Clinical Policy: Ixekizumab (Taltz)

Reference Number: ERX.SPA.122
Effective Date: 10.01.16
Last Review Date: 05.21
Line of Business: Commercial, Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description
Ixekizumab (Taltz®) is an interleukin-17A (IL-17A) antagonist.

FDA Approved Indication(s)
Taltz is 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 (nr-axSpA) with objective signs of inflammation

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.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ that Taltz is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Axial Spondyloarthritis (must meet all)**:**
1. Diagnosis of AS or nr-axSpA;
2. Prescribed by or in consultation with a rheumatologist;
3. Age ≥ 18 years;
4. Failure of at least TWO non-steroidal anti-inflammatory drugs (NSAIDs), each used for ≥ 4 weeks at up to maximally indicated doses unless clinically significant adverse effects are experienced or all are contraindicated;
5. For AS: Failure of 2 of the following, each used for ≥ 3 consecutive months unless clinically significant adverse effects are experienced or all are contraindicated: Cosentyx®, etanercept (*Enbrel® is preferred*), adalimumab (*Humira® is preferred*), infliximab (*Remicade® is preferred*), golimumab (*Simponi Aria® is preferred);*
   **Prior authorization may be required for Cosentyx, adalimumab, etanercept, infliximab, and golimumab*
6. For nr-axSpA: Failure of Cosentyx, unless contraindicated or clinically adverse effects are experienced;
7. Dose does not exceed one of the following (a or b):
   a. For AS: 160 mg at weeks 0, followed by maintenance dose of 80 mg every 4 weeks;
   b. For nr-axSpA: 80 mg every 4 weeks.

Approval duration: 6 months

B. Plaque Psoriasis (must meet all)**:**
1. Diagnosis of PsO as evidenced by involvement of one of the following (a or b):
   a. ≥ 3% of total body surface area;
   b. Hands, feet, scalp, face, or genital area;

2. Prescribed by or in consultation with a dermatologist or rheumatologist;
3. Age ≥ 6 years;
4. Member meets one of the following (a or b):
   a. Failure of a ≥ 3 consecutive month trial of methotrexate (MTX) 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 at up to maximally indicated doses, unless clinically significant adverse effects are experienced or both are contraindicated;
5. Failure of 2 of the following, each used for ≥ 3 consecutive months unless clinically significant adverse effects are experienced or all are contraindicated: Cosentyx, adalimumab (*Humira is preferred*), infliximab (*Remicade is preferred*), Skyrizi®, subcutaneous Stelara®, Tremfya®;
   **Prior authorization may be required for Cosentyx, adalimumab, infliximab, Skyrizi, Stelara, and Tremfya*
6. Dose does not exceed one of the following (a – d):
   a. For adults: 160 mg at week 0, 80 mg at weeks 2, 4, 6, 8, 10, and 12, followed by maintenance dose of 80 mg every 4 weeks thereafter;
   b. For pediatric members weighing < 25 kg: 40 mg at week 0, followed by 20 mg every 4 weeks;
   c. For pediatric members weighing 25 – 50 kg: 80 mg at week 0, followed by 40 mg every 4 weeks;
   d. For pediatric members weighing > 50 kg: 160 mg (two 80 mg injections) at week 0, followed by 80 mg every 4 weeks.

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. Failure of 2 of the following, each used for ≥ 3 consecutive months unless clinically significant adverse effects are experienced or all are contraindicated: Cosentyx, etanercept (*Enbrel is preferred*), adalimumab (*Humira is preferred*), Otezla®, infliximab (*Remicade is preferred*), golimumab (*Simponi Aria is preferred*), subcutaneous Stelara, Xeljanz®, Xeljanz XR®;
   **Prior authorization may be required for Cosentyx, etanercept, adalimumab, Otezla, infliximab, golimumab, Stelara, Xeljanz, and Xeljanz XR*
5. Dose does not exceed one of the following (a or b):
   a. PsA alone: 160 mg at weeks 0, followed by maintenance dose of 80 mg every 4 weeks;
   b. PsA with coexistent PsO: 160 mg at Week 0, 80 mg at weeks 2, 4, 6, 8, 10, and 12, followed by maintenance dose of 80 mg every 4 weeks.

Approval duration: 6 months

D. Other diagnoses/indications
1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. All Indications in Section I (must meet all)**:**
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions 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 80 mg every 4 weeks.

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or

2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

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 policy – ERX.PA.01 or evidence of coverage documents;

B. Combination use of biological disease-modifying antirheumatic drugs (bDMARDs), including any tumor necrosis factor (TNF) antagonists [Cimzia®, Enbrel®, Simponi®, Avsola™, Inflectra™, Remicade®, Renflexis™], interleukin agents [Arcalyst® (IL-1 blocker), Ilaris® (IL-1 blocker), Kineret® (IL-1RA), Actemra® (IL-6RA), Kevzara® (IL-6RA), Stelara® (IL-12/23 inhibitor), Cosentyx® (IL-17A inhibitor), Taltz® (IL-17A inhibitor), Siliq™ (IL-17RA), Ilumya™ (IL-23 inhibitor), Skyrizi™ (IL-23 inhibitor), Tremfya® (IL-23 inhibitor)], janus kinase inhibitors (JAKi) [Xeljanz®/Xeljanz® XR, Rinvoq™], anti-CD20 monoclonal antibodies [Rituxan®, Riabni™, Ruxience™, Truxima®, and Rituxan Hycela®], selective co-stimulation modulators [Orencia®], or integrin receptor antagonists [Entyvio®] because of the possibility of increased immunosuppression, neutropenia and increased risk of infection.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

ACR: American College of Rheumatology
AS: ankylosing spondylitis
FDA: Food and Drug Administration
IL-17A: interleukin-17A
MTX: methotrexate
nr-axSpA: non-radiographic axial spondyloarthritis
PsA: psoriatic arthritis
PsO: plaque psoriasis

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 and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
acitretin (Soriatane®)	**PsO** 25 or 50 mg PO daily	50 mg/day
cyclosporine (Sandimmune®, Neoral®)	**PsO** 2.5 – 4 mg/kg/day PO divided BID	PsO: 4 mg/kg/day
methotrexate (Rheumatrex®)	**PsO** 10 – 25 mg/week PO or 2.5 mg PO Q12 hr for 3 doses/week	30 mg/week
NSAIDs (e.g., indomethacin, ibuprofen, naproxen, celecoxib)	**AS, nr-axSpA** Varies	Varies
Cosentyx® (secukinumab)	**AS** With loading dose: 150 mg at weeks 0, 1, 2, 3, and 4, followed by 150 mg every 4 weeks Without loading dose: 150 mg every 4 weeks **PsA** With loading dose: 150 mg SC at week 0, 1, 2, 3, and 4, followed by 150 mg every 4 weeks Without loading dose: 150 mg SC every 4 weeks If a patient continues to have active psoriatic arthritis, consider a dosage of 300 mg.	AS, nr-axSpA: 150 mg every 4 weeks PsA, PsO: 300 mg every 4 weeks

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	PsO (with or without PsA) 300 mg SC at week 0, 1, 2, 3, and 4, followed by 300 mg every 4 weeks **nr-axSpA** With loading dose: 150 mg at weeks 0, 1, 2, 3, and 4, followed by 150 mg every 4 weeks Without loading dose: 150 mg every 4 weeks	
Enbrel® (etanercept)	**AS** 50 mg SC once weekly **PsA** 50 mg SC once weekly	50 mg/week
Humira® (adalimumab)	**AS, PsA** 40 mg SC every other week **PsO** Initial dose: 80 mg SC Maintenance dose: 40 mg SC every other week starting one week after initial dose	40 mg every other week
Otezla® (apremilast)	**PsA** 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
Remicade® (infliximab)	**AS** Initial dose: 5 mg/kg IV at weeks 0, 2 and 6 Maintenance dose: 5 mg/kg IV every 6 weeks **PsA, PsO** Initial dose: 5 mg/kg IV at weeks 0, 2 and 6 Maintenance dose: 5 mg/kg IV every 8 weeks	AS: 5 mg/kg every 6 weeks PsA, PsO: 5 mg/kg every 8 weeks
Simponi Aria® (golimumab)	**AS, PsA, RA** Initial dose: 2 mg/kg IV at weeks 0 and 4 Maintenance dose: 2 mg/kg IV every 8 weeks	2 mg/kg every 8 weeks
Skyrizi® (risankizumab-rzaa)	**PsO** 150 mg (two 75 mg injections) SC at Week 0, Week 4 and every 12 weeks thereafter	150 mg every 12 weeks

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Stelara® (ustekinumab)	**PsA** 45 mg SC at weeks 0 and 4, followed by 45 mg every 12 weeks **PsO** Weight based dosing SC at weeks 0 and 4, followed by maintenance dose every 12 weeks *Adult:* Weight ≤ 100 kg: 45 mg Weight > 100 kg: 90 mg *Pediatrics (Age 12 years and older):* Weight < 60 kg: 0.75 mg/kg Weight 60 to 100 kg: 45 mg Weight > 100kg: 90 mg	PsA: 45 mg every 12 weeks PsO: 90 mg every 12 weeks
Tremfya® (guselkumab)	**PsO** Initial dose: 100 mg SC at weeks 0 and 4 Maintenance dose: 100 mg SC every 8 weeks	100 mg every 8 weeks
Xeljanz® (tofacitinib, immediate-release)	**PsA** 5 mg PO BID	PsA: 10 mg/day
Xeljanz XR® (tofacitinib, extended-release)	**PsA** 11 mg PO QD	PsA: 11 mg/day

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): previous serious hypersensitivity reaction, such as anaphylaxis, to ixekizumab or to any of the excipients
- Boxed warning(s): none reported

Appendix D: General Information
- Definition of failure of MTX or 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.
- Examples of positive response to therapy may include, but are not limited to:
  - Reduction in joint pain/swelling/tenderness
  - Improvement in erythrocyte sedimentation rates/C-reactive protein (ESR/CRP) levels
  - Improvements in activities of daily living
- 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.

- AS and nr-axSpA: Although the 2019 ACR guidelines for AS recommend the use of TNF inhibitors over IL-17A antagonists such as Taltz or Cosentyx, this recommendation was based on "greater experience with TNF inhibitors and familiarity with their long-term safety and toxicity" rather than differences in efficacy.

V. Dosage and Administration

<table>
<tr><th>Indication</th><th>Dosing Regimen</th><th>Maximum Dose</th></tr>
<tr><td>PsO (with or without coexistent PsA)</td><td>Adults:
Initial dose: 160 mg (two 80 mg injections) SC at week 0, then 80 mg SC at weeks 2, 4, 6, 8, 10, and 12
Maintenance dose:
80 mg SC every 4 weeks

Pediatrics between ages of 6 and 18 years:
<table>
<tr><th>Pediatric Patient's Weight</th><th>Starting Dose (Week 0)</th><th>Dose every 4 weeks (Q4W) Thereafter</th></tr>
<tr><td>> 50 kg</td><td>160 mg (two 80 mg injections)</td><td>80 mg</td></tr>
<tr><td>25 to 50 kg</td><td>80 mg</td><td>40 mg</td></tr>
<tr><td>< 25 kg</td><td>40 mg</td><td>20 mg</td></tr>
</table></td><td>80 mg every 4 weeks</td></tr>
<tr><td>PsA, AS</td><td>Initial dose: 160 mg (two 80 mg injections) SC at week 0
Maintenance dose:
80 mg SC every 4 weeks</td><td>80 mg every 4 weeks</td></tr>
<tr><td>nr-axSpA</td><td>80 mg SC every 4 weeks</td><td>80 mg every 4 weeks</td></tr>
</table>

VI. Product Availability

- Single-dose prefilled autoinjector: 80 mg/mL
- Single-dose prefilled syringe: 80 mg/mL

VII. References

1. Taltz Prescribing Information. Indianapolis, IN: Eli Lilly and Company; May 2020. Available at Available at http://www.taltz.com. Accessed January 13, 2021.
2. Pariser DM, Bagel J, Gelfand JM et al. National psoriasis foundation clinical consensus on disease severity. *Arch Dermatol*. 2007 Feb; 143: 239-242.
3. Menter A, Gottlieb A, Feldman SR, Van Voorhees AS, Leonardi CL, Gordon KB, et al. American Academy of Dermatology. 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. *J Am Acad Dermatol.* 2008;58(5):826-50.
4. Menter A, Korman NJ, Elmets CA, Feldman SR, Gelfand JM, Gordon KM, et al. American Academy of Dermatology. Guidelines of care for the management of psoriasis and psoriatic arthritis: section 4. Guidelines of care for the management and treatment of psoriasis with traditional systemic agents. *J Am Acad Dermatol*. 2009;61(3):451-85.
5. Hsu S, Papp KA, Lebwohl MG et al. Consensus guidelines for the management of plaque psoriasis. *Arch Dermatol*. 2012; 148(1):95-102
6. Gossec L, Smolen JS, Ramiro S, et al. European League Against Rheumatism (EULAR) recommendations for the management of psoriatic arthritis with pharmacological therapies: 2015 update. *Ann Rheum Dis.* 2015;0:1-12. doi:10.1136/annrheumdis-2015-208337
7. Van der Heijde D, Ramiro S, Landewe R, et al. 2016 update of the ASAS-EULAR management recommendations for axial spondyloarthritis. *Ann Rheum Dis*. 2017;76:978-991. doi:10.1136/annrheumdis-2016-210770.

8. 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.
9. 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.
10. Ward MM, Deodhar A, Gensler LS, et al. 2019 Update of the American College of Rheumatology/Spondylitis Association of America/Spondyloarthritis Research and Treatment Network recommendations for the treatment of ankylosing spondylitis and nonradiographic axial spondyloarthritis. *Arthritis Care & Research*. 2019. Available at: https://www.rheumatology.org/Practice-Quality/Clinical-Support/Clinical-Practice-Guidelines/Axial-Spondyloarthritis. Accessed June 24, 2020.
11. DeoDhar A, van der Heijde D, Gensler LS, et al. Ixekizumab for patients with non-radiographic axial spondyloarthritis (COAST-X): a randomised, placebo-controlled trial. *Lancet*. 2020; 395: 53-64.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Added criteria for TB test per PI. Added rheumatologist as option for prescriber. Removed Member had failed topical treatment (e.g. corticosteroids, calcipotriene, tazarotene) and phototherapy, unless contraindicated. Per AAD topical treatments are for mild or limited disease.	07.01.17	08.17
2Q 2018 annual review: criteria added for new FDA indication: psoriatic arthritis; removed specific diagnosis requirements for PsO; removed trial and failure of phototherapy and topical therapy for PsO, modified requirement for trial and failure of MTX (and if intolerance or contraindication to MTX, trial and failure of cyclosporine or acitretin) for PsO; removed TB testing for PsO; references reviewed and updated.	02.27.18	05.18
4Q 2018 annual review: allowed bypassing conventional DMARDs for axial PsA and required trial of NSAIDs; references reviewed and updated.	09.04.18	11.18
2Q 2019 annual review: removed trial and failure of conventional DMARDs (e.g., MTX)/NSAIDs for PsA per 2018 ACR/NPF guidelines; added trial and failure requirement of TNF inhibitors and Otezla for PsA per ACR/NPF 2018 guidelines; references reviewed and updated.	03.05.19	05.19
Criteria added for new FDA indication: ankylosing spondylitis; references reviewed and updated.	10.22.19	02.20
2Q 2020 annual review: no significant changes; for PsO, added pediatric age extension from 18 years old to 6 years old, added redirection to preferred alternatives per formulary status: Cosentyx, Humira, Remicade, Stelara, and Tremfya; for PsA, added Cosentyx, SC Stelara, Xeljanz, and Xeljanz XR as preferred options for redirection per formulary status; for AS, added redirection to preferred alternatives per formulary status: Cosentyx, Enbrel, Humira, Remicade, and Simponi Aria; references reviewed and updated.	04.28.20	05.20
Criteria added for new FDA indication: nr-axSpA; references reviewed and updated.	06.26.20	11.20
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, updated dosing limits to reflect pediatric limits; added Skyrizi as a preferred option for PsO per formulary status; added combination of bDMARDs under Section III; references reviewed and updated.	02.23.21	05.21

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.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. 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.