mg orally once daily	Xeljanz®: PsA AS: 10 mg/day Xeljanz® XR: 11 mg/day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Orencia®	**PsA:** Intravenous: weight-based dose at weeks 0, 2, and 4, followed by every 4 weeks Weight < 60 kg: 500 mg per dose Weight 60 to 100 kg: 750 mg per dose Weight > 100 kg: 1,000 mg per dose Subcutaneous: 125 mg once weekly **PsA:** Patients switching from intravenous use to subcutaneous use, administer first subcutaneous dose instead of next scheduled intravenous dose. (For RA: Prior to the first subcutaneous dose, may administer an optional loading dose as a single intravenous infusion as per body weight categories above.) For PsA: Intravenous loading dose is not recommended.	**PsA:** Intravenous: 1,000 mg every 4 weeks Subcutaneous: 125 mg/week
Siliq®	**PsO:** Initial dose: 210 mg subcutaneous at weeks 0, 1, and 2 Maintenance dose: 210 mg subcutaneous every 2 weeks	210 mg every 2 weeks
Cimzia®	**PsA:** Initial dose: 400 mg subcutaneous at 0, 2, and 4 weeks. Maintenance dose: 200 mg subcutaneous every other week (or 400 mg subcutaneous every 4 weeks) **PsO:** 400 mg subcutaneous every other week. For some patients (with body weight ≤ 90 kg), a dose of 400 mg subcutaneous at 0, 2 and 4 weeks, followed by 200 mg subcutaneous every other week may be considered.	**PsA:** 400 mg every 4 weeks **PsO:** 400 mg every other week
Simponi®	**PsA:** 50 mg subcutaneous once monthly	50 mg/month
Tremfya®	**PsO, PsA:** Initial dose: 100 mg subcutaneous at weeks 0 and 4 Maintenance dose: 100 mg subcutaneous every 8 weeks Can be used alone or in combination with conventional DMARD e.g. methotrexate	100 mg every 8 weeks
Taltz®	**PsO:** Adult Plaque Psoriasis: Recommended dose is 160 mg subcutaneously (two 80 mg injections) at Week 0, followed by 80 mg at Weeks 2, 4, 6, 8, 10, and 12, then 80 mg every 4 weeks Pediatric Plaque Psoriasis (age 6 years or older): For patients weighing greater than 50 kg:160 mg subcutaneously	**PsO:** 80 mg every 4 weeks **PsA:** 80 mg every 4 weeks

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	(two 80 mg injections) at Week 0, followed by 80 mg every 4 weeks. For patients weighing 25-50 kg: 80 mg subcutaneoulsy at Week 0, followed by 40 mg every 4 weeks. For patients weighing less than 25 kg:40 mg subcutaneously at Week 0, followed by 20 mg every 4 weeks **PsA:** Initial dose: 160 mg (two 80 mg injections) subcutaneous Maintenance dose: 80 mg subcutaneous every 4 weeks.	
Skyrizi®	**PsO:** 150 mg subcutaneous at weeks 0, 4, and every 12 weeks thereafter	150 mg/12 Weeks
Ilumya™	**PsO:** Initial dose: 100 mg subcutaneous at weeks 0 and 4 Maintenance dose: 100 mg subcutaneous every 12 weeks Tildrakizumab should only be administered by a healthcare professional.	100 mg every 12 weeks
Rinvoq®	**PsA:** 15 mg orally once daily Can be used as monotherapy or in combination with methotrexate or other non biologic DMARDs. *For use in adults who have had an inadequate response or intolerance to one or more TNF blockers	15 mg/day
Stelara®	**PsO:** Weight based dosing subcutaneous at weeks 0 and 4, followed by maintenance dose every 12 weeks Adult: Weight ≤ 100 kg: 45 mg (some patients may require doses of 90 mg or maintenance dosing of every 8 weeks) Weight > 100 kg: 90 mg (some patients may require maintenance dosing of every 8 weeks) Pediatrics (Age 6 years and older): Weight < 60 kg: 0.75 mg/kg Weight ≥ 60 to ≤100 kg: 45 mg Weight > 100kg: 90 mg **PsA:** 45 mg subcutaneous at weeks 0 and 4, followed by 45 mg every 12 weeks	**PsO:** 90 mg every 8 weeks **PsA:** 45 mg every 12 weeks
Enbrel®	**PsA:** 25 mg subcutaneous twice weekly or 50 mg subcutaneous once Weekly **PsO:** Adults: Initial dose: 50 mg subcutaneous twice weekly for 3 months (Starting	50 mg/week

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	doses of 25 mg or 50 mg per week are also shown to be efficacious) Maintenance dose: 50 mg subcutaneous once weekly Pediatrics: Weight < 63 kg: 0.8 mg/kg subcutaneous once weekly Weight ≥ 63 kg: 50 mg subcutaneous once weekly	

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

APPENDIX C: Contraindications*/Boxed Warnings

- Contraindication(s):
  - Known hypersensitivity to apremilast or any excipients in formulation.

  *Contraindications listed reflect direct statements made in the manufacturer's package insert; for additional uses, warnings, and precautions, please refer to clinical guidelines.

- Boxed Warning(s):
  - None reported.

APPENDIX D: General Information

- Diarrhea, Nausea, and Vomiting: Consider Otezla® dose reduction or suspension if patients develop severe diarrhea, nausea, or vomiting.
- Depression: Advise patients, their caregivers, and families to be alert for the emergence or worsening of depression, suicidal thoughts or other mood changes and if such changes occur to contact their healthcare provider. Carefully weigh risks and benefits of treatment with Otezla® in patients with a history of depression and/or suicidal thoughts or behavior.
- Weight Decrease: Monitor weight regularly. If unexplained or clinically significant weight loss occurs, evaluate weight loss and consider discontinuation of Otezla®.
- Drug Interactions: Use with strong cytochrome P450 enzyme inducers (e.g., rifampin, phenobarbital, carbamazepine, phenytoin) is not recommended because loss of efficacy may occur.
- 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.

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Review/Revision History	Review/Revision Date	P&T Approval Date
RxA.592.Biologic_DMARDs was last reviewed and updated on 01/05/2022 and archived on 04/18/2022. For details, please refer to RxA.592.Biologic_DMARDs.	01/05/2022	4/18/2022
Drug specific policy for Otezla was created	2/14/2022	4/18/2022

based on RxA.592.Biologic_DMARDs 1. Dosing Information, Dosing Regimen: Updated to include renal impairment dosing information for indication PsO, PsA, BD. 2. Initial Approval Criteria I.B.3: Updated trial and failure criteria to rephrase and include phototherapy (psoralen plus ultraviolet A light [PUVA]). 3. Appendix A: Updated to include abbreviations PUVA. 4. Appendix B, Drug Name: Updated to remove discontinued brand-name therapeutic alternative Soriatane®. 5. Appendix B, Drug Name: Updated to include brand-name therapeutic alternative of other biological DMARDs. 6. Disclaimer about contraindications "Contraindications listed reflect statements made in the manufacturer's package insert..." was added to Appendix C. 7. Appendix D, General Information: Updated to include new information regarding Warnings and Precautions. 8. References were reviewed and updated.		