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Policy Number: 060.000

Title: Coverage Determination Policy for Spesolimab-Sbzo (Spevigo)

Regions:	☒ **Texas**	☐ **Florida**	☐ **Indiana**	☐ **New Jersey**	☒ **New Mexico**

Impacted Areas:

- ☒ Network Management/Provider Services
- ☐ Member services
- ☐ Quality Management
- ☐ Credentialing
- ☐ IT
- ☐ Administration
- ☐ Compliance/delegation
- ☒ Utilization Management
- ☐ Case management
- ☐ Disease management
- ☒ Claims
- ☐ Human resources
- ☐ Finance
- ☒ Pharmacy
- ☐ ALL

Available LCD/NCD/LCA: None

Disclaimer:

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Title: Coverage Determination Policy for Spesolimab-Sbzo (Spevigo)

Coverage Policy Number: 060.000

Line of Business: Medicare Part B

Policy Type: Prior Authorization

Coverage Determination:

Initial/New Requests

Note: All patients should be evaluated for tuberculosis (TB) prior to initiating treatment. Spevigo should not be initiated in patients with clinically important active infection.

Spesolimab-Sbzo (Spevigo) is medically necessary for the treatment of **generalized pustular psoriasis (GPP) flares** when **ALL** of the following criteria are met:

A. Diagnosis of generalized pustular psoriasis (GPP) based on **BOTH** of the following:
   I. Presence of primary, sterile, macroscopically visible pustules on non-acral skin
   II. Pustulation is not restricted to psoriatic plaques
B. **ONE** of the following:
   I. Patient has a moderate to severe GPP flare based on ONE of the following:
      a. Generalized Pustular Psoriasis Physician Global Assessment (GPPPGA) total score ≥ 3 (moderate)
      b. Generalized Pustular Psoriasis Physician Global Assessment (GPPPGA) pustulation subscore ≥ 2 (mild)
      c. Erythema and pustules cover ≥ 5% of body-surface area
      d. New appearance or worsening of pustules
C. Patient is NOT receiving Spevigo in combination with **ANY** of the following:
   I. Biologic disease-modifying antirheumatic drug (DMARD) [e.g., Enbrel (etanercept), Humira (adalimumab), Cosentyx (secukinumab), Stelara (ustekinumab)]
   II. Janus kinase inhibitor [e.g., Xeljanz (tofacitinib)]
   III. Phosphodiesterase 4 (PDE4) inhibitor [e.g., Otezla (apremilast)]
D. Spevigo is dosed according to FDA approved dosing for GPP flares
E. Total dose of Spevigo does not exceed two doses per single GPP flare. One dose will be approved for initial requests.

   Note: If the patient has been treated with Spevigo for a previous GPP flare, then a new (different) GPP flare may be treated with up to two doses of Spevigo

Renewal/Continuation of Therapy Requests

1. **Spesolimab-Sbzo (Spevigo)** is medically necessary for renewal for the treatment of generalized pustular psoriasis (GPP) flares when **ALL** of the following criteria are met:

   A. **ALL** of the following:
      I. Patient has already received one initial dose of Spevigo for a current GPP flare
      II. Documentation that the patient requires a second dose of Spevigo in order to treat persistent GPP flare symptoms including **ONE** of the following:
         a. GPPPGA total score ≥ 2
         b. GPPPGA pustulation subscore ≥ 2
         c. Fever
         d. Asthenia
         e. Myalgia
         f. Elevated C-reactive protein
         g. Leukocytosis with peripheral blood neutrophilia (above the upper limit of normal [ULN]).
      III. The second dose of Spevigo is to be administered no sooner than one week after the initial dose of Spevigo
   B. Patient is NOT receiving Spevigo in combination with **ANY** of the following:
      I. Biologic disease-modifying antirheumatic drug (DMARD) [e.g., Enbrel (etanercept), Humira (adalimumab), Cosentyx (secukinumab), Stelara (ustekinumab)]
      II. Janus kinase inhibitor [e.g., Xeljanz (tofacitinib)]
      III. Phosphodiesterase 4 (PDE4) inhibitor [e.g., Otezla (apremilast)]
   C. Spevigo is dosed according to FDA approved dosing for GPP flares
   D. Total dose of Spevigo does NOT exceed two doses per single GPP flare

   Note: If the patient has been treated with Spevigo for a previous GPP flare, then a new (different) GPP flare may be treated with up to two doses of Spevigo

2. **Spesolimab-Sbzo (Spevigo)** is **unproven and not medically necessary** for the treatment of the following conditions and situations:

   A. Administration in excess of 2 doses per single GPP flare
   B. Atopic dermatitis
   C. Crohn´s disease
   D. Hidradenitis suppurativa
   E. Palmoplantar pustulosis
   F. Plaque psoriasis
   G. Prevention of GPP flares
   H. Ulcerative colitis

FDA Approved Dose and Indication

FDA Approved Indication	FDA Approved Dosing
Generalized pustular psoriasis, Flares	• 900 mg IV infusion over 90 minutes as a single administration • If GPP flare symptoms persist, an additional 900 mg IV infusion over 90 minutes may be administered 1 week after the initial dose

General Background

Generalized pustular psoriasis (GPP) is also known as von Zombusch psoriasis, is a rare and persistent auto inflammatory disease[1]. It typically presents as pustules, which cover large areas of the body and are accompanied with fever, shivers, intense episodes of itching, rapid pulse, fatigue, headache, nausea, muscle weakness, and even joint pain. GPP can lead to life threatening complications such as heart failure, renal failure and sepsis.

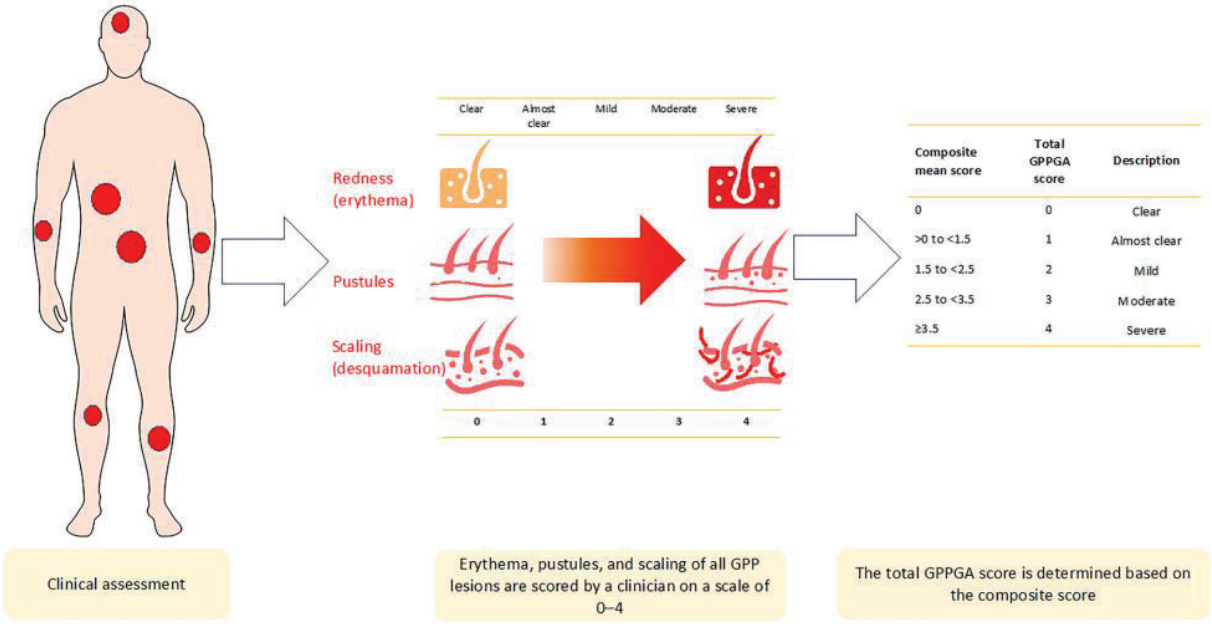
GPP is distinct from plaque psoriasis in clinical presentation, pathophysiology, histopathology, response to therapies, epidemiology and genetics. The clinical presentation of GPP is different from psoriasis vulgaris (PV) in its' episodic nature, often with normal appearing skin between very acute and severe disease flares. GPP is clinically characterized by the preponderance of pustules as the primary lesion on an erythematous base rather than red plaques covered with silvery scales representing the primary lesion of typical plaque psoriasis. GPP may be associated with systemic symptoms (fever, increased CRP and neutrophilia) and severe extra-cutaneous organ manifestations (liver, kidney failure, CV shock).

The European Rare And Severe Psoriasis Expert Network (ERASPEN) has defined consensus criteria that include as key diagnosis criteria for acute GPP the presence of primary, sterile, macroscopically visible pustules on non-acral skin (excluding cases where pustulation is restricted to psoriatic plaques), with or without systemic inflammation, with or without plaque-type psoriasis, either relapsing (> 1 episode) or persistent (> 3 months). Chronic GPP describes the state in between disease flares that may be characterized by the complete absence of symptoms or the persistence of residual skin symptoms such as erythema and scaling and minor pustulation.

Prior to Spevigo's approval, there were no FDA approved therapies for GPP, and treatment was limited to retinoids, cyclosporine, and methotrexate for non-biologic therapies[2].

Spevigo is a humanized antagonistic monoclonal immunoglobulin G1 antibody that blocks the activation of the interleukin-36 receptor (IL-36R), a signaling pathway within the immune system that is involved in the pathogenesis of generalized pustular psoriasis (GPP). 2 Binding of spesolimab-sbzo to IL36R prevents the subsequent activation of IL36R by cognate ligands (IL36 α, β and γ) and downstream activation of pro-inflammatory and pro-fibrotic pathways. IL36R signaling is differentiated from TNF-α, integrin and IL-23 inhibitory pathways by directly and simultaneously blocking both inflammatory and pro-fibrotic pathways.

Generalized Pustular Psoriasis Physician Global Assessment (GPPPGA)[3]



Composite mean score	Total GPPGA score	Description
0	0	Clear
>0 to <1.5	1	Almost clear
1.5 to <2.5	2	Mild
2.5 to <3.5	3	Moderate
≥3.5	4	Severe

Fig. 1 Generalized Pustular Psoriasis Physician Global Assessment (GPPGA) score is based on averaging the individual scores for erythema, scaling, and pustulation [13]. *GPP* generalized pustular psoriasis

Clinical Evidence

A phase 2, multicenter, randomized, double blind, placebo-controlled trial evaluated the safety and efficacy of spesolimab-sbzo in patients age 18 to 75 years who had generalized pustular psoriasis (GPP) and had a GPP flare of moderate-to-severe intensity. 2 A GPP flare of moderate-to-severe intensity was defined as: a GPPGA total score of ≥ 3, new or worsening pustules, a GPPGA pustulation subscore of ≥ 2, and ≥ 5% of bodysurface area with erythema and the presence of pustules. Patients who presented with a GPP flare were randomly assigned in a 2:1 ratio to receive a single intravenous dose of 900 mg of spesolimabsbzo or placebo. On day 8, patients from both groups were eligible to receive a single, open-label, intravenous dose of 900 mg of spesolimab-sbzo (which led to a crossover from placebo to open-label spesolimab-sbzo for some patients) if they had persistent symptoms, on the basis of a predefined threshold that consisted of a Generalized Pustular Psoriasis Physician Global Assessment (GPPGA) total score of 2 or higher at the end of week 1 (range, 0 [clear skin] to 4 [severe disease]) and a clinician assessment of GPP severity based on a modified Physician Global Assessment and a GPPGA pustulation subscore of 2 or higher at week 1 (range, 0 [no visible pustules] to 4 [severe pustulation]). The GPPGA total score is the average of the subscores for pustulation, erythema, and scaling. After week 1, rescue treatment with a single intravenous dose of 900 mg of spesolimab-sbzo could be administered in case of reoccurrence of a flare (defined as an increase of ≥ 2 points in both the GPPGA total score and the pustulation subscore after a GPPGA total score of 0 or 1 had been reached). Escape treatment was defined as standard-of-care therapy, according to the treating physician's choice, that was allowed for patients who had worsening of disease that warranted immediate treatment during week 1 and for patients with disease worsening who did not qualify for a rescue medication with open-label spesolimab-sbzo after week 1. The primary end point was a GPPGA pustulation subscore of 0 (no visible pustules) at the end of week 1. At the end of week 1, a total of 19 of the 35 patients (54%) who were assigned to the spesolimab-sbzo group and 1 of the 18 patients (6%) who were assigned to the placebo group had a GPPGA pustulation subscore of 0 (no visible pustules) (difference, 49 percentage points; 95% confidence interval [CI], 21 to 67; P < 0.001). A total of 15 patients (43%) who were assigned to the spesolimab-sbzo group and 2 patients (11%) who were assigned to the placebo group had a GPPGA total score of 0 or 1 (clear or almost clear skin) (difference, 32 percentage points; 95% CI, 2 to 53; P = 0.02). In Study Effisayil-1, subjects in either treatment group who continued to experience flare symptoms at Week 1 were eligible to receive a single open-label intravenous dose of 900 mg of Spevigo (second dose and first dose for subjects in the Spevigo and placebo groups, respectively). At Week 1, 12 (34%) subjects and 15 subjects (83%) in the SPEVIGO and placebo groups, respectively, received open-label Spevigo. In subjects who were randomized to Spevigo and received an open-label dose of Spevigo at Week 1, 5 (42%) subjects had a GPPPGA pustulation sub score of 0 at Week 2 (one week after their second dose of Spevigo).

Through the first week of treatment, adverse events were reported in 66% of the patients assigned to the spesolimab-sbzo group and 56% of those assigned to the placebo group. Pyrexia occurred in 6% of the patients who received spesolimab-sbzo and in 22% of those who received placebo; all pyrexia events occurred in the context of the underlying GPP flare, but pyrexia attributable to the drug cannot be ruled out. Infections were reported in 17% of the patients in the spesolimab-sbzo group and in 6% of those in the placebo group through the first week. At week 1, in the spesolimab-sbzo group, there were two cases of urinary tract infection and one case each of various other infections. Serious adverse events were reported in 6% of the patients who received spesolimab-sbzo and in none of the patients who received placebo in the first week. At week 12, a total of 82% of the patients who received at least one dose of spesolimab-sbzo (including those assigned to the placebo group who received open-label spesolimab-sbzo at day 8) had an adverse event, and 12% had a serious adverse event; in the spesolimab-sbzo group, the percentages of patients with adverse events remained unchanged or increased and the time-adjusted incidence rates decreased from week 1 to week 12. Infections were reported in 47% of the patients. There were three cases each of urinary tract infection and influenza; two cases each of folliculitis, otitis externa, upper respiratory tract infection, and pustule; and one case each of other infections. Symptoms that were observed in two patients who received spesolimab-sbzo were reported as a drug reaction with eosinophilia and systemic symptoms (DRESS) with RegiSCAR (European Registry of Severe Cutaneous Adverse Reactions) scores of 1 and 3.

HCPCS Code

HCPCS Code	Description
J1747	Spesolimab-Sbzo (Spevigo)

Acronyms

GPP = Generalized pustular psoriasis

DMARD = Biologic disease-modifying antirheumatic drug

TB = Tuberculosis

GPPPGA = Generalized Pustular Psoriasis Physician Global Assessment

PDE4 = Phosphodiesterase 4

ERASPEN = European Rare And Severe Psoriasis Expert Network

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