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## Subject: Ixekizumab (Taltz®) Injection

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<a href="#">Dosage/ Administration</a>	<a href="#">Position Statement</a>	<a href="#">Billing/Coding</a>	<a href="#">Reimbursement</a>	<a href="#">Program Exceptions</a>	<a href="#">Definitions</a>
<a href="#">Related Guidelines</a>	<a href="#">Other</a>	<a href="#">References</a>	<a href="#">Updates</a>		

### DESCRIPTION:

Ixekizumab (Taltz) was approved by the US Food and Drug Administration (FDA) in March 2016 for moderate to severe plaque psoriasis in adults who are candidates for systemic therapy or phototherapy. In December 2017, the FDA-approved indications for use were expanded to include the treatment of adults with active psoriatic arthritis (PsA). In August 2019, the FDA granted approval for the treatment of adult patients with active ankylosing spondylitis. In March 2020, the indication for plaque psoriasis was expanded to include pediatric patients 6 to less than 18 years of age. In May 2020, the FDA granted approval for the treatment of adult patients with active non-radiographic axial spondyloarthritis (nr-axSpA) with objective signs of inflammation. In May 2022, a new, citrate-free formulation of ixekizumab injection was FDA-approved and then released in August 2022. The new formulation reduced injection site pain experienced by some people immediately following injection. The original formulation will only remain on the market until it is replaced by the citrate-free formulation (timing unknown); both products share the same NDC. Ixekizumab is a humanized IgG4 monoclonal antibody that selectively binds to the interleukin-17A (IL-17A) cytokine and inhibits its interaction with the IL-17 receptor. Secukinumab (Cosentyx), approved by the FDA in January 2015 for moderate to severe plaque psoriasis, was the first-in-class biologic agent to target IL-17. Interleukin-17A is a naturally occurring cytokine that is involved in normal inflammatory and immune responses. Elevated concentrations of IL-17A are found in psoriatic plaques. Ixekizumab inhibits the release of proinflammatory cytokines and chemokines.

### RHEUMATOID DISORDERS

#### Ankylosing spondylitis (AS)

Ankylosing spondylitis (AS) is a form of chronic inflammatory arthritis characterized by sacroiliitis, enthesitis, and a marked propensity for sacroiliac joint and spinal fusion. AS is distinguished by universal

involvement with sacroiliac joint inflammation or fusion and more prevalent spinal ankylosis. Goals of treatment for AS are to reduce symptoms, maintain spinal flexibility and normal posture, reduce functional limitations, maintain work ability, and decrease disease complications. The mainstay of treatment has been NSAIDs and exercise, with the additional use of DMARDs in patients with peripheral arthritis. The American College of Rheumatology (ACR), Spondylitis Association of America (SAA), and Spondyloarthritis Research and Treatment Network (SPARTAN) recommend the following pharmacological treatment for AS:

- Stable AS: First line therapy with on demand NSAIDs; there is also a conditional recommendation for continuation of TNF inhibitor as monotherapy
- Active AS:
  - First line therapy with continuous NSAIDs and physical therapy
  - TNF inhibitor recommended for patients with active AS despite an adequate trial with NSAIDs
    - Lack of response (or intolerance) to at least 2 different NSAIDs over 1 month or incomplete response to at least 2 different NSAIDs over 2 months would be an adequate NSAID trial to judge response
  - Recommendations for nonresponse to TNF therapy (all conditional):
    - Primary nonresponse: switch to secukinumab or ixekizumab over another TNF
    - Secondary nonresponse: switch to another TNF over a non-TNF biologic
    - Recommend against addition of sulfasalazine or MTX
    - Recommend against switching to a biosimilar of the failed TNF
  - TNF-inhibitors are conditionally recommended over secukinumab or ixekizumab
  - Secukinumab or ixekizumab are conditionally recommended over DMARDs in patients that have failed NSAIDs and have contraindications to TNF-inhibitors
  - DMARDs (i.e., methotrexate [MTX], sulfasalazine, leflunomide, pamidronate, thalidomide, apremilast) are only conditionally recommended in patients that have failed NSAIDs and have contraindications to TNF-inhibitors
  - Methotrexate is not recommended as add on therapy to TNF inhibitors in stable and active AS
  - If patient has concomitant inflammatory bowel disease (IBD) or recurrent uveitis, TNF-inhibitors are recommended over other biologics
  - Glucocorticoids are not recommended

### **Nonradiographic Axial Spondyloarthritis (nr-axSpA)**

Nonradiographic axial spondyloarthritis (nr-axSpA) falls under the same spondyloarthritis family as ankylosing spondylitis (AS). Nr-axSpA includes patients with chronic back pain and features suggestive of spondyloarthritis (SpA), but do not meet the classification of AS. The goals of treatment are to reduce symptoms, maintain spinal flexibility and normal posture, reduce functional limitations, maintain work ability, and decrease disease complications. The mainstay of treatment has been NSAIDs and exercise, with the additional use of DMARDs in patients with peripheral arthritis. The American College of

Rheumatology (ACR), Spondylitis Association of America (SAA), and Spondyloarthritis Research and Treatment Network (SPARTAN) recommendation for nr-axSpA are the same as AS:

- Stable SpA: conditional recommendation for on-demand treatment with NSAIDs
- Active SpA:
  - First line therapy with continuous NSAIDs and physical therapy
  - TNF inhibitor conditionally recommended for patients with active SpA despite an adequate trial with NSAIDs
    - Lack of response (or intolerance) to at least 2 different NSAIDs over 1 month or incomplete response to at least 2 different NSAIDs over 2 months would be an adequate NSAID trial to judge response
  - TNF-inhibitors are conditionally recommended over secukinumab or ixekizumab
  - Secukinumab or ixekizumab are conditionally recommended over DMARDs in patients that have failed NSAIDs and have contraindications to TNF-inhibitors
  - Recommendations for nonresponse to TNF therapy (all conditional):
    - Primary nonresponse: switch to secukinumab or ixekizumab over another TNF
    - Secondary nonresponse: switch to another TNF over a non-TNF biologic
    - Recommend against addition of sulfasalazine or MTX
    - Recommend against switching to a biosimilar of the failed TNF
  - DMARDs (i.e., methotrexate, sulfasalazine, leflunomide, pamidronate, thalidomide, apremilast) are only conditionally recommended in patients that have failed NSAIDs and have contraindications to TNF-inhibitors
  - Methotrexate is not recommended as add on therapy to TNF inhibitors in stable and active AS
  - If patient has concomitant inflammatory bowel disease or recurrent uveitis, TNF-inhibitors are recommended over other biologics
  - Glucocorticoids are not recommended

### **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.

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.

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:

- 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

## DERMATOLOGICAL DISORDERS

### 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.

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:

- 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 it occurs in select locations (e.g., hands, feet, scalp, face, or genital area) or when it causes intractable pruritus. The AAD psoriasis treatment guidelines recommend the following:

- 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:

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

## POSITION STATEMENT:

### Comparative Effectiveness

The Food and Drug Administration has deemed the drug(s) or biological product(s) in this coverage policy to be appropriate for self-administration or administration by a caregiver (i.e., not a healthcare professional). Therefore, coverage (i.e., administration) in a provider-administered setting such as an outpatient hospital, ambulatory surgical suite, physician office, or emergency facility is not considered medically necessary.

**NOTE:** The self-administered products with prerequisites for certain indications are as follows:

**Table 1**

Disease State	Step 1				

	Step 1a	Step 1b (Directed to ONE TNF inhibitor) NOTE: Please see Step 1a for preferred TNF inhibitors	Step 2 (Directed to ONE step 1 agent)	Step 3a (Directed to TWO step 1 agents)	Step 3b (Directed to TWO agents from step 1 and/or step 2)	Step 3c (Directed to THREE step 1 agents)
<b>Rheumatoid Disorders</b>						
Ankylosing Spondylitis (AS)	SQ: Cosentyx, Enbrel, Humira	Oral: Rinvoq, Xeljanz, Xeljanz XR	N/A	SQ: Cimzia, Simponi, <b>Taltz</b>	N/A	N/A
Nonradiographic Axial Spondyloarthritis (nr-axSpA)	SQ: Cimzia, Cosentyx	Oral: Rinvoq	N/A	SQ: <b>Taltz</b>	N/A	N/A
Polyarticular Juvenile Idiopathic Arthritis (PJIA)	SQ: Enbrel, Humira	Oral: Xeljanz	SQ: Actemra (Humira is required Step 1 agent)	N/A	SQ: Orencia	N/A
Psoriatic Arthritis (PsA)	SQ: Cosentyx, Enbrel, Humira, Skyrizi, Stelara, Tremfya Oral: Otezla	Oral: Rinvoq, Xeljanz, Xeljanz XR	N/A	SQ: Cimzia, Orencia, Simponi, <b>Taltz</b>	N/A	N/A
Rheumatoid Arthritis	SQ: Enbrel, Humira	Oral: Rinvoq, Xeljanz, Xeljanz XR	SQ: Actemra (Humira is required Step 1 agent)	Oral: Olumiant SQ: Cimzia, Kevzara, Kineret, Orencia, Simponi	N/A	N/A
<b>Dermatological Disorders</b>						
Hidradenitis Suppurativa (HS)	SQ: Humira	N/A	N/A	N/A	N/A	N/A
Psoriasis (PS)	SQ: Cosentyx, Enbrel, Humira, Skyrizi, Stelara, Tremfya Oral: Otezla	N/A	N/A	SQ: Cimzia, Ilumya	N/A	SQ: Siliq, <b>Taltz</b> Oral: Sotyktu
<b>Inflammatory Bowel Disease</b>						
Crohn's Disease	SQ: Humira, Skyrizi, Stelara	N/A	N/A	SQ: Cimzia (Humira is a required Step 1 agent)	N/A	N/A
Ulcerative Colitis	SQ: Humira, Stelara	Oral: Rinvoq, Xeljanz, Xeljanz XR	SQ: Simponi (Humira is required Step 1 agent)	N/A	Zeposia (Humira, Rinvoq, Stelara, OR Xeljanz/Xeljanz XR are required Step agents)	N/A
<b>Other</b>						
Uveitis	SQ: Humira	N/A	N/A	N/A	N/A	N/A
<b>Indications Without Prerequisite Biologic Immunomodulators</b>						

Alopecia Areata (AA)						
Atopic Dermatitis						
Deficiency of IL-1 Receptor Antagonist (DIRA)						
Enthesitis-Related Arthritis (ERA)						
Giant Cell Arteritis (GCA)						
Neonatal-Onset Multisystem Inflammatory Disease (NOMID)	N/A	N/A	N/A	N/A	N/A	N/A
Systemic Juvenile Idiopathic Arthritis (SJIA)						
Systemic Sclerosis-associated Interstitial Lung Disease (SSc-ILD)						

**\*Note:** A trial of either or both Xeljanz products (Xeljanz and Xeljanz XR) collectively counts as **ONE** product

Initiation of ixekizumab (Taltz) **meets the definition of medical necessity** when **ALL** of the following are met (“1” to “6”):

1. **ONE** of the following (“a”, “b”, or “c”):
  - a. Information has been provided that indicates the member has been treated with ixekizumab (starting on samples is not approvable) within the past 90 days
  - b. The prescriber states the member has been treated with ixekizumab (starting on samples is not approvable) within the past 90 days **AND** is at risk if therapy is changed
  - c. **BOTH** of the following (“i” and “ii”):
    - i. Ixekizumab will be used for the treatment of an indication listed in Table 2, and **ALL** of the indication-specific criteria are met
    - ii. **EITHER** of the following (“I” or “II”)
      - I. The member’s age is within FDA labeling for the requested indication for ixekizumab
      - II. The prescriber has provided information in support of using ixekizumab for the member’s age
2. The prescriber is a specialist in the area of the member’s diagnosis (e.g., rheumatologist for PsA, dermatologist for PS) or the prescriber has consulted with a specialist in the area of the member’s diagnosis
3. Member does **NOT** have any FDA labeled contraindications to ixekizumab



4. Member has been tested for latent tuberculosis (TB) **AND**, if positive, the member has begun therapy for latent TB
5. Member will **NOT** be using ixekizumab in combination with another biologic immunomodulator agent (full list in “Other” section); Janus kinase (JAK) inhibitor [Cibinqo (abrocitinib), Olumiant (baricitinib), Opzelura (ruxolitinib), Rinvoq (upadacitinib), Xeljanz (tofacitinib), and Xeljanz XR (tofacitinib extended release)]; Otezla (apremilast); Sotyktu (deucravacitinib); or Zeposia (ozanimod)
6. **ANY** of the following (“a”, “b”, or “c”):
  - a. The dosage does not exceed
    - Loading dose
      - AS, and PsA: Initial dose of 160 mg (2 x 80 mg) at week 0, then maintenance doses starting 4 weeks later (i.e., week 4)
      - Adult PS and PS with PsA: Initial dose of 160 mg (2 x 80 mg) at week 0, followed by 80 mg at weeks 2, 4, 6, 8, 10, and 12, then maintenance doses starting 4 weeks later (i.e., week 16)
      - nr-axSpA: No loading dose
    - Maintenance dose - 80 mg every 4 weeks (28 days)
      - QL: 80 mg/mL autoinjector - 1 syringe/28 days
      - QL: 80 mg/mL syringe - 1 syringe/28 days
  - b. The requested quantity (dose) is greater than program’s quantity limit but does **NOT** exceed the maximum FDA labeled dose OR the maximum compendia-supported dose (i.e., DrugDex with 1 or 2a level of evidence, AHFS, or NCCN compendium recommended use 1 or 2a) for the requested indication, **AND** the requested quantity (dose) cannot be achieved with a lower quantity of a higher strength and/or package size that does not exceed the program quantity limit
  - c. The requested quantity (dose) is greater than the program’s quantity limit and greater than the maximum FDA labeled dose AND the maximum compendia-supported dose (i.e., DrugDex with 1 or 2a level of evidence, AHFS, or NCCN compendium recommended use 1 or 2a) for the requested indication, **AND** the prescriber has provided information in support of therapy with a higher dose for the requested indication (submitted copy required, e.g., clinical trials, phase III studies, guidelines required)

**Approval duration:**

- AS and PsA - Loading dose (doses on week 0) for 1 month, then maintenance dose for 11 additional months [12 months for total duration of approval]
- Adult PS and Adult PS with PsA - Loading dose (doses on week weeks 0, 2, 4, 6, 8, 10, and 12) for 4 months, then maintenance dose for 8 additional months [12 months for total duration of approval]
- nr-axSpA and other indications – 12 months

**Table 2**

Diagnosis	Criteria
Active psoriatic arthritis (PsA)	<p><b>BOTH</b> of the following:</p> <ol style="list-style-type: none"> <li>1. <b>ONE</b> of the following:           <ol style="list-style-type: none"> <li>a. The member has tried and had an inadequate response to <b>ONE</b> conventional agent (i.e., cyclosporine, leflunomide, methotrexate, sulfasalazine) used in the treatment of PsA for at least 3 months</li> <li><b>OR</b></li> <li>b. The member has an intolerance or hypersensitivity to <b>ONE</b> of the conventional agents used in the treatment of PsA</li> <li><b>OR</b></li> <li>c. The member has an FDA labeled contraindication to <b>ALL</b> of the conventional agents used in the treatment of PsA</li> <li><b>OR</b></li> <li>d. The member has severe active PsA (e.g., erosive disease, elevated markers of inflammation [e.g., ESR, CRP] attributable to PsA, long-term damage that interferes with function [i.e., joint deformities], rapidly progressive)</li> <li><b>OR</b></li> <li>e. The member has concomitant severe psoriasis (PS) (e.g., greater than 10% body surface area involvement, occurring on select locations [i.e., hands, feet, scalp, face, or genitals], intractable pruritus, serious emotional consequences)</li> <li><b>OR</b></li> <li>f. The member’s medication history indicates use of another biologic immunomodulator agent <b>OR</b> Otezla that is FDA labeled or supported in DrugDex with 1 or 2a level of evidence or AHFS for the treatment of PsA</li> </ol> </li> <li>2. <b>ANY</b> of the following:           <ol style="list-style-type: none"> <li>a. The member has tried and had an inadequate response to at least <b>TWO</b> of the following for at least 3 months:               <ul style="list-style-type: none"> <li>• Cosentyx (secukinumab)</li> <li>• Enbrel (etanercept)</li> <li>• Humira (adalimumab)</li> <li>• Otezla (apremilast)</li> </ul> </li> </ol> </li> </ol>

- Rinvoq (upadacitinib)
- Skyrizi (risankizumab-rzaa)
- Stelara (ustekinumab)
- Tremfya (guselkumab)
- Xeljanz/Xeljanz XR (tofacitinib)

**OR**

b. The member has an intolerance (defined as an intolerance to the drug or its excipients, not to the route of administration) or hypersensitivity to **TWO** of the following:

- Cosentyx (secukinumab)
- Enbrel (etanercept)
- Humira (adalimumab)
- Otezla (apremilast)
- Rinvoq (upadacitinib)
- Skyrizi (risankizumab-rzaa)
- Stelara (ustekinumab)
- Tremfya (guselkumab)
- Xeljanz/Xeljanz XR (tofacitinib)

**OR**

c. The member has an FDA labeled contraindication to **ALL** of the following:

- Cosentyx (secukinumab)
- Enbrel (etanercept)
- Humira (adalimumab)
- Otezla (apremilast)
- Rinvoq (upadacitinib)
- Skyrizi (risankizumab-rzaa)
- Stelara (ustekinumab)
- Tremfya (guselkumab)
- Xeljanz/Xeljanz XR (tofacitinib)

**OR**

d. The prescriber has provided information indicating why **ALL** of the following are not clinically appropriate for the member, **AND**

	<p>the prescriber has provided a complete list of previously tried agents for the requested indication:</p> <ul style="list-style-type: none"><li>• Cosentyx (secukinumab)</li><li>• Enbrel (etanercept)</li><li>• Humira (adalimumab)</li><li>• Otezla (apremilast)</li><li>• Rinvoq (upadacitinib)</li><li>• Skyrizi (risankizumab-rzaa)</li><li>• Stelara (ustekinumab)</li><li>• Tremfya (guselkumab)</li><li>• Xeljanz/Xeljanz XR (tofacitinib)</li></ul>
Moderate to severe plaque psoriasis (PS)	<p><b>BOTH</b> of the following:</p> <ol style="list-style-type: none"><li>1. <b>ONE</b> of the following:<ol style="list-style-type: none"><li>a. The member has tried and had an inadequate response to <b>ONE</b> 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</li><li><b>OR</b></li><li>b. The member has an intolerance or hypersensitivity to <b>ONE</b> conventional agent used in the treatment of PS</li><li><b>OR</b></li><li>c. The member has an FDA labeled contraindication to <b>ALL</b> conventional agents used in the treatment of PS</li><li><b>OR</b></li><li>d. The member has severe active PS (e.g., greater than 10% body surface area involvement, occurring on select locations [i.e., hands, feet, scalp, face, or genitals], intractable pruritus, serious emotional consequences)</li><li><b>OR</b></li><li>e. The member has concomitant severe psoriatic arthritis (PsA) (e.g., erosive disease, elevated markers of inflammation [e.g., ESR, CRP] attributable to PsA, long-term damage that interferes with function [i.e., joint deformities], rapidly progressive)</li></ol></li></ol>

**OR**

- f. The member's medication history indicates use of another biologic immunomodulator agent OR Otezla that is FDA labeled or supported in DrugDex with 1 or 2a level of evidence or AHFS for the treatment of PS

2. **ANY** of the following:

- a. The member has tried and had an inadequate response to at least **THREE** of the following for at least 3 months:

- Cosentyx (secukinumab)
- Enbrel (etanercept)
- Humira (adalimumab)
- Otezla (apremilast)
- Skyrizi (risankizumab)
- Stelara (ustekinumab)
- Tremfya (guselkumab)

**OR**

- b. The member has an intolerance (defined as an intolerance to the drug or its excipients, not to the route of administration) or hypersensitivity to **THREE** of the following:

- Cosentyx (secukinumab)
- Enbrel (etanercept)
- Humira (adalimumab)
- Otezla (apremilast)
- Skyrizi (risankizumab)
- Stelara (ustekinumab)
- Tremfya (guselkumab)

**OR**

- c. The member has an FDA labeled contraindication to **ALL** of the following:

- Cosentyx (secukinumab)
- Enbrel (etanercept)
- Humira (adalimumab)
- Otezla (apremilast)

	<ul style="list-style-type: none"> <li>• Skyrizi (risankizumab)</li> <li>• Stelara (ustekinumab)</li> <li>• Tremfya (guselkumab)</li> </ul> <p><b>OR</b></p> <p>d. The prescriber has provided information indicating why <b>ALL</b> of the following are not clinically appropriate for the member, <b>AND</b> the prescriber has provided a complete list of previously <b>tried</b> agents for the requested indication:</p> <ul style="list-style-type: none"> <li>• Cosentyx (secukinumab)</li> <li>• Enbrel (etanercept)</li> <li>• Humira (adalimumab)</li> <li>• Otezla (apremilast)</li> <li>• Skyrizi (risankizumab)</li> <li>• Stelara (ustekinumab)</li> <li>• Tremfya (guselkumab)</li> </ul>
Active ankylosing spondylitis (AS)	<p><b>BOTH</b> of the following:</p> <p>1. <b>ONE</b> of the following:</p> <p>a. The member has tried and had an inadequate response to <b>TWO</b> different NSAIDs used in the treatment of AS for at least a 4-week total trial</p> <p><b>OR</b></p> <p>b. The member has an intolerance or hypersensitivity to <b>TWO</b> different NSAIDs used in the treatment of AS</p> <p><b>OR</b></p> <p>c. The member has an FDA labeled contraindication to <b>ALL</b> NSAIDs used in the treatment of AS</p> <p><b>OR</b></p> <p>d. The member’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 AS</p> <p>2. <b>ANY</b> of the following:</p> <p>a. The member has tried and had an inadequate response to at least <b>TWO</b> of the following for at least 3 months:</p>

- Cosentyx (secukinumab)
- Enbrel (etanercept)
- Humira (adalimumab)
- Rinvoq (upadacitinib)
- Xeljanz/Xeljanz XR (tofacitinib)

**OR**

b. The member has an intolerance (defined as an intolerance to the drug or its excipients, not to the route of administration) or hypersensitivity to **TWO** of the following:

- Cosentyx (secukinumab)
- Enbrel (etanercept)
- Humira (adalimumab)
- Rinvoq (upadacitinib)
- Xeljanz/Xeljanz XR (tofacitinib)

**OR**

c. The member has an FDA labeled contraindication to **ALL** of the following:

- Cosentyx (secukinumab)
- Enbrel (etanercept)
- Humira (adalimumab)
- Rinvoq (upadacitinib)
- Xeljanz/Xeljanz XR (tofacitinib)

**OR**

d. The prescriber has provided information indicating why **ALL** of the following are not clinically appropriate for the patient, **AND** the prescriber has provided a complete list of previously tried agents for the requested indication:

- Cosentyx (secukinumab)
- Enbrel (etanercept)
- Humira (adalimumab)
- Rinvoq (upadacitinib)
- Xeljanz/Xeljanz XR (tofacitinib)

Active non-radiographic axial spondyloarthritis (nr-axSpA)

**BOTH** of the following:

1. **ONE** of the following:

a. The member has tried and had an inadequate response to **TWO** different NSAIDs used in the treatment of nr-axSpA for at least a 4-week total trial

**OR**

b. The member has an intolerance or hypersensitivity to **TWO** different NSAIDs used in the treatment of AS

**OR**

c. The member has an FDA labeled contraindication to **ALL** NSAIDs used in the treatment of nr-axSpA

**OR**

d. The member'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 nr-axSpA

2. **ANY** of the following:

a. The member has tried and had an inadequate response to at least **TWO** of the following for at least 3 months:

- Cimzia (certolizumab pegol)
- Cosentyx (secukinumab)
- Rinvoq (upadacitinib)

**OR**

b. The member has an intolerance (defined as an intolerance to the drug or its excipients, not to the route of administration) to at least **TWO** of the following:

- Cimzia (certolizumab pegol)
- Cosentyx (secukinumab)
- Rinvoq (upadacitinib)

**OR**

c. The member has an FDA labeled contraindication to **ALL** of the following:

- Cimzia (certolizumab pegol)
- Cosentyx (secukinumab)
- Rinvoq (upadacitinib)



	<p style="text-align: center;"><b>OR</b></p> <p>d. The prescriber has provided information indicating why <b>ALL</b> of the following are not clinically appropriate for the member, <b>AND</b> the prescriber has provided a complete list of previously tried agents for the requested indication:</p> <ul style="list-style-type: none"> <li>• Cimzia (certolizumab pegol)</li> <li>• Cosentyx (secukinumab)</li> <li>• Rinvoq (upadacitinib)</li> </ul>
Other indications	The member has another FDA labeled indication or an indication supported in DrugDex with 1 or 2a level of evidence, AHFS, or NCCN compendium recommended use 1 or 2a

Continuation of ixekizumab (Taltz) **meets the definition of medical necessity** when **ALL** of the following are met (“1” to “6”):

1. An authorization or reauthorization for ixekizumab has been previously approved by Florida Blue
2. Member has had clinical benefit with ixekizumab therapy
3. The prescriber is a specialist in the area of the member’s diagnosis (e.g., rheumatologist for PsA, dermatologist for PS) or the prescriber has consulted with a specialist in the area of the member’s diagnosis
4. Member does **NOT** have any FDA labeled contraindications to ixekizumab
5. Member will **NOT** be using ixekizumab in combination with another biologic immunomodulator agent (full list in “Other” section); Janus kinase (JAK) inhibitor [Cibinqo (abrocitinib), Olumiant (baricitinib), Opzelura (ruxolitinib), Rinvoq (upadacitinib), Xeljanz (tofacitinib), and Xeljanz XR (tofacitinib extended release)]; Otezla (apremilast); Sotyktu (deucravacitinib); or Zeposia (ozanimod)
6. **ANY** of the following (“a”, “b”, or “c”):
  - a. The dosage does not exceed 80 mg every 4 weeks (28 days)
    - QL: 80 mg/mL autoinjector - 1 syringe/28 days
    - QL: 80 mg/mL syringe - 1 syringe/28 days
  - b. The requested quantity (dose) is greater than program’s quantity limit but does **NOT** exceed the maximum FDA labeled dose **OR** the maximum compendia-supported dose (i.e., DrugDex with 1 or 2a level of evidence, AHFS, or NCCN compendium recommended use 1 or 2a) for the requested indication, **AND** the requested quantity (dose) cannot be achieved with a lower quantity of a higher strength and/or package size that does not exceed the program quantity limit
  - c. The requested quantity (dose) is greater than the program’s quantity limit and greater than the maximum FDA labeled dose **AND** the maximum compendia-supported dose (i.e., DrugDex with 1 or 2a level of evidence, AHFS, or NCCN compendium recommended use 1 or 2a) for the requested indication, **AND** the prescriber has provided information in support of therapy with a

higher dose for the requested indication (submitted copy required, e.g., clinical trials, phase III studies, guidelines required)

**Approval duration:** 12 months

## **DOSAGE/ADMINISTRATION:**

**THIS INFORMATION IS PROVIDED FOR INFORMATIONAL PURPOSES ONLY AND SHOULD NOT BE USED AS A SOURCE FOR MAKING PRESCRIBING OR OTHER MEDICAL DETERMINATIONS. PROVIDERS SHOULD REFER TO THE MANUFACTURER'S FULL PRESCRIBING INFORMATION FOR DOSAGE GUIDELINES AND OTHER INFORMATION RELATED TO THIS MEDICATION BEFORE MAKING ANY CLINICAL DECISIONS REGARDING ITS USAGE.**

### **FDA-approved**

- Indicated for (1) the treatment of patients 6 years of age and older with moderate-to-severe plaque psoriasis who are candidates for systemic therapy or phototherapy, (2) the treatment of adult patients with active psoriatic arthritis (PsA), and (3) the treatment of adult patients with active ankylosing spondylitis (AS), and (4) the treatment of adult patients with active non-radiographic axial spondyloarthritis (nr-axSpA) with objective signs of inflammation.
- Administered by subcutaneous injection. The recommended dose is for adult plaque psoriasis is 160 mg (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. Dosing for pediatric PS (6 to <18 years old) is weight based. Refer to the product labeling for the recommended loading and maintenance dosing. The recommended dose for PsA and AS is 160 mg by subcutaneous injection (two 80 mg injections) at week 0, followed by 80 mg every 4 weeks. For PsA patients with coexistent moderate-to-severe plaque psoriasis, use the dosing regimen for plaque psoriasis. For nr-axSpA the recommended dose is 80 mg every 4 weeks (no loading dose). For PsA patients, ixekizumab may be administered alone or in combination with a csDMARD (e.g., methotrexate).
- Ixekizumab is intended for use under the guidance and supervision of a physician. Patients may self-inject after training in subcutaneous injection technique using the autoinjector or prefilled syringe. Administer each injection at a different anatomic location (such as upper arms, thighs or any quadrant of abdomen) than the previous injection, and not into areas where the skin is tender, bruised, erythematous, indurated or affected by psoriasis. Administration the upper, outer arm may be performed by a caregiver or healthcare provider. However, doses of 20 mg or 40 mg must be prepared and administered by a qualified healthcare professional. Use only the commercial 80 mg/1 mL prefilled syringe when preparing the prescribed 20 mg and 40 mg pediatric dose.
- Before injection, remove ixekizumab from the refrigerator and allow to reach room temperature (30 minutes) without removing the needle cap.

### **Dose Adjustments**

- Specific guidelines for dosage adjustments in hepatic or renal impairment are not available; it appears no dosage adjustments are needed

### **Drug Availability**

- Autoinjector - 80 mg/mL solution in a single-dose prefilled autoinjector (cartons of 1, 2, or 3)
- Prefilled Syringe - 80 mg/mL solution in a single-dose prefilled syringe (carton of 1)

## PRECAUTIONS:

### Boxed Warning

- None

### Contraindications

- Patients with a previous serious hypersensitivity reaction, such as anaphylaxis, to ixekizumab or to any of the excipients

### Precautions/Warnings

- **Infections:** Serious infections have occurred. Instruct patients to seek medical advice if signs or symptoms of clinically important chronic or acute infection occur. If a serious infection develops, discontinue ixekizumab until the infection resolves.
- **Tuberculosis (TB):** Evaluate for TB prior to initiating treatment. Do not administer to patients with active TB infection. Initiate treatment of latent TB prior to administering ixekizumab. Consider anti-TB therapy prior to initiating in patients with a history of latent or active TB in whom an adequate course of treatment cannot be confirmed. Patients receiving ixekizumab should be monitored closely for signs and symptoms of active TB during and after treatment.
- **Hypersensitivity:** Serious hypersensitivity reactions, including angioedema and urticaria (each  $\leq 0.1\%$ ), occurred in clinical trials. Anaphylaxis, including cases leading to hospitalization, has been reported in post marketing use. If a serious allergic reaction occurs, discontinue ixekizumab immediately and initiate appropriate therapy.
- **Inflammatory Bowel Disease:** Crohn's disease and ulcerative colitis, including exacerbations, occurred during clinical trials. Patients who are treated with ixekizumab and have inflammatory bowel disease should be monitored closely.
- **Adverse Reactions:** Most common ( $\geq 1\%$ ) adverse reactions associated with ixekizumab treatment are injection site reactions, upper respiratory tract infections, nausea, and tinea infections.
- **Immunizations:** Prior to initiating therapy with ixekizumab, consider completion of all age-appropriate immunizations according to current immunization guidelines. Avoid use of live vaccines in patients treated with ixekizumab. No data are available on the response to live or inactive vaccines.
- **Pregnancy:** There are no available data on ixekizumab use in pregnant women to inform any drug associated risks. Human IgG is known to cross the placental barrier; therefore, ixekizumab may be transmitted from the mother to the developing fetus. An embryofetal development study conducted in pregnant monkeys at doses up to 19 times the maximum recommended human dose (MRHD) revealed no evidence of harm to the developing fetus.
- **Pediatric Use:** The safety and effectiveness of ixekizumab in pediatric patients (<18 years of age) have not been evaluated.
- **Cytochrome P450 Substrates:** The formation of CYP450 enzymes can be altered by increased levels of certain cytokines (e.g., IL-1, IL-6, IL-10, TNF $\alpha$ , IFN) during chronic inflammation. Thus, ixekizumab, an antagonist of IL-17A, could normalize the formation of CYP450 enzymes. Therefore, upon initiation or discontinuation in patients who are receiving concomitant drugs which are CYP450

substrates, particularly those with a narrow therapeutic index, consider monitoring for effect (e.g., for warfarin) or drug concentration (e.g., for cyclosporine) and consider dosage modification of the CYP450 substrate.

## BILLING/CODING INFORMATION:

### HCPCS Coding

J3590	Unclassified biologics
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### ICD-10 Diagnosis Codes That Support Medical Necessity

L40.0	Psoriasis vulgaris
L40.50	Arthropathic psoriasis, unspecified
L40.51	Distal interphalangeal psoriatic arthropathy
L40.52	Psoriatic arthritis mutilans
L40.53	Psoriatic spondylitis
L40.59	Other psoriatic arthropathy
M45.0 – M45.9	Ankylosing spondylitis
M45.A0 – M45.AB	Non-radiographic axial spondyloarthritis
M46.81 – M46.89	Other specified inflammatory spondylopathies

## REIMBURSEMENT INFORMATION:

Refer to section entitled [POSITION STATEMENT](#).

### PROGRAM EXCEPTIONS:

**Federal Employee Program (FEP):** Follow FEP guidelines.

**State Account Organization (SAO):** Follow SAO guidelines.

**Medicare Part D:** Florida Blue has delegated to Prime Therapeutics authority to make coverage determinations for the Medicare Part D services referenced in this guideline.

**Medicare Advantage:** No National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) were found at the time of the last guideline review date.

### DEFINITIONS:

**DMARDs:** An acronym for disease-modifying antirheumatic drugs. These are drugs that modify the rheumatic disease processes, and slow or inhibit structural damage to cartilage and bone. These drugs are unlike symptomatic treatments such as NSAIDs that do not alter disease progression. DMARDs can be further subcategorized. With the release of biologic agents (e.g., anti-TNF drugs), DMARDs were divided into either: (1) conventional, traditional, synthetic, or non-biological DMARDs; or as (2) biological DMARDs. However, with the release of newer targeted non-biologic drugs and biosimilars, DMARDs are now best categorized as: (1) conventional synthetic DMARDs (csDMARD) (e.g., MTX, sulfasalazine), (2) targeted synthetic DMARDs (tsDMARD) (e.g., baricitinib, tofacitinib, apremilast), and

(3) biological DMARDs (bDMARD), which can be either a biosimilar DMARD (bsDMARD) or biological originator DMARD (boDMARD).

**Plaque psoriasis:** It is the most common form of psoriasis. It affects 80 to 90% of people with psoriasis. Plaque psoriasis typically appears as raised areas of inflamed skin covered with silvery white scaly skin. These areas are called plaques.

**Psoriatic arthritis (PsA):** joint inflammation that occurs in about 5% to 10% of people with psoriasis (a common skin disorder). It is a severe form of arthritis accompanied by inflammation, psoriasis of the skin or nails, and a negative test for rheumatoid factor. Enthesitis refers to inflammation of entheses, the site where ligaments or tendons insert into the bones. It is a distinctive feature of PsA and does not occur with other forms of arthritis. Common locations for enthesitis include the bottoms of the feet, the Achilles' tendons, and the places where ligaments attach to the ribs, spine, and pelvis.

## RELATED GUIDELINES:

[Adalimumab \(Humira\), 09-J0000-46](#)

[Apremilast \(Otezla\) Tablet, 09-J2000-19](#)

[Brodalumab \(Siliq\) Injection, 09-J2000-74](#)

[Certolizumab Pegol \(Cimzia\), 09-J0000-77](#)

[Etanercept \(Enbrel\), 09-J0000-38](#)

[Golimumab \(Simponi, Simponi Aria\), 09-J1000-11](#)

[Guselkumab \(Tremfya\), 09-J2000-87](#)

[Infliximab Products \[infliximab \(Remicade\), infliximab-dyyb \(Inflectra\), and infliximab-abda \(Renflexis\)\], 09-J0000-39](#)

[Psoralens with Ultraviolet A \(PUVA\), 09-10000-16](#)

[Risankizumab \(Skyrizi\), 09-J3000-45](#)

[Secukinumab \(Cosentyx\), 09-J2000-30](#)

[Tildrakizumab-asmn \(Ilumya\), 09-J3000-04](#)

[Ustekinumab \(Stelara\), 09-J1000-16](#)

## OTHER:

### Biologic Immunomodulator Agents Not Permitted as Concomitant Therapy

Actemra (tocilizumab)

Adbry (tralokinumab-ldrm)

Arcalyst (rilonacept)

Avsola (infliximab-axxq)

Benlysta (belimumab)

Cimzia (certolizumab)

Cinqair (reslizumab)

Cosentyx (secukinumab)

Dupixent (dupilumab)

Fasenra (benralizumab)

Enbrel (etanercept)  
 Entyvio (vedolizumab)  
 Humira (adalimumab)  
 Ilaris (canakinumab)  
 Ilumya (tildrakizumab-asmn)  
 Inflectra (infliximab-dyyb)  
 Infliximab  
 Kevzara (sarilumab)  
 Kineret (anakinra)  
 Nucala (mepolizumab)  
 Orencia (abatacept)  
 Remicade (infliximab)  
 Renflexis (infliximab-abda)  
 Riabni (rituximab-arrx)  
 Rituxan (rituximab)  
 Rituxan Hycela (rituximab/hyaluronidase human)  
 Ruxience (rituximab-pvvr)  
 Siliq (brodalumab)  
 Simponi (golimumab)  
 Simponi Aria (golimumab)  
 Skyrizi (risankizumab-rzaa)  
 Stelara (ustekinumab)  
 Tezspire (tezepelumab-ekko)  
 Tremfya (guselkumab)  
 Truxima (rituximab-abbs)  
 Tysabri (natalizumab)  
 Xolair (omalizumab)

**Table 4: Conventional Synthetic DMARDs**

<b>Generic Name</b>	<b>Brand Name</b>
Auranofin (oral gold)	Ridaura
Azathioprine	Imuran
Cyclosporine	Neoral, Sandimmune
Hydroxychloroquine	Plaquenil
Leflunomide	Arava
Methotrexate	Rheumatrex, Trexall
Sulfasalazine	Azulfidine, Azulfidine EN-Tabs

## REFERENCES:

1. Armstrong AW, Siegel MP, Bagel J, et al. From the Medical Board of the National Psoriasis Foundation: Treatment targets for plaque psoriasis. *J Am Acad Dermatol*. 2017 Feb;76(2):290-298.
2. Blauvelt A, Papp KA, Griffiths CEM, et al. Efficacy and Safety of Switching to Ixekizumab in Etanercept Non-Responders: A Subanalysis from Two Phase III Randomized Clinical Trials in Moderate-to-Severe Plaque Psoriasis (UNCOVER-2 and -3). *Am J Clin Dermatol*. 2017 Apr;18(2):273-280.
3. Canadian Psoriasis Guidelines Addendum Committee. 2016 Addendum to the Canadian Guidelines for the Management of Plaque Psoriasis 2009. *J Cutan Med Surg*. 2016 Sep;20(5):375-431.
4. Clinical Pharmacology powered by ClinicalKey [Internet]. Tampa, FL: Elsevier.; 2022. Available at: <https://www.clinicalkey.com/pharmacology/>. Accessed 10/25/22.
5. Coates LC, Kavanaugh A, Mease PJ et al. Group for Research and Assessment of Psoriasis and Psoriatic Arthritis: Treatment Recommendations for Psoriatic Arthritis 2015. *Arthritis Rheumatol* 2016; 68:1060–71.
6. Dogra S, Jain A, Kanwar AJ. Efficacy and safety of acitretin in three fixed doses of 25, 35 and 50 mg in adult patients with severe plaque type psoriasis: a randomized, double blind, parallel group, dose ranging study. *J Eur Acad Dermatol Venereol*. 2013 Mar;27(3):e305-11.
7. Dogra S, Krishna V, Kanwar AJ. Efficacy and safety of systemic methotrexate in two fixed doses of 10 mg or 25 mg orally once weekly in adult patients with severe plaque-type psoriasis: a prospective, randomized, double-blind, dose-ranging study. *Clin Exp Dermatol*. 2012 Oct;37(7):729-34.
8. Elmets CA, Leonardi CL, Davis DM, et al. Joint AAD-NPF guidelines of care for the management and treatment of psoriasis with awareness and attention to comorbidities. *J Am Acad Dermatol*. 2019 Apr;80(4):1073-1113. Epub 2019 Feb 13.
9. Elmets CA, Lim HW, Stoff H, et al. Joint American Academy of Dermatology–National Psoriasis Foundation guidelines of care for the management and treatment of psoriasis with phototherapy. *J Am Acad Dermatol*. Epub 2019 July 25.
10. FDA Orphan Drug Designations and Approvals [Internet]. Washington, D.C. [cited 2022 Oct 25]. Available from: <http://www.accessdata.fda.gov/scripts/opdlisting/oopd/>.
11. Gordon KB, Blauvelt A, Papp KA, et al.; UNCOVER-1 Study Group; UNCOVER-2 Study Group; UNCOVER-3 Study Group. Phase 3 Trials of Ixekizumab in Moderate-to-Severe Plaque Psoriasis. *N Engl J Med*. 2016 Jul 28;375(4):345-56.
12. Griffiths C, Reich K, Lebwohl M, et al: Comparison of ixekizumab with etanercept or placebo in moderate-to-severe psoriasis (UNCOVER-2 and UNCOVER-3): results from two phase 3 randomised trials. *Lancet* 2015; 386(9993):541-551.
13. Heydendael VM, Spuls PI, Opmeer BC, et al. Methotrexate versus cyclosporine in moderate-to-severe chronic plaque psoriasis. *N Engl J Med* 2003; 349:658-65.
14. Kalb RE, Strober B, Weinstein G, Lebwohl M. Methotrexate and psoriasis: 2009 National Psoriasis Foundation Consensus Conference. *J Am Acad Dermatol* 2009; 60:824-37.
15. Krause ML, Amin A, and Makol A. Use of DMARDs and biologics during pregnancy and lactation in rheumatoid arthritis: what the rheumatologist needs to know. *Ther Adv Musculoskelet Dis*. 2014 Oct; 6(5): 169–184.
16. Kroon FP, van der Burg LR, Ramiro S, et al. Non-steroidal anti-inflammatory drugs (NSAIDs) for axial spondyloarthritis (ankylosing spondylitis and non-radiographic axial spondyloarthritis). *Cochrane Database Syst Rev*. 2015 Jul 17;7:CD010952.

17. Menter A, Korman NJ, Elmets CA, Feldman SR, Gelfand JM, Gordon KB, et al. 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 Sep;61(3):451-85.
18. Menter A, Korman NJ, Elmets CA, et al. Guidelines of care for the management of psoriasis and psoriatic arthritis: Section 6. Guidelines of care for the treatment of psoriasis and psoriatic arthritis: Case-based presentations and evidence-based conclusions. *J Am Acad Dermatol* 2011; 65:137-74.
19. 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 Apr;80(4):1029-1072. Epub 2019 Feb 13.
20. Micromedex Healthcare Series [Internet Database]. Greenwood Village, Colo: Thomson Healthcare. Updated periodically. Accessed 10/25/22.
21. Rahimi R, Nikfar S, Rezaie A, et al. Pregnancy outcome in women with inflammatory bowel disease following exposure to 5-aminosalicylic acid drugs: a meta-analysis. *Reprod. Toxicol*; 2008;25,271–275.
22. Ramiro S, Nikiphorou E, Sepriano A, et al. ASAS-EULAR recommendations for the management of axial spondyloarthritis: 2022 update. *Ann Rheum Dis*. 2022 Oct 19:ard-2022-223297. Epub ahead of print.
23. Rudwaleit M, van der Heijde D, Landewé R, et al. The Assessment of SpondyloArthritis International Society classification criteria for peripheral spondyloarthritis and for spondyloarthritis in general. *Ann Rheum Dis*. 2011 Jan;70(1):25-31.
24. Sbidian E, Chaimani A, Garcia-Doval, et al. Systemic pharmacological treatments for chronic plaque psoriasis: a network meta-analysis. *Cochrane Database Syst Rev*. 2021 Apr 19;4(4):CD011535. Update in: *Cochrane Database Syst Rev*. 2022 May 23;5:CD011535.
25. Singh JA, Guyatt G, Ogdie A, et al. Special Article: 2018 American College of Rheumatology/National Psoriasis Foundation Guideline for the Treatment of Psoriatic Arthritis. *Arthritis Rheumatol*. 2019 Jan;71(1):5-32. Epub 2018 Nov 30.
26. Smith CH, Jabbar-Lopez JK, Yiu ZZ, et al. British Association of Dermatologists guidelines for biologic therapy for psoriasis 2017. *Br J Dermatol* 2017; 177: 628-136.
27. Taltz (ixekizumab) [prescribing information]. Eli Lilly and Company; Indianapolis, IN. September 2022.
28. 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 Rheumatol*. 2019 Aug 22. [Epub ahead of print].

### COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 11/09/22.

### GUIDELINE UPDATE INFORMATION:

06/15/16	New Medical Coverage Guideline.
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10/15/17	Review and revision to guideline consisting of updating description, position statement, dosage/administration, definitions, related guidelines, and references.
01/01/18	Revision to guideline consisting of updating the preferred self-administered biologic products according to indication for use. Secukinumab (Cosentyx) is now a preferred product for plaque psoriasis.
01/15/18	Revision to guideline consisting of the description section, position statement, dosage/administration, billing/coding information, related guidelines, definitions, and referenced, based on the new FDA-approved indication for the treatment of adults with active psoriatic arthritis.
07/01/18	Revision to guideline consisting of updating the position statement.
10/15/18	Review and revision to guideline consisting of updating the position statement and references.
07/01/19	Revision to guideline consisting of updating the position statement.
09/01/19	Revision to guideline consisting of updating the position statement.
10/15/19	Review and revision to guideline consisting of updating the description, position statement, dosage/administration, billing/coding, definitions, other section, and references.
01/01/20	Revision to guideline consisting of updating the position statement due to changes in preferred and non-preferred products.
07/01/20	Revision to guideline consisting of updating the description, position statement, dosage/administration, definitions, other, and references.
01/01/21	Review and revision to guideline consisting of updating the position statement and references.
03/15/21	Revision to guideline consisting of updating Table 1 in the position statement.
10/01/21	Revision: Addition of new ICD-10 code range M45.A0 – M45.AB.
11/15/21	Revision to guideline consisting of updating the position statement.
01/01/22	Review and revision to guideline consisting of updating the position statement, other section, and references.
02/15/22	Update to Table 1 in Position Statement.
03/15/22	Revision to guideline consisting of updating the position statement and other section.
05/15/22	Update to Table 1 in Position Statement.
07/15/22	Revision to guideline consisting of updating the position statement.
09/15/22	Revision to guideline consisting of updating the description, position statement, and references.
01/01/23	Review and revision to guideline consisting of updating the position statement, other section, and references. Rinvoq was added as a preferred agent for nr-AxSpA. New drugs were added to the list of drugs that are not permitted for use in combination.