Clinical Policy Title:	ixekizumab
Policy Number:	RxA.748
Drug(s) Applied:	Taltz®
Original Policy Date:	04/18/2022
Last Review Date:	04/18/2022
Line of Business Policy Applies to:	All lines of business

Background

Taltz® is a humanized interleukin-17A antagonist indicated for the treatment of:

- Patients aged 6 years or older with moderate-to-severe plaque psoriasis (PsO) who are candidates for systemic therapy or phototherapy
- Adults with active psoriatic arthritis (PsA)
- Adults with active ankylosing spondylitis (AS)
- Adults with active non-radiographic axial spondyloarthritis with objective signs of inflammation (nr-axSpA)

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
ixekizumab (Taltz®)	PsO	<u>Adult Plaque Psoriasis:</u> 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 <u>Pediatric Plaque Psoriasis (age 6 years or older):</u> For patients weighing greater than 50 kg:160 mg subcutaneously (two 80 mg injections) at Week 0, followed by 80 mg every 4 weeks. For patients weighing 25-50 kg: 80 mg subcutaneously 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	80 mg every 4 weeks
	PsA, AS	<u>Initial dose:</u> 160 mg (two 80 mg injections) subcutaneously <u>Maintenance dose:</u> 80 mg subcutaneously every 4 weeks	
	nr-axSpA	80 mg subcutaneously every 4 weeks	

Dosage Forms

Autoinjector

- Injection: 80 mg/mL solution in a single-dose prefilled autoinjector

Prefilled Syringe

- Injection: 80 mg/mL solution in a single-dose prefilled syringe

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. Ankylosing Spondylitis (must meet all):

1. Diagnosis of active ankylosing spondylitis (AS) or non-radiographic axial spondyloarthritis (nr-axSpA);
2. Prescribed by or in consultation with a rheumatologist;
3. Age ≥ 18 years;
4. Trial and failure of at least two (2) non-steroidal anti-inflammatory drugs (NSAIDs) at up to maximally indicated doses, each used for at least ≥ 4 weeks unless contraindicated or clinically significant adverse effects are experienced;
5. Member meets (a or b):
   a. For Ankylosing Spondylitis: Trial and failure of at least one (1) of the following agents: Humira®, Cimzia®, Simponi Aria® or Simponi® unless contraindicated or clinically significant adverse effects are experienced;
   b. For non-radiographic axial spondyloarthritis : Trial and failure of Cimzia® unless contraindicated or clinically significant adverse effects are experienced;
6. Dose does not exceed 80 mg every 4 weeks.

Approval Duration
Commercial: 12 months
Medicaid: 12 months

B. Plaque Psoriasis (must meet all):

1. Diagnosis of Plaque Psoriasis (PsO);
2. Prescribed by or in consultation with a dermatologist or a rheumatologist;
3. Age ≥ 6 years;
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. Trial and failure of at least one (1) of the following agents: Humira®, Cimzia®, Skyrizi®, Tremfya® or Stelara® unless contraindicated or clinically significant adverse effects are experienced;
6. Dose does not exceed 80 mg every 4 weeks.

Approval Duration
Commercial: 12 months

Medicaid: 12 months

C. Psoriatic Arthritis (must meet all):

1. Diagnosis of Psoriatic Arthritis (PsA);
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 following agents: Humira®, Cimzia®, Stelara®, Skyrizi®, Tremfya®, Rinvoq®, Xeljanz®/XR, Simponi Aria®, Simponi® unless contraindicated or clinically significant adverse effects are experienced;
5. Dose does not exceed 80 mg every 4 weeks.

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 80 mg every 4 weeks.

Approval Duration
Commercial: 12 months
Medicaid: 12 months

III. Appendices

APPENDIX A: Abbreviation/Acronym Key
AS: ankylosing spondylitis
nr-axSpA: non-radiographic axial spondyloarthritis
NSAIDs: Non-Steroidal Anti-Inflammatory Drugs
PsO: plaque psoriasis
PsA: psoriatic arthritis
DMARDs: Disease-Modifying Antirheumatic Drugs
FDA: Food and Drug Administration
TNF: tumor necrosing factor
MT: methotrexate
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

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
methotrexate	**PsO:** 10 – 25 mg/week orally or 2.5 mg orally every 12 hr for 3 doses/week	30 mg/week
NSAIDs (e.g., indomethacin, ibuprofen, naproxen, celecoxib)	**AS, nr-axSpA:** Varies	Varies
Biologic DMARDs		
Humira®	**PsO**: Initial dose: 80 mg Maintenance dose: 40 mg subcutaneously every other week starting one week after initial dose **AS, PsA:** 40 mg subcutaneously every other week	40 mg every other week
Cosentyx®	**PsA:** With loading dose: 150 mg subcutaneously at week 0, 1, 2, 3, and 4, followed by 150 mg subcutaneously every 4 weeks Without loading dose: 150 mg subcutaneously 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. **AS, nr-axSpA:** With loading dose: 150 mg subcutaneously at weeks 0, 1, 2, 3, and 4, followed by 150 mg subcutaneously every 4 weeks thereafter Without loading dose: 150 mg subcutaneously every 4 weeks If the patient continues to have active ankylosing spondylitis: 300 mg every 4 weeks can be considered **PsO:** Adults: Recommended dosage is 300 mg by subcutaneous injection at Weeks 0, 1, 2, 3, and 4 followed by 300 mg every 4 weeks. For some patients, a dose of 150 mg may be acceptable. Children and Adolescents 6 to 17 years weighing 50 kg or more: 150 mg subcutaneously at weeks 0, 1, 2, 3, and 4. Then give 150 mg subcutaneously every 4 weeks. Children and Adolescents 6 to 17 years weighing less than 50 kg:	PsA: 300 mg every 4 weeks AS: 300mg every 4 weeks nr-axSpA: 150 mg every 4 weeks PsO Adults: 300 mg/dose subcutaneously Adolescents weighing 50 kg or more: 150 mg/dose subcutaneously. weighing less than 50 kg: 75 mg/dose subcutaneously.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	75 mg subcutaneously at weeks 0, 1, 2, 3, and 4. Then give 75 mg subcutaneously every 4 weeks	
infliximab (Remicade®), Renflexis®, Inflectra®, Avsola®	**PsA, PsO:** Initial dose: 5 mg/kg intravenously at weeks 0, 2 and 6 Maintenance dose: 5 mg/kg intravenously every 8 weeks **AS:** Initial dose: 5 mg/kg intravenously at weeks 0, 2 and 6 Maintenance dose: 5 mg/kg intravenously every 6 weeks	PsA, PsO: 5 mg/kg every 8 weeks AS: 5 mg/kg every 6 weeks
Simponi Aria®	**AS, PsA:** Initial dose: 2 mg/kg intravenously at weeks 0 and 4 Maintenance dose: 2 mg/kg intravenously every 8 weeks	AS, PsA: 2 mg/kg every 8 weeks
Otezla®	**PsO, PsA** 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	60 mg/day
Xeljanz® / Xeljanz® oral Solution, Xeljanz® XR	Xeljanz®: **PsA, AS**: 5 mg orally twice daily PsA: use in combination with nonbiologic disease-modifying antirheumatic drugs Xeljanz® XR: **PsA, AS**: 11 mg orally once daily	Xeljanz®: PsA AS: 10 mg/day Xeljanz® / Xeljanz® oral Solution: 5 mg or 5 ml twice daily Xeljanz® XR: PsA, AS: 11 mg/day
Enbrel®	**PsA**: Adult: 50 mg once weekly with or without methotrexate (MTX) **AS:** 50 mg once weekly **PsO:** Adult PsO: 50 mg twice weekly for 3 months, followed by 50 mg	PsA**:** Adults 50 mg/week subcutaneously. Induction therapy for psoriatic arthritis should not exceed 100 mg/week with no

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	once weekly Pediatric PsO: Weight < 63 kg: 0.8 mg/kg subcutaneously once weekly Weight ≥ 63 kg: 50 mg subcutaneously once weekly	more than 50 mg/dose subcutaneously. AS, PsO: 50 mg/week
Ilumya®	**PsO:** Initial dose: 100 mg subcutaneously at weeks 0 and 4 Maintenance dose: 100 mg subcutaneously every 12 weeks Tildrakizumab should only be administered by a healthcare professional.	100 mg every 12 weeks
Orencia®	**PsA:** Intravenously: 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 PsA: Intravenous loading dose is not recommended	PsA: Intravenous: 1,000 mg every 4 weeks Subcutaneous: 125 mg/week
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
Siliq®	**PsO:** Initial dose: 210 mg subcutaneously at weeks 0, 1, and 2 Maintenance dose: 210 mg subcutaneously every 2 weeks	210 mg every 2 weeks
Simponi®	**AS, PsA:** 50 mg subcutaneously once monthly	50 mg/month
Tremfya®	**PsO, PsA:** Initial dose: 100 mg subcutaneously at weeks 0 and 4 Maintenance dose: 100 mg subcutaneously every 8 weeks Can be used alone or in combination with conventional DMARD e.g., methotrexate	100 mg every 8 weeks
Skyrizi®	**PsO:** 150 mg subcutaneously at weeks 0, 4, and every 12 weeks thereafter	150 mg/12 Weeks

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Stelara®	**PsO:** Weight based dosing subcutaneously 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 subcutaneously at weeks 0 and 4, followed by 45 mg every 12 weeks	PsO: 90 mg every 8 weeks PsA: 45 mg every 12 weeks
Cimzia®	**PsA, AS:** <u>Initial dose:</u> 400 mg subcutaneously at 0, 2, and 4 weeks. <u>Maintenance dose:</u> 200 mg subcutaneously every other week (or 400 mg subcutaneously every 4 weeks) **PsO:** 400 mg subcutaneously every other week. For some patients (with body weight ≤ 90 kg), a dose of 400 mg subcutaneously at 0, 2 and 4 weeks, followed by 200 mg subcutaneously every other week may be considered.	PsA, AS :400 mg every 4 weeks PsO: 400 mg every other week

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):
  - Serious hypersensitivity reaction to ixekizumab or to any of the excipients.

  *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

- Ankylosing Spondylitis: Several AS treatment guidelines recommend a trial of 2 or 3 NSAIDs prior to use of an anti-TNF agent. A two-year trial showed that continuous NSAID use reduced radiographic progression of AS versus on demand use of NSAID.

- Psoriatic Arthritis: 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.
- Plaque Psoriasis: Joint guidelines from the American Academy of Dermatology (AAD) and National Psoriasis Medical Board (2019) have been published for management of psoriasis with biologics. These guidelines list Taltz as a monotherapy treatment option for patients with moderate to severe plaque psoriasis. Guidelines from the European Dermatology Forum (EDF) [2015] recommend biologics (i.e., etanercept, adalimumab, infliximab, ustekinumab) as second-line therapy for induction and long-term treatment if phototherapy and conventional systemic agents have failed, are contraindicated, or are not tolerated.

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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.Biologics DMARDs.	02/16/2022	04/18/2022
Drug specific policy for Taltz was created based on RxA.592.Biologic DMARDs: 1. Initial Approval Criteria, 1.A: Updated indication from Axial Spondylitis to Ankylosing Spondylitis. 2. Initial Approval Criteria, 1.A.5, 1.B.5 and 1.C.4: Updated to include new trial and failure criteria Trial and failure of at least one (1) of the following agents: Humira®, Cimzia®, Simponi Aria® or Simponi® unless contraindicated or clinically significant adverse effects are experienced. 3. Initial Approval Criteria, 1.B.4: Updated trial and failure criteria to include phototherapy	02/16/2022	04/18/2022

{psoralen plus ultraviolet A light (PUVA). 4. Appendix A: Updated to include abbreviation PUVA. 5. Appendix A: Updated to remove abbreviations ESR and CRP. 6. Appendix B, Drug Name: Updated to include brand-name therapeutic alternative of other biological DMARDs. 7. Appendix D, General Information: Updated to remove information regarding: (a, b and c): a. Taltz®: Ixekizumab is currently being studied for the treatment of rheumatoid arthritis, radiographic axial spondyloarthritis, ankylosing spondylitis, and psoriatic arthritis; b. Definition of failure of MTX or DMARDs; c. Examples of positive response to therapy. 8. References were reviewed and updated.		