09-J3000-04

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Reviewed: 11/09/22

Revised: 01/01/23

Subject: Tildrakizumab-asmn (Ilumya®) Injection

THIS MEDICAL COVERAGE GUIDELINE IS NOT AN AUTHORIZATION, CERTIFICATION, EXPLANATION OF BENEFITS, OR A GUARANTEE OF PAYMENT, NOR DOES IT SUBSTITUTE FOR OR CONSTITUTE MEDICAL ADVICE. ALL MEDICAL DECISIONS ARE SOLELY THE RESPONSIBILITY OF THE PATIENT AND PHYSICIAN. BENEFITS ARE DETERMINED BY THE GROUP CONTRACT, MEMBER BENEFIT BOOKLET, AND/OR INDIVIDUAL SUBSCRIBER CERTIFICATE IN EFFECT AT THE TIME SERVICES WERE RENDERED. THIS MEDICAL COVERAGE GUIDELINE APPLIES TO ALL LINES OF BUSINESS UNLESS OTHERWISE NOTED IN THE PROGRAM EXCEPTIONS SECTION.

Dosage/ Administration | Position Statement | Billing/Coding | Reimbursement | Program Exceptions | Definitions
Related Guidelines | Other | References | Updates

DESCRIPTION:

Tildrakizumab-asmn (Ilumya) was initially approved by the U.S. Food and Drug Administration (FDA) in March 2018 for the treatment of adults with moderate-to-severe plaque psoriasis who are candidates for systemic therapy or phototherapy. Tildrakizumab is an injectable humanized IgG1/k monoclonal antibody that selectively binds to the p19 subunit of interleukin-23 (IL-23) and inhibits its interaction with the IL-23 receptor. Interleukin-23 is a naturally occurring cytokine that is involved in inflammatory and immune response, and its blockade inhibits the release of proinflammatory cytokines and chemokines. Tildrakizumab was the second IL-23 antagonist to be approved by the FDA for the treatment of plaque psoriasis. The first IL-23 antagonist to be approved was guselkumab (Tremfya) in July 2017. Risankizumab was the third IL-23 to be approved by the FDA in May 2019. Ustekinumab (Stelara) was FDA-approved for plaque psoriasis in 2009 but inhibits both IL-12 and IL-23 via the p40 subunit found on both interleukins.

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 is 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 ≤1% after 3 months
- Acceptable response is either a BSA ≤3% or a BSA improvement ≥75% from baseline at 3 months after treatment initiation

POSITION STATEMENT:

Initiation of tildrakizumab-asmn (Ilumya) **meets the definition of medical necessity** when **ALL** of the following criteria are met ("1" to "6"):

1. Tildrakizumab will be used for the treatment of an indication listed in **Table 1**, and **ALL** indication-specific and maximum-allowable dosage criteria are met
2. The prescriber is a specialist in the area of the member's diagnosis (e.g., 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 tildrakizumab
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 tildrakizumab 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. The member is 18 years of age or older

Approval duration: 6 months (to allow for the first three initial doses)

Table 1

Indications and Specific Criteria		
Indication	**Criteria**	**Maximum Allowable Dosage***
Moderate to severe plaque psoriasis (PS)	**ONE** of the following: 1. The member has tried and had an inadequate response to **ONE** 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 **OR**	Initial: • 100 mg at Weeks 0 and 4 Maintenance: • 100 mg every 12 weeks starting at

	2. The member has an intolerance or hypersensitivity to **ONE** conventional agent used in the treatment of PS **OR** 3. The member has an FDA labeled contraindication to **ALL** conventional agents used in the treatment of PS **OR** 4. 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) **OR** 5. 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) **OR** 6. 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	Week 16 (i.e., Weeks 16, 28, 40, etc.)
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	Maximum dose supported by the FDA labeled indication or maximum dose supported in DrugDex with 1 or 2a level of evidence, AHFS, or NCCN compendium recommended use 1 or 2a
*The maximum allowable dose can be exceeded if - (1) the dose is supported in DrugDex with 1 or 2a level of evidence, AHFS, or NCCN compendium recommended use 1 or 2a for the requested indication **OR** (2) 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)		

Continuation of tildrakizumab-asmn (Ilumya) **meets the definition of medical necessity** when **ALL** of the following criteria are met ("1" to "6"):

1. An authorization or reauthorization for tildrakizumab 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 1**, **OR** the member has previously met **ALL** indication-specific initiation criteria
2. The prescriber is a specialist in the area of the member's diagnosis (e.g., 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 tildrakizumab
4. Member has had clinical benefit with tildrakizumab therapy
5. Member will **NOT** be using tildrakizumab 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. **EITHER** of the following ("a" or "b"):
    a. The dosage of tildrakizumab does not exceed 100 mg every 12 weeks
    b. The dose is supported in DrugDex with 1 or 2a level of evidence, AHFS, or NCCN compendium recommended use 1 or 2a for the requested indication, **OR** 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

- For the treatment of adults with moderate-to-severe plaque psoriasis who are candidates for systemic therapy or phototherapy.
- The recommended dose is 100 mg at Weeks 0, 4, and every twelve weeks thereafter. Tildrakizumab is administered by subcutaneous injection by a healthcare provider ONLY. Each pre-filled syringe is for single dose only.

Dose Adjustments

- Hepatic impairment: specific guidelines for dosage adjustments in hepatic impairment are not available; it appears that no dosage adjustments are needed.
- Renal impairment: specific guidelines for dosage adjustments in renal impairment are not available; it appears that no dosage adjustments are needed.

Drug Availability

- One single-dose prefilled syringe per carton that delivers 1 mL of a 100 mg/mL solution. Store refrigerated at 2°C to 8°C (36°F to 46°F) in the original carton to protect from light until the time of use. Do not freeze. Do not shake. Can be kept at room temperature at 25°C (77°F) for up to 30 days in the original carton to protect from light.

PRECAUTIONS:

Boxed Warning

- None

Contraindications

- Previous serious hypersensitivity reaction to tildrakizumab or to any of the excipients

Precautions/Warnings

- **Hypersensitivity**: Cases of angioedema and urticaria occurred in in clinical trials. If a serious hypersensitivity reaction occurs, discontinue tildrakizumab immediately and initiate appropriate therapy.
- **Infections**: Tildrakizumab may increase the risk of infection. Treatment should not be initiated in patients with any clinically important active infection until the infection resolves or is adequately treated. In patients with a chronic infection or a history of recurrent infection, consider the risks and benefits prior to prescribing tildrakizumab. Instruct patients to seek medical help if signs or symptoms of clinically important chronic or acute infection occur. If a patient develops a clinically important or serious infection or is not responding to standard therapy, monitor the patient closely and consider discontinuation until the infection resolves.
- **Pretreatment Evaluation for Tuberculosis**: Evaluate patients for tuberculosis (TB) infection prior to initiating treatment with tildrakizumab. Initiate treatment of latent TB prior to administering tildrakizumab. Monitor patients for signs and symptoms of active TB during and after treatment. Consider anti-TB therapy prior to initiation of tildrakizumab in patients with a past history of latent or active TB in whom an adequate course of treatment cannot be confirmed. Do not administer to patients with active TB infection.
- **Immunizations**: Prior to initiating therapy with tildrakizumab, consider completion of all age-appropriate immunizations according to current immunization guidelines. Avoid the use of live vaccines. No data are available on the response to live or inactive vaccines.

BILLING/CODING INFORMATION:

HCPCS Coding

J3245	Injection, tildrakizumab, 1 mg

ICD-10 Diagnosis Codes That Support Medical Necessity

L40.0	Psoriasis vulgaris

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:

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.

RELATED GUIDELINES:

Adalimumab (Humira), 09-J0000-46
Apremilast (Otezla), 09-J2000-19
Brodalumab (Siliq) Injection, 09-J2000-79
Certolizumab Pegol (Cimzia), 09-J0000-77
Etanercept (Enbrel), 09-J0000-38
Guselkumab (Tremfya), 09-J2000-87
Infliximab Products [infliximab (Remicade), infliximab-dyyb (Inflectra), and infliximab-abda (Renflexis)], 09-J0000-39
Ixekizumab (Taltz) Injection, 09-J2000-62
Psoralens with Ultraviolet A (PUVA), 02-10000-16
Risankizumab (Skyrizi), 09-J3000-45
Secukinumab (Cosentyx), 09-J2000-30

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)
Enbrel (etanercept)
Entyvio (vedolizumab)
Fasenra (benralizumab)

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)
Taltz (ixekizumab)
Tezspire (tezepelumab-ekko)
Tremfya (guselkumab)
Truxima (rituximab-abbs)
Tysabri (natalizumab)
Xolair (omalizumab)

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. Bilal J, Berlinberg A, Bhattacharjee S, et al. A Systematic Review and Meta-Analysis of the Efficacy and Safety of the Interleukin (IL)-12/23 and IL-17 Inhibitors Ustekinumab, Secukinumab, Ixekizumab, Brodalumab, Guselkumab, and Tildrakizumab for the Treatment of Moderate to Severe Plaque Psoriasis. J Dermatolog Treat. 2018 Mar 13:1-37.
3. Blauvelt A, Sofen H, Papp K, et al. Tildrakizumab Efficacy and Impact on Quality of Life Up to 52 Weeks in Patients with Moderate-to-Severe Psoriasis: A Pooled Analysis of Two Randomized Controlled Trials. J Eur Acad Dermatol Venereol. 2019 Aug 13.
4. 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.
5. Clinical Pharmacology powered by ClinicalKey [Internet]. Tampa, FL: Elsevier.; 2022. Available at: https://www.clinicalkey.com/pharmacology/. Accessed 10/25/22.
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. 2012; 27:305-311.

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. 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.
11. Ilumya (tildrakizumab-asmn injection) [package insert]. Merck & Co., Inc.; Whitehouse Station, NJ. April 2022.
12. 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.
13. Kimball AB, Papp KA, Reich K, et al. Efficacy and safety of tildrakizumab for plaque psoriasis with continuous dosing, treatment interruption, dose adjustments, and switching from etanercept: results from phase 3 studies. Br J Dermatol. 2019 Sep 5. [Epub ahead of print].
14. 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.
15. 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.
16. 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.
17. Micromedex Healthcare Series [Internet Database]. Greenwood Village, Colo: Thomson Healthcare. Updated periodically. Accessed 10/25/22.
18. Orphan Drug Designations and Approval [Internet]. Silver Spring (MD): US Food and Drug Administration; 2022 [cited 2022 Oct 25]. Available from: http://www.accessdata.fda.gov/scripts/opdlisting/oopd/index.cfm.
19. Papp K, Thaçi D, Reich K, et al. Tildrakizumab (MK-3222), an anti-interleukin-23p19 monoclonal antibody, improves psoriasis in a phase IIb randomized placebo-controlled trial. Br J Dermatol. 2015 Oct;173(4):930-9.
20. 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.
21. Reich K, Papp KA, Blauvelt A, et al. Tildrakizumab versus placebo or etanercept for chronic plaque psoriasis (reSURFACE 1 and reSURFACE 2): results from two randomised controlled, phase 3 trials. Lancet. 2017 Jul 15;390(10091):276-288.
22. Reich K, Warren RB, Iversen L, et al. Long-term efficacy and safety of tildrakizumab for moderate-to-severe psoriasis: pooled analyses of two randomized phase III clinical trials (reSURFACE 1 and reSURFACE 2) through 148 weeks. Br J Dermatol. 2019 Jun 19. [Epub ahead of print].
23. 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.

COMMITTEE APPROVAL:

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

GUIDELINE UPDATE INFORMATION:

06/15/18	New Medical Coverage Guideline.
01/01/19	Revision: HCPCS code updates. Added J3245 and removed C9399 and J3590.
10/15/19	Review and revision to guideline consisting of updating the description, position statement, related guidelines, definitions, and references.
07/01/20	Revision to guideline consisting of updating the description, position statement, and definitions.
01/01/21	Review and revision to guideline consisting of updating the position statement and references.
01/01/22	Review and revision to guideline consisting of updating the position statement and references.
03/15/22	Revision to guideline consisting of updating the position statement and other section.
01/01/23	Review and revision to guideline consisting of updating the description section, position statement, other section, and references. New drugs were added to the list of drugs that are not permitted for use in combination.