Blue Cross Blue Shield Blue Care Network of Michigan

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Effective Date: 06/06/2024

Spevigo® (spesolimab-sbvo)

HCPCS: J1747

Policy:

Requests must be supported by submission of chart notes and patient specific documentation.

A. Coverage of the requested drug is provided when all the following are met:
   a. FDA approved indication
   b. FDA approved age
   c. Patient has a history of generalized pustular psoriasis (GPP) as defined by the European Rare and Severe Psoriasis Expert Network
   d. For the treatment of GPP flares:
      i. Patient is experiencing a GPP flare of moderate-to-severe intensity defined by all of the following:
         a) A Generalized Pustular Psoriasis Physician Global Assessment (GPPGA) total score ≥ 3
         b) New or worsening pustules
         c) GPPGA pustulation sub-score ≥ 2
         d) ≥ 5% of body surface area (BSA) with erythema and the presence of pustules
      ii. Trial and failure, contraindication, or intolerance to one of the following systemic therapies: acitretin, cyclosporine, methotrexate, infliximab
   e. For the prevention of GPP flares:
      i. A GPPGA total score of 0 or 1
      ii. A history of at least 2 past moderate-to-severe GPP flares with new or worsening pustulation
      iii. Member must have tried at least one of the following systemic therapies for the prevention of GPP flares and continued to experience GPP flares either during treatment, following dose reduction, or following/within one year of treatment discontinuation, unless contraindicated or not tolerated: acitretin, methotrexate, cyclosporine, infliximab.
   f. Not to be used in combination with other biologics or targeted DMARDs
   g. Trial and failure, contraindication, OR intolerance to the preferred drugs as listed in BCBSM/BCN's utilization management medical drug list and/or BCBSM/BCN's prior authorization and step therapy documents.

B. Quantity Limitations, Authorization Period and Renewal Criteria
   a. Quantity Limits: Align with FDA recommended dosing
   b. Authorization Period:
      i. Spevigo IV: 12 weeks

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ii. Spevigo SC: One year at a time

c. Renewal Criteria:
   i. Spevigo IV: Not applicable as no further authorization will be provided.
   ii. Spevigo SC: Clinical documentation must be provided to confirm that current criteria are met and that the medication is providing clinical benefit.

***Note: Coverage and approval duration may differ for Medicare Part B members based on any applicable criteria outlined in Local Coverage Determinations (LCD) or National Coverage Determinations (NCD) as determined by Center for Medicare and Medicaid Services (CMS). See the CMS website at http://www.cms.hhs.gov/. Determination of coverage of Part B drugs is based on medically accepted indications which have supported citations included or approved for inclusion determined by CMS approved compendia.

Background Information:

- Generalized pustular psoriasis (GPP) is a rare and potentially life-threatening neutrophilic skin disease characterized by flares consisting of widespread eruptions of painful, sterile pustules. Patients with acute GPP may appear systemically ill and require hospital admission for adequate supportive care, and flares can be so disruptive to the system that they can trigger sepsis, cardiovascular complications, and renal failure. It is estimated that 1 out of every 10,000 people has GPP, and because it is so rare the condition is often under- or mis-diagnosed. Mortality ranges from 2% to 16% with deaths often attributed to septic shock and cardiorespiratory failure. Clinical course of GPP varies and can be relapsing with recurrent flares or persistent with intermittent flares. Flare frequency varies among patients and may be spontaneous or triggered by stress, infection, medication, or pregnancy.

- The European Rare and Severe Psoriasis Expert Network (ERASPEN) consensus statement on phenotypes of pustular psoriasis (2017) define GPP as macroscopically visible primary sterile pustules occurring on non-acral skin and not within psoriasis plaques. Per the ERASPEN, GPP may occur with or without systemic inflammation and with or without psoriasis vulgaris and should only be diagnosed when the condition has relapsed at least once or when it persists for more than 3 months. Of note, the National Psoriasis Foundation (NPF), in its 2023 consensus statement on GPP, indicates that our experience in the United States has shown that GPP can also occur on acral surfaces and may last fewer than three months.The ERASPEN also advises against counting pustules to measure GPP intensity as the spectrum can vary from discrete to confluent forms and notes there is an unmet need for development of a clinically validated standard to measure GPP severity.

- The goals of treatment of GPP are to improve skin manifestations, alleviate systemic symptoms, and minimize the risk for life-threatening systemic complications. There are no standard US or international guidelines for the treatment of GPP as high-quality data on the efficacy of treatments is lacking. Treatment options include systemic therapies, topicals, and phototherapy. Phototherapy has a delayed onset of action, and due to the widespread nature of GPP topicals may not be practical; therefore, these therapies are typically reserved as adjuncts to systemic therapy for the treatment of GPP.

- Japanese guidelines for the treatment of GPP (2018), a 2012 consensus statement on GPP from the NPF Medical Board, and joint guidelines on the treatment of psoriasis from the American Academy of Dermatology and NPF (2019, 2020) recommend an oral retinoid (e.g. acitretin), cyclosporine, methotrexate, and various biologics as potential systemic treatments for GPP. In the United States, these therapies are used off-label to treat GPP flares. The choice of systemic agent is based on disease severity and may differ between those with severe acute disease and those with stable disease. It should be noted that demonstration of efficacy with any of these agents is solely based on limited evidence from case reports and small, uncontrolled trials. No randomized controlled trials or other comparative studies have been done comparing treatment methods.

- A retinoid like acitretin is considered a first-line agent for GPP. Improvement (i.e., cessation of new pustule formation, initial improvement in other clinical signs) is typically seen within 7 to 10 days of initiating therapy, and a complete

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response is noted after 2 to 3 months of treatment. Methotrexate is an alternative, particularly for those intolerant to retinoids, with significant clinical improvement expected within 8 to 12 weeks of treatment. These agents can be continued for long-term maintenance treatment once the flare has resolved; however, due to their slow onset of action they are best suited for patients with less severe disease.

- More severe, acute GPP flares require rapid stabilization and improvement. For these patients, faster-acting drugs such as cyclosporine, infliximab, and interleukin (IL)-17 and IL -23 receptor antagonists are preferred. Cyclosporine and infliximab have a longer history of use compared to the IL-17 and IL-23 biologics, and both therapies are supported by the AAD, NPF, and Japanese guidelines. Marked improvement is often seen within the first few days of treatment with either of these agents. Some case reports with cyclosporine have demonstrated near-complete remission within 2 weeks, and Japanese guidelines cite the effects of infliximab as apparent within 24-48 hours in many cases and a clear effect often seen after 1 to 3 administrations. Once the flare has resolved, patients can be transitioned to alternative therapies like methotrexate or a retinoid for maintenance, or they can remain on infliximab. For those treated with cyclosporine, however, transitioning to another drug for maintenance is recommended due to side effect concerns with prolonged cyclosporine use.

- IL-17 inhibitors that have demonstrated benefit in small studies and case reports in GPP flares include secukinumab, ixekizumab and brodalumab. These drugs are approved to treat GPP in Japan and the Japanese guidelines support their use. Ustekinumab, an IL-23 inhibitor, has shown some efficacy in case reports for GPP; however, it is not approved for this indication in Japan and the Japanese guidelines suggest reserving use for those resistant to other treatment modalities. Dosing of interleukin receptor antagonists generally reflects doses recommended for plaque psoriasis; however, the optimal treatment regimen for GPP is unknown.

- In addition to select interleukin receptor antagonists, the tumor necrosis factor (TNF) inhibitors adalimumab and etanercept have demonstrated successful control of GPP in small numbers of patients. These drugs are considered second-line therapies for GPP flares by the 2012 NPF consensus and Japanese guidelines. Of note, there are reports of TNF inhibitors inducing pustular psoriasis, including GPP.

- Spevigo (spesolimab-sbvo) is the first and only therapy approved in the United States to treat GPP in adults and pediatric patients 12 years and older weighing at least 40 kg. It is an IL-36 inhibitor and is the first approved drug in this class. Loss-of-function mutations in the IL-36 receptor antagonist gene and other associated genes as well as overexpression of IL-36 cytokines in GPP skin lesions have been found in patients with GPP and support the role of the IL-36 pathway in the disease process.

- Spevigo for GPP flares was evaluated in the Phase II, randomized, multicenter, double-blind, placebo-controlled Effisayil-1 trial. Adults 18 to 75 years of age who had a history of GPP consistent with the ERASPEN diagnostic criteria and presenting with a GPP flare were randomly assigned in a 2:1 ratio to receive a single IV dose of Spevigo (n=35) or placebo (n=18). Patients were followed through week 12. The primary endpoint was a Generalized Pustular Psoriasis Physician Global Assessment (GPPGA) pustulation sub-score of 0 (no visible pustules) at the end of week 1. The key secondary end point was a GPPGA total score of 0 or 1 (clear or almost clear skin) at the end of week 1. Scores range from 0 to 4, with higher scores indicating greater disease severity. Refer to Appendix A for a full description of the GPPGA.

    - Trial participants were required to have a GPP flare of moderate to severe intensity as defined by the following:

        - A GPPGA total score of $\geq$ 3,

        - New or worsening pustules,

        - A GPPGA pustulation sub-score of $\geq$ 2, and

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- ≥5% of body-surface area with erythema and the presence of pustules.

- At the end of week 1, 54% (19 of 35) patients in the Spevigo group met the primary endpoint compared to 6% (1 in 18) in the placebo group ($p<0.001$). Additionally, 43% (15 of 35) of patients treated with Spevigo showed clear/almost clear skin compared to 11% (2 of 18) in the placebo group ($p=0.02$).

- Patients in both groups were eligible to receive a single open-label dose of Spevigo on day 8 if the flare symptoms persisted as defined by a GPPGA total score ≥ 2 at the end of week 1, a clinician assessment of GPP severity based on a modified Physician Global Assessment, and a GPPGA pustulation sub-score of ≥2 at week 1.

- Both groups were also eligible to receive rescue treatment with a single dose of Spevigo in the case of flare reoccurrence after week 1, which was defined as an increase of ≥2 points in both the GPPGA total score and the pustulation sub-score after a GPPGA total score of 0 or 1 had been reached. It should be noted that only one rescue dose with Spevigo was allowed in the trial if a patient experienced a reoccurrence of a GPP flare after achieving clinical response to either Spevigo at day 1, placebo at day 1, escape medication, or an open-label dose of Spevigo at Day 8. Subsequent flares were treated with standard of care therapy per the physician's discretion.

- All patients in the trial were followed through 12 weeks. Effect on pustular and skin clearance was sustained over 12 weeks, with 84.4% who received Spevigo having no visible pustules after the 12 week trial duration, and 81.3% having clear/almost clear skin. Additionally, clearance was accompanied by clinically significant improvements in quality of life and symptoms such as pain and fatigue.

- For patients not experiencing a flare, the Phase IIb, randomized, double-blind, placebo-controlled Effisayil-2 trial evaluated the safety and efficacy of Spevigo for SC administration in patients 12 to 75 years of age with a documented history of GPP consistent with the ERASPEN diagnostic criteria, a history of at least 2 GPP flares of moderate to severe intensity with new or worsening pustulation, and a GPPGA score of 0 or 1. Patients already receiving GPP treatment prior to randomization were required to discontinue treatment and must have had a history of flaring while on concomitant treatment for GPP or in case of dose reduction or discontinuation of these concomitant medications. Patients who were not on concomitant GPP treatment at randomization were required to have had at least two moderate to severe GPP flares in the past year, with at least one displaying evidence of either fever and/or elevated C-reactive protein and/or elevated white blood count, and/or asthenia, and/or myalgia.

    - Participants (n=123) were randomized 1:1:1:1 to one of four treatment arms: Spevigo 600 mg SC loading dose followed by 300 mg SC every 4 weeks (high dose); Spevigo 600 mg SC loading dose followed by 300 mg SC every 12 weeks (medium dose); Spevigo 300 mg SC loading dose followed by 150 mg SC every 12 weeks (low dose); or matched placebo.

    - The primary endpoint was the time to first GPP flare up to week 48, defined by a Generalized Pustular Psoriasis Physician Global Assessment (GPPGA) pustulation sub-score > 2 and an increase in GPPPGA total score by > 2 from baseline.

    - Results demonstrated that treatment with SC Spevigo (high dose) significantly reduced the risk of GPP flares by 84% over 48 weeks compared to placebo; by week 48, 3 (10%) of 30 patients in the high dose group experienced GPP flares compared to 16 (52%) of 31 patients in the placebo group.

- To treat a GPP flare, Spevigo is recommended as a single IV infusion. If flare symptoms persist, an additional dose may be administered one week after the initial dose. For patients not experiencing a flare, Spevigo is recommended

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as a subcutaneous (SC) injection for maintenance to prevent flare occurrence. Should a patient experience a flare during treatment with SC Spevigo, the flare can be treated with IV Spevigo.

- Spevigo fills an unmet need as the only FDA-approved treatment for GPP. The off-label alternatives that have been used historically can also be used for both flares and prevention and provide more cost-effective alternatives by comparison. It is unknown how Spevigo compares to the alternatives used for treating GPP or how these alternatives compare to one another.

References:

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Policy History		
#	Date	Change Description
1.6	Effective Date: 07/01/2024	UM medical management system update for MAPPO and BCNA for Spevigo SC
1.5	Effective Date: 06/06/2024	Updated to add FDA approved indication criteria and criteria for members with GPP not experiencing a flare and authorization period and renewal criteria specific to Spevigo SC
1.4	Effective Date: 04/25/2024	UM medical management system update for BCBS and BCN for Spevigo SC
1.3	Effective Date: 10/12/2023	Annual review of criteria performed, no changes were made
1.2	Effective Date: 10/13/2022	UM medical management system update for BCBS and BCN for Spevigo IV
1.1	Effective Date: 10/06/2022	New policy
1.0	Effective Date: 09/26/2022	UM medical management system update for MAPPO and BCNA for Spevigo IV

** The prescribing information for a drug is subject to change. To ensure you are reading the most current information it is advised that you reference the most updated prescribing information by visiting the drug or manufacturer website or http://dailymed.nlm.nih.gov/dailymed/index.cfm.*

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