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# 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 is 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. 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 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 for the management of psoriasis and psoriatic arthritis 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, despite is being normally less effective than other traditional systemic agents, is also mentioned as an important systemic option 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 tildrakizumab: 9.1 - Tildrakizumab is recommended as a monotherapy treatment option in adult patients with moderate-to-severe plaque psoriasis (Strength of recommendation A) and 9.2 - The recommended dose is 100 mg given by in office physician-administered subcutaneous injection at wk 0 and wk 4 and every 12 wks thereafter (A).

The safety and efficacy of tildrakizumab leading to its FDA-approval for moderate-to-severe plaque psoriasis was assessed in two multicenter, randomized, double-blind, placebo-controlled, phase III trials known as reSURFACE 1 and reSURFACE 2. In both trials a total of 926 subjects were treated with either tildrakizumab (n=616) or placebo (n=310). Subjects had a Physician Global Assessment (PGA) score of ≥3 (moderate) on a 5-point scale of overall psoriasis disease severity, Psoriasis Area and Severity Index (PASI) score ≥12, AND a minimum body surface area (BSA) involvement of 10%. Subjects with guttate, erythrodermic, or pustular psoriasis were excluded. Subjects were randomized to either placebo or tildrakizumab (100 mg at Week 0, Week 4, and every twelve weeks thereafter [Q12W]) up to 64 weeks. The two co-primary endpoints, measured by the changes from baseline to Week 12, were (1) the proportion of subjects who achieved at least a 75% reduction in the PASI composite score (PASI75), and (2) the proportion of subjects with a PGA of 0 (“cleared”) or 1 (“minimal”) and at least a 2-point improvement. Other evaluated outcomes included the proportion of subjects who achieved a reduction from baseline in PASI score of at least 90% (PASI 90), a reduction of 100% in PASI score (PASI 100) at Week 12, and maintenance of efficacy up to Week 64. Subjects were predominantly men (69%) and white (80%), with a mean age of 46 years. At baseline, these subjects had a median affected BSA of 27%, a median PASI score of 17.8, and approximately 33% had a PGA score of 4 (“marked”) or 5 (“severe”). Approximately 34% had received prior phototherapy, 39% had received prior conventional systemic therapy, and 18% had received prior biologic therapy for the treatment of psoriasis. Approximately 16% of subjects had a history of psoriatic arthritis. The major efficacy results are presented in Table 1 below.

**Table 1: Efficacy Results at Week 12 in reSURFACE 1 and reSURFACE 2 Studies**

| | **reSURFACE 1** | | **reSURFACE 2** | |
|---|---|---|---|---|
| | **Ilumya 100 mg (n=309)** | **Placebo (n=154)** | **Ilumya 100 mg (n=307)** | **Placebo (n=156)** |
| **PGA of 0 or 1** | 58% | 7% | 55% | 4% |
| **PASI 75** | 64% | 6% | 61% | 6% |
| **PASI 90** | 35% | 3% | 39% | 1% |
| **PASI 100** | 14% | 1% | 12% | 0% |

Examination of age, gender, race, and previous treatment with a biologic did not identify differences in response to tildrakizumab among these subgroups at Week 12. In reSURFACE 1, subjects originally randomized to tildrakizumab and who were responders at Week 28 (i.e., PASI 75) were re-randomized to an additional 36 weeks of either maintaining the same dose of tildrakizumab Q12W or placebo. At Week

28, 229 (74%) subjects treated with tildrakizumab 100 mg were PASI 75 responders. At Week 64, 84% of subjects who continued on tildrakizumab 100 mg Q12W maintained PASI 75 compared to 22% of subjects who were re-randomized to placebo. In addition, for subjects who were re-randomized and also had a PGA score of 0 or 1 at Week 28, 69% of subjects who continued on tildrakizumab 100 mg Q12W maintained this response (PGA 0 or 1) at Week 64 compared to 14% of subjects who were rerandomized to placebo. For PASI 75 responders at Week 28 who were re-randomized to treatment withdrawal (i.e., placebo), the median time to loss of PASI 75 was approximately 20 weeks. In addition, for subjects who were re-randomized to placebo and also had a PGA score of 0 or 1 at Week 28, the median time to loss of PGA score of 0 or 1 was approximately 16 weeks**.** In the data collected from three phase III clinicals trials (n=705 for tildrakizumab 100 mg), adverse events occurred in 48.2% of subjects in the tildrakizumab group vs. 53.8% of subjects in the placebo group. The rates of serious adverse events were 1.4% in the tildrakizumab group and 1.7% in the placebo group. The adverse reactions that occurred in at least 1% of subjects treated with tildrakizumab 100 mg and more frequently than placebo included: upper respiratory infections (14% vs. 12%), injection site reactions (3% vs. 2%), and diarrhea (2% vs. 1%).

## POSITION STATEMENT:

Initiation of tildrakizumab-asmn (Ilumya) **meets the definition of medical necessity** when **ALL** of the following criteria are met ("1", "2", and "3"):

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

**Table 2**

| **Indications and Specific Criteria** | | |
|---|---|---|
| **Indication** | **Criteria** | **Maximum Allowable Dosage** |
| Plaque psoriasis | When **BOTH** of the following are met ("1" and "2"):<br>1. Member's disease is moderate to severe as evidenced by **EITHER** of the following before or after systemic drug therapy ("a" or "b"):<br>a. Psoriasis covers 10% or more of the member's body surface area (BSA)<br>b. Psoriasis covers less than 10% of the member's BSA, but affects crucial body areas necessary for daily living activities (i.e., face, palms of hands, soles of feet, or genitals)<br>2. **EITHER** of the following* ("a" or "b"):<br>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)<br>b. **BOTH** of the following ("i" and "ii"):<br>i. Member has a contraindication to or intolerable adverse effects with methotrexate [the specific contraindication and/or adverse effect(s) must be provided]<br>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] | Initial:<br>• 100 mg at Weeks 0 and 4<br>Maintenance:<br>• 100 mg every 12 weeks starting at Week 16 (i.e., Weeks 16, 28, 40, etc.) |
| **Approval duration**: 12 weeks (to allow for the first two initial doses) | | |
| *__NOTE:__ If the member has had an inadequate response to previous biologic therapy, other than tildrakizumab, that is FDA-approved for the requested indication listed in Table 2, the member is **NOT** required to have had an inadequate therapeutic 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).

Continuation of tildrakizumab-asmn (Ilumya) **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 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 2, **OR** the member has previously met **ALL** indication-specific initiation criteria
2. Member has demonstrated a beneficial clinical response to tildrakizumab therapy
3. Tildrakizumab will **NOT** be administered in combination with **ANY** of the following:
    a. abatacept (Orencia)
    b. adalimumab (Humira)
    c. anakinra (Kineret)
    d. apremilast (Otezla)
    e. brodalumab (Siliq)
    f. certolizumab (Cimzia)
    g. etanercept (Enbrel)
    h. golimumab (Simponi, Simponi Aria)
    i. guselkumab (Tremfya)
    j. infliximab products (Remicade, Inflectra, Renflexis)
    k. ixekizumab (Taltz)
    l. risankizumab (Skyrizi)
    m. sarilumab (Kevzara)
    n. secukinumab (Cosentyx)
    o. tocilizumab (Actemra)
    p. tofacitinib (Xeljanz, Xeljanz XR)
    q. upadacitinib (Rinvoq)
    r. ustekinumab (Stelara)
    s. vedolizumab (Entyvio)
4. The dosage of tildrakizumab does not exceed 100 mg every 12 weeks

**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**

- 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:

The following codes may be used to describe:

### HCPCS Coding

| | |
|---|---|
| J3245 | Injection, tildrakizumab, 1 mg |

### ICD-10 Diagnoses 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:** 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:

**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.

**Psoriasis Area Severity Index (PASI):** An index used to express the severity of psoriasis. It combines the severity (erythema, induration and desquamation) and percentage of affected area. The score ranges from 0 (no psoriasis on the body) to 72 (the most severe case of psoriasis). A score of 11 or greater suggests moderate-to-severe psoriasis. A web-based calculator can be found at: http://www.pasitraining.com

## 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:

None

## 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 [Internet]. Tampa (FL): Gold Standard, Inc.; 2010 [cited 2019 Aug 28]. Available from: http://www.clinicalpharmacology.com/
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. DRUGDEX System [Internet]. Greenwood Village (CO): Thomson Micromedex; Updated periodically [cited 2019 Aug 28]. Available from: http://www.thomsonhc.com/.
9. 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.
10. 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.

11. 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.
12. Ilumya (tildrakizumab-asmn injection) [package insert]. Merck & Co., Inc.; Whitehouse Station, NJ. August 2018.
13. 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.
14. 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]
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. 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
17. 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.
18. Orphan Drug Designations and Approval [Internet]. Silver Spring (MD): US Food and Drug Administration; 2019[cited 2019 Aug 28]. 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]

## COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the BCBSF Pharmacy Policy Committee on 09/11/19.

## GUIDELINE UPDATE INFORMATION:

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| 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. |