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Subject: Ixekizumab (Taltz®) Injection

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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. 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.

Psoriasis is a chronic, inflammatory disease that affects approximately 3% of the adult US population. Approximately 80% of patients with psoriasis have limited disease, and, for the majority of these patients, topical treatments are safe, effective, and convenient. However, some patients require systemic treatment. Without appropriate treatment, patients may experience substantial disease burden and decreased quality of life. The American Academy of Dermatology (AAD) guidelines state that methotrexate is a logical first choice of systemic agent, because it is the most cost-effective systemic psoriasis agent with the longest safety follow-up data. Cyclosporine is cited as particularly useful in the treatment of significant flares of psoriasis unresponsive to other therapies. Intermittent, short-term therapy (12 to 16 weeks) is the most frequently recommended regimen, with treatment withdrawn once significant improvement is achieved. When relapse occurs, cyclosporine therapy is reinstituted at the previously established effective dose, or maintenance therapy for up to 1 year can be used. Acitretin is also mentioned as an important oral option, despite it being normally less effective than other traditional

systemic agents, due to its lack of immunosuppression and value in patients with known infection, active malignancy, or HIV. The AAD and National Psoriasis Foundation (NPF) are expected to release updated joint guidelines for the management of psoriasis with non-biologics in 2020. The AAD-NPF did release a joint guideline in 2019 for the management and treatment of psoriasis with biologics. The prior AAD guidelines did not include many of the biologics approved in the past decade. The 2019 guidelines provide the following recommendations regarding ixekizumab: 6.1 - ixekizumab is recommended as a monotherapy treatment option for use in adult patients with moderate-to-severe plaque psoriasis (Strength of recommendation A), 6.2 - the recommended starting dose of ixekizumab is 160 mg by self-administered subcutaneous injection followed by 80 mg at wk 2, wk 4, wk 6, wk 8, wk 1, and wk 12 (A), 6.3 - the recommended maintenance dose of ixekizumab after the initial 12 wk is 80 mg every4 wk (A), 6.4 - ixekizumab can be recommended as a monotherapy treatment option in adult patients with moderate-to-severe plaque psoriasis affecting the scalp (B), 6.5 - ixekizumab can be recommended as a monotherapy treatment option in adult patients with erythrodermic psoriasis (B), 6.6 - ixekizumab can be recommended as a monotherapy treatment option in adult patients with moderate-to-severe plaque psoriasis affecting the nails (B), 6.7 - ixekizumab can be recommended as a monotherapy treatment option in adult patients with generalized pustular psoriasis (B), 6.8 - ixekizumab is recommended as a monotherapy treatment option in adult patients with plaque psoriasis when associated with psoriatic arthritis (A).

The safety and efficacy of ixekizumab in plaque psoriasis were evaluated in three, double-blind, multicenter, phase 3 studies (UNCOVER-1, UNCOVER-2 and UNCOVER-3) in a total of 3,866 adult patients with moderate to severe chronic plaque psoriasis. In all three trials, subjects were randomized to either placebo or ixekizumab (80 mg every two weeks [Q2W]) for 12 weeks, following a 160 mg starting dose. In the two active comparator trials (UNCOVER-2 and UNCOVER-3), subjects were also randomized to etanercept (Enbrel) 50 mg twice weekly for 12 weeks. All three trials assessed the changes from baseline to Week 12 in two co-primary endpoints: (1) PASI 75 [the proportion of subjects who achieved at least a 75% reduction in the Psoriasis Area and Severity Index (PASI) composite score], and (2) sPGA of “0” (clear) or “1” (minimal) [the proportion of subjects with an static Physician Global Assessment (sPGA) score of 0 or 1 and at least a 2-point improvement]. Other evaluated outcomes included the proportion of subjects with a sPGA score of 0, PASI 90, and PASI 100. Subjects in all treatment groups had a median baseline PASI score ranging from about 17 to 18. Of all subjects, 44% had received prior phototherapy, 49% had received prior conventional systemic therapy, and 26% had received prior biologic therapy for the treatment of psoriasis.

The results of UNCOVER-1, UNCOVER-2 and UNCOVER-3 in the intent-to-treat (ITT) population are presented in Table 1 below.

Table 1

	UNCOVER-1		**UNCOVER-2**		**UNCOVER-3**	
	Taltz (n=433)	**Placebo** (n=431)	**Taltz** (n=351)	**Placebo** (n=168)	**Taltz** (n=385)	**Placebo** (n=193)
sPGA of 0 or 1	82%	3%	83%	2%	81%	7%
sPGA of 0	37%	0%	42%	1%	40%	0%
PASI 75	89%	4%	90%	4%	87%	7%
PASI 90	71%	1%	71%	1%	68%	3%
PASI 100	35%	0%	40%	1%	38%	0%

In an integrated analysis of the US sites in the two active comparator studies using etanercept, ixekizumab demonstrated superiority to etanercept 50 mg twice weekly on sPGA and PASI scores during the 12 week treatment period. The respective response rates for ixekizumab and etanercept were: sPGA of 0 or 1 (73% vs. 27%); PASI 75 (87% vs. 41%); sPGA of 0 (34% vs. 5%); PASI 90 (64% vs. 18%), and PASI 100 (34% vs. 4%).

The safety and efficacy of ixekizumab in PsA were evaluated in two randomized, double-blind, placebo-controlled Phase 3 studies (SPIRIT-P1 and SPIRIT-P2) which included 679 adult patients with active PsA. SPIRIT-P1 evaluated the safety and efficacy of ixekizumab compared to placebo in patients with active PsA who had never been treated with a biologic DMARD. SPIRIT-P2 evaluated the safety and efficacy of ixekizumab compared to placebo in TNFi-experienced patients with active PsA who failed one or two TNF inhibitors. Across both studies, patients were required to have a diagnosis of active PsA for at least six months and at least three tender and three swollen joints. In addition, approximately 47% of patients from both studies had concomitant methotrexate use. Inadequate responders (defined by blinded tender and swollen joint count criteria) at Week 16 received rescue therapy and were analyzed as non-responders. The primary endpoint was the percentage of patients achieving an ACR20 response at Week 24. In both studies, patients treated with ixekizumab 80 mg Q2W or 80 mg Q4W demonstrated a greater clinical response including ACR20, ACR50, and ACR70 compared to placebo at Week 24. The results of SPIRIT-P1 and SPIRIT-P2 in the intent-to-treat (ITT) population are presented in Table 2 below.

Table 2

	SPIRIT-P1			**SPIRIT-P2**		
	Taltz 80 mg Q4W (n=107)	Placebo (n=106)	Δ vs Placebo (95% CI)	Taltz 80 mg Q4W (n=122)	Placebo (n=118)	Δ vs Placebo (95% CI)
ACR20						
Week 12	57%	31%	26% (13, 39)	50%	22%	28% (16, 40)
Week 24	58%	30%	28% (15, 41)	53%	20%	34% (22, 45)
ACR50						
Week 12	34%	5%	29% (19, 39)	31%	3%	28% (19, 37)
Week 24	40%	15%	25% (14, 37)	35%	5%	30% (21, 40)
A**CR70**						
Week 12	15%	0%	15% (8, 22)	15%	2%	13% (6, 20)
Week 24	23%	6%	18% (9, 27)	22%	0%	22% (15, 30)

POSITION STATEMENT:

NOTE: The preferred self-administered specialty products for certain indications are:

- Axial spondyloarthritis - adalimumab (Humira), etanercept (Enbrel), and secukinumab (Cosentyx)
- Crohn’s disease - adalimumab (Humira) and ustekinumab (Stelara)
- Hidradenitis suppurativa - adalimumab (Humira)
- Plaque psoriasis - adalimumab (Humira), etanercept (Enbrel), guselkumab (Tremfya), risankizumab (Skyrizi), secukinumab (Cosentyx), and ustekinumab (Stelara)
- Juvenile idiopathic arthritis [non-systemic] - adalimumab (Humira) and etanercept (Enbrel)
- Psoriatic arthritis - adalimumab (Humira), etanercept (Enbrel), secukinumab (Cosentyx), and ustekinumab (Stelara)

- Rheumatoid arthritis - adalimumab (Humira), etanercept (Enbrel), and upadacitinib (Rinvoq)
- Ulcerative colitis - adalimumab (Humira) and ustekinumab (Stelara)
- Uveitis - adalimumab (Humira)

Initiation of ixekizumab (Taltz) **meets the definition of medical necessity** when **ALL** of the following criteria are met (“1”, “2”, and “3”):

1. Ixekizumab will be used for the treatment of an indication listed in Table 3, and **ALL** of the indication-specific and maximum-allowable dose criteria are met
2. Ixekizumab will **NOT** be used in combination with **ANY** of the following:
    a. abatacept (Orencia)
    b. adalimumab (Humira)
    c. anakinra (Kineret)
    d. apremilast (Otezla)
    e. baricitinib (Olumiant)
    f. brodalumab (Siliq)
    g. certolizumab (Cimzia)
    h. etanercept (Enbrel)
    i. golimumab (Simponi, Simponi Aria)
    j. guselkumab (Tremfya)
    k. infliximab products (Remicade, Inflectra, Renflexis)
    l. risankizumab (Skyrizi)
    m. sarilumab (Kevzara)
    n. secukinumab (Cosentyx)
    o. tildrakizumab-asmn (Ilumya)
    p. tocilizumab (Actemra)
    q. tofacitinib (Xeljanz, Xeljanz XR)
    r. upadacitinib (Rinvoq)
    s. ustekinumab (Stelara)
    t. vedolizumab (Entyvio)
3. The member is 18 years of age or older

Table 3

Indications and Specific Criteria		
Indication	**Criteria**	**Max Allowable Dosage**
Axial spondyloarthritis	When **ALL** of the following are met (“1”, “2”, “3”, and “4”):	Initial:

(axSpA) [including both ankylosing spondylitis (AS) and non-radiographic axial spondyloarthritis (nr-axSpA)]	1. Member has a diagnosis of axial spondyloarthritis per ASAS criteria 2. Member has had an inadequate response to, intolerable adverse effects with, or has a contraindication to at least **TWO** different NSAID therapies taken continuously for at least 2 weeks each at maximal doses* (e.g., celecoxib, diclofenac, ibuprofen, meloxicam, naproxen) [the specific adverse effect(s) and/or contraindication must be provided] 3. **EITHER** of the following ("a" or "b"): a. Member has had inadequate responses to **TWO** or more of the following self-administered therapies, **OR** has had intolerable adverse effects with or has contraindications to **ALL** of the following self-administered therapies [the specific adverse effect(s) and/or contraindication(s) must be provided]: • adalimumab (Humira) • etanercept (Enbrel) • secukinumab (Cosentyx) b. Member has had an inadequate response to, intolerable adverse effects with, or has a contraindication to secukinumab (Cosentyx), AND alternatives to the use of an anti-TNF biologic should be considered due to the member having current or worsening congestive heart failure or demyelinating disease (e.g., multiple sclerosis) 4. **EITHER** of the following ("a" or "b"): a. Member has had an inadequate response to, intolerable adverse effects with, or has a contraindication to certolizumab pegol (Cimzia) b. Alternatives to the use of an anti-TNF biologic should be considered due to the member having current or worsening congestive heart failure or a demyelinating disease (e.g., multiple sclerosis)	• 160 mg (two 80 mg injections) at Week 0 Maintenance: • 80 mg every 4 weeks starting at Week 4
Plaque psoriasis	When **ALL** of the following are met ("1", "2", "3", and "4"): 1. Member's disease is moderate to severe as evidenced by **EITHER** of the following before or after systemic drug therapy ("a" or "b"): a. Psoriasis covers 10% or more of member's BSA b. Psoriasis covers less than 10% of member's BSA, but affects crucial body areas necessary for	Initial: • 160 mg (two 80 mg injections) at Week 0, followed by 80 mg at Weeks 2, 4, 6, 8, 10, and 12

	daily living activities (i.e., face, palms of hands, soles of feet, or genitals) 2. **EITHER** of the following* ("a" or "b"): a. Member has had an inadequate response to at least 3 months of continuous treatment with maximally tolerated methotrexate* (e.g., titrated to a dosage of 25 mg per week) b. **BOTH** of the following* ("i" and "ii"): i. Member has a contraindication to or intolerable adverse effects with methotrexate* [the specific contraindication and/or adverse effect(s) must be provided] ii. Member has had an inadequate response to at least 3 months of continuous treatment with **EITHER** oral cyclosporine* (at a dosage of at least 4 mg/kg per day) or acitretin (at a dosage of at least 25 mg per day), **OR** has contraindication(s) to and/or intolerable adverse effect(s) with **BOTH** cyclosporine and acitretin* [the specific contraindication(s) and/or adverse effect(s) must be provided; pregnancy is not considered a contraindication to the use of cyclosporine] 3. Member has had inadequate responses to **THREE** or more of the following self-administered therapies, **OR** has had intolerable adverse effects with or contraindications to **ALL** of the following self-administered therapies [the specific adverse effect(s) and/or contraindication(s) must be provided]: • adalimumab (Humira) • etanercept (Enbrel) • guselkumab (Tremfya) • risankizumab (Skyrizi) • secukinumab (Cosentyx) • ustekinumab (Stelara) 4. **EITHER** of the following ("a" or "b"): a. Member has had an inadequate response to, intolerable adverse effects with, or a contraindication to certolizumab pegol (Cimzia) b. Alternatives to the use of an anti-TNF biologic should be considered due to current or worsening congestive heart failure or demyelinating disease (e.g., multiple sclerosis)	Maintenance: • 80 mg every 4 weeks starting on week 16

Psoriatic arthritis (PsA) [including both axial and non-axial (peripheral) PsA]	When **ALL** of the following are met ("1", "2", "3", and "4"): 1. Member's disease is active (i.e., persistent joint inflammation) 2. **EITHER** of the following based on the dominate disease type* ("a" or "b"): a. **Axial PsA**: Member has had an inadequate response to, intolerable adverse effects with, or has a contraindication to at least **TWO** different NSAID therapies taken continuously for at least 2 weeks each at maximal doses* (e.g., celecoxib, diclofenac, ibuprofen, meloxicam, naproxen) [the specific adverse effect(s) or contraindication must be provided] b. **Peripheral PsA**: Member has had an inadequate response to, intolerable adverse effects with, or has a contraindication to at least **ONE** NSAID therapy taken continuously for at least 2 weeks at maximal doses* (e.g., celecoxib, diclofenac, ibuprofen, meloxicam, naproxen) [the specific adverse effect(s) or contraindication must be provided] **AND** **c.** Member has had an inadequate response to, intolerable adverse effects with, or has a contraindication to methotrexate at the maximally tolerated dosage (e.g., methotrexate titrated to 25 mg weekly), **OR**, if methotrexate is contraindicated or not tolerated, an inadequate response to another csDMARD* (e.g., cyclosporine, leflunomide, sulfasalazine) [the specific adverse effect(s) or contraindication must be provided] 3. Member has had an inadequate response to **TWO** or more of the following self-administered therapies, **OR** has had intolerable adverse effects with or has contraindications to **ALL** of the following self-administered therapies [the specific adverse effect(s) and/or contraindication(s) must be provided]: • adalimumab (Humira) • etanercept (Enbrel) • secukinumab (Cosentyx) • ustekinumab (Stelara) 4. **EITHER** of the following ("a" or "b"): a. Member has had an inadequate response to, intolerable adverse effects with, or a contraindication to certolizumab pegol (Cimzia) b. Alternatives to the use of an anti-TNF biologic	Initial: • 160 mg (two 80 mg injections) at Week 0 Maintenance: • 80 mg every 4 weeks starting at Week 4 For PsA members with coexistent moderate-to-severe plaque psoriasis, use the dosing regimen for plaque psoriasis

	should be considered due to current or worsening congestive heart failure or demyelinating disease (e.g., multiple sclerosis)	
Approval duration:12 weeks		
ASAS, Assessment of SpondyloArthritis International Society; BSA, body surface area; csDMARD, conventional synthetic disease modifying anti-rheumatic drug; NSAID, non-steroidal anti-inflammatory drug ***NOTE:** If the member has had an inadequate response to previous biologic therapy, other than ixekizumab, that is FDA-approved for the requested indication listed in Table 3, the member is not required to have had an inadequate response to non-biologic prerequisite therapy (e.g., for psoriasis, if member has previously had an inadequate response to etanercept, but does not have a history of inadequate response to methotrexate, they do not have to try methotrexate to meet medical necessity criteria). However, members must still meet the preferred self-administered product requirement.		

Continuation of ixekizumab (Taltz) **meets the definition of medical necessity** when **ALL** of the following criteria are met ("1", "2", "3", and "4"):

1. An authorization or reauthorization for ixekizumab has been previously approved by Florida Blue or another health plan in the past 2 years for the treatment of a condition listed in Table 3, **OR** the member previously met **ALL** indication-specific initiation criteria
2. Member has demonstrated a beneficial clinical response to ixekizumab therapy
3. Ixekizumab is **NOT** used in combination with **ANY** of the following:
    a. abatacept (Orencia)
    b. adalimumab (Humira)
    c. anakinra (Kineret)
    d. apremilast (Otezla)
    e. baricitinib (Olumiant)
    f. brodalumab (Siliq)
    g. certolizumab (Cimzia)
    h. etanercept (Enbrel)
    i. golimumab (Simponi, Simponi Aria)
    j. guselkumab (Tremfya)
    k. infliximab products (Remicade, Inflectra, Renflexis)
    l. risankizumab (Skyrizi)
    m. sarilumab (Kevzara)
    n. secukinumab (Cosentyx)
    o. tildrakizumab-asmn (Ilumya)
    p. tocilizumab (Actemra)

q. tofacitinib (Xeljanz, Xeljanz XR)
r. upadacitinib (Rinvoq)
s. ustekinumab (Stelara)
t. vedolizumab (Entyvio)

4. The dosage of ixekizumab does not exceed the following based on the indication for use:
   a. Plaque psoriasis
      - First 12 week of treatment – 80 mg every 2 weeks (weeks 2, 4, 6, 8, 10, and 12)
      - After 12 weeks of treatment - 80 mg every 4 weeks starting on week 16
   b. PsA and axial spondyloarthritis - 80 mg every 4 weeks starting on week 4

Approval duration: 1 year

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 adults 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).
- Administered by subcutaneous injection. The recommended dose is for 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. 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 PsA patients, ixekizumab may be administered alone or in combination with a csDMARD (e.g., methotrexate). For AS patients, csDMARDs (e.g., sulfasalazine), corticosteroids, NSAIDs, and/or analgesics may be used during treatment with ixekizumab.
- 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.
- 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 (cartons of 1, 2, or 3)

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 past 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 ≤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 (≥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, TNFα, 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:

The following codes may be used to describe:

HCPCS Coding

J3590	Unclassified biologics

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
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: BCBSF 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:

Axial PsA (a.k.a., psoriatic spondylitis): a subset of psoriatic arthritis that affects the spine (i.e., spondylitis) and/or spinal joints (e.g., the sacroiliac joint between the sacrum and ilium of pelvis). Axial PsA shares similar clinical findings to patients with ankylosing spondylitis (AS); however, patients with axial PsA are often less symptomatic, have asymmetric disease, and tend to have less severe disease. In addition, the psoriatic plaques or nail changes present in patients with axial PsA are absent in patients with AS. About 5% of PsA patients have exclusively axial involvement, and 20 to 50% have both spinal and peripheral involvement, with peripheral joint involvement being the predominant pattern.

Axial Spondyloarthritis (SpA): an inflammatory disease where the main symptom is back pain, and where the x-ray changes of sacroiliitis may or may not be present. In ankylosing spondylitis (AS), the x-ray changes are clearly present. In non-radiographic axial spondyloarthritis (nr-axSpA); the x-ray changes are not present but you have symptoms. It is thought that nr-axSpA may be an earlier form of AS.

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).

Non-axial or peripheral PsA: a subset of psoriatic arthritis that does NOT affect the spine or spinal joints [e.g. elbow, wrist, knees, hands, feet, and digits (dactylitis)]. Peripheral involvement may be polyarticular (5 or more joints affected) or oligoarticular (a.k.a., pauciarticular) (4 or fewer joints affected). Approximately 95% of patients with PsA have involvement of the peripheral joints, predominantly the polyarticular form, whereas a minority has the oligoarticular form.

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:

Table 4: Conventional Synthetic DMARDs

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

Assessment of Spondyloarthritis International Society (ASAS) Diagnostic Criteria for Axial Spondylarthritis (SpA)

Patients with chronic (≥3 months) back pain, the onset of which occurs at <45 years of age, AND EITHER of the following:

1. Imaging arm:
    a. Sacroiliitis on imaging*****

        AND

    b. ≥1 SpA feature
2. Clinical arm:
    a. HLA-B27 positive

        AND

    b. ≥2 other SpA features

SpA features:

- Inflammatory back pain
- Arthritis
- Enthesitis (heel)
- Uveitis
- Dactylitis
- Psoriasis
- Crohn's/colitis
- Good response to NSAIDs
- Family history of SpA
- HLA-B27
- Elevated CRP

*****Active (acute) inflammation on MRI highly suggestive of sacroiliitis associated with SpA, or definite radiographic sacroiliitis according to modified New York criteria

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COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 11/13/19.

GUIDELINE UPDATE INFORMATION:

06/15/16	New Medical Coverage Guideline.
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.