Spevigo® (Spesolimab-Sbzo)

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➲ Instructions for Use

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Coverage Rationale

Generalized Pustular Psoriasis (GPP)

Spevigo for intravenous use is proven for the treatment of generalized pustular psoriasis flares when all of the following criteria are met: [1,2]

- Diagnosis of generalized pustular psoriasis (GPP); **and**
- Patient has a GPP flare; **and**
- Spevigo is dosed according to U.S. Food and Drug Administration labeled dosing for GPP flares; **and**
- 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.] **and**
- Authorization will be for no more than 21 days

Spevigo for intravenous use is medically necessary for the treatment of generalized pustular psoriasis flares when all of the following criteria are met: [1,2,3]

- Diagnosis of generalized pustular psoriasis (GPP) based on **both** of the following:[2,3]
  - Presence of primary, sterile, macroscopically visible pustules on non-acral skin; **and**
  - Pustulation is not restricted to psoriatic plaques

  and
- One of the following:
  - Patient has a moderate to severe GPP flare based on **one** of the following:
    - Generalized Pustular Psoriasis Physician Global Assessment (GPPPGA) total score ≥ 3 (moderate); **or**
    - Generalized Pustular Psoriasis Physician Global Assessment (GPPPGA) pustulation subscore ≥ 2 (mild); **or**
    - Erythema and pustules cover ≥ 5% of body-surface area; **or**
    - New appearance or worsening of pustules

    or
  - **All** of the following:
    - Patient has already received one initial dose of Spevigo for a current GPP flare; **and**
    - Documentation that the patient requires a second dose of Spevigo in order to treat persistent GPP flare symptoms including **one** of the following:
      - GPPPGA total score ≥ 2; **or**
      - GPPPGA pustulation subscore ≥ 2; **or**
      - Fever; **or**
      - Asthenia; **or**
      - Myalgia; **or**

- Elevated C-reactive protein; **or**
- Leukocytosis with peripheral blood neutrophilia [above the upper limit of normal (ULN)]

and

- The second dose of Spevigo is to be administered no sooner than one week after the initial dose of Spevigo

and

- Patient is not receiving Spevigo in combination with another targeted immunomodulator [e.g., Enbrel (etanercept), Cimzia (certolizumab), Simponi (golimumab), Orencia (abatacept), adalimumab, Xeljanz (tofacitinib), Olumiant (baricitinib), Rinvoq (upadacitinib), Stelara (ustekinumab), Skyrizi (risankizumab)]; **and**
- Spevigo is dosed according to U.S. Food and Drug Administration labeled dosing for GPP flares; **and**
- 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) **and**
- Prescribed by a dermatologist; **and**
- Authorization will be for no more than 21 days

Spevigo for subcutaneous use is proven for the treatment of generalized pustular psoriasis. Spevigo for subcutaneous use is medically necessary for the treatment of generalized pustular psoriasis when all of the following criteria are met:[1]

- For **initial therapy**, **all** of the following:
  - Diagnosis of generalized pustular psoriasis (GPP) based on **both** of the following:[2,3]
    - Presence of primary, sterile, macroscopically visible pustules on non-acral skin; **and**
    - Pustulation is not restricted to psoriatic plaques

    and
  - **Both** of the following:
    - Used to prevent GPP flares; **and**
    - Patient is not currently experiencing a GPP flare

    and
  - **One** of the following:
    - Patient has previously been treated with intravenous **Spevigo** for a GPP flare; **or**
    - **All** of the following:
      - Patient has **not** previously been treated with intravenous **Spevigo** for a GPP flare; **and**
      - During the previous 12 months prior to initiating subcutaneous Spevigo the patient has had one or more moderate to severe GPP flares based on **one** of the following:
        - Generalized Pustular Psoriasis Physician Global Assessment (GPPPGA) total score ≥ 3 (moderate); **or**
        - Generalized Pustular Psoriasis Physician Global Assessment (GPPPGA) pustulation subscore ≥ 2 (mild); **or**
        - Erythema and pustules cover ≥ 5% of body-surface area; **or**
        - New appearance or worsening of pustules

        and
      - Prescriber attests that the patient has experienced flares of a severity and/or frequency such that they would clinically benefit from prophylactic therapy with subcutaneous Spevigo

    and
  - Patient is not receiving Spevigo in combination with another targeted immunomodulator [e.g., Enbrel (etanercept), Cimzia (certolizumab), Simponi (golimumab), Orencia (abatacept), adalimumab, Xeljanz (tofacitinib), Olumiant (baricitinib), Rinvoq (upadacitinib), Stelara (ustekinumab), Skyrizi (risankizumab)]; **and**
  - **One** of the following:
    - Spevigo is to be administered subcutaneously as a single loading dose for a patient that is not following treatment of a GPP flare with intravenous Spevigo; **or**
    - Prescriber attestation that the patient or caregiver is not able to be trained or is physically unable to administer maintenance subcutaneous Spevigo; prescriber must submit explanation

    and
  - Spevigo is dosed according to U.S. Food and Drug Administration labeled dosing for treatment of GPP when not experiencing a flare; **and**
  - Prescribed by a dermatologist; **and**
  - **For subcutaneous use not following treatment of GPP flare with intravenous Spevigo:** Authorization will be for one loading dose
  - **For subcutaneous use following treatment of GPP flare with intravenous Spevigo:** Initial authorization will be for no more than 12 months

- For **continuation of therapy**, **all** of the following:
  - Documentation of positive clinical response to subcutaneous Spevigo therapy; **and**
  - Patient is not receiving Spevigo in combination with another targeted immunomodulator [e.g., Enbrel (etanercept), Cimzia (certolizumab), Simponi (golimumab), Orencia (abatacept), adalimumab, Xeljanz (tofacitinib), Olumiant (baricitinib), Rinvoq (upadacitinib), Stelara (ustekinumab), Skyrizi (risankizumab)]; **and**
  - Prescriber attestation that the patient or caregiver is not able to be trained or is physically unable to administer maintenance subcutaneous Spevigo; prescriber must submit explanation; **and**
  - Spevigo is dosed according to U.S. Food and Drug Administration labeled dosing for treatment of GPP when not experiencing a flare; **and**
  - Prescribed by a dermatologist; **and**
  - Authorization will be for no more than 12 months

Spevigo (spesolimab-sbzo) is unproven and not medically necessary for the treatment of the following conditions and situations:

- Administration of intravenous Spevigo in excess of 2 doses per single GPP flare
- Atopic dermatitis
- Crohn´s disease
- Hidradenitis suppurativa
- Palmoplantar pustulosis
- Plaque psoriasis
- Ulcerative colitis

Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this policy does not imply that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

HCPCS Code	Description
J1747	Injection, spesolimab-sbzo, 1 mg

Diagnosis Code	Description
L40.1	Generalized pustular psoriasis

Background

Generalized pustular psoriasis is a severe skin disease characterized by the repeated occurrence of acute flares caused by systemic inflammation affecting the skin and internal organs.[4,9] GPP is distinct from plaque psoriasis in clinical presentation, pathophysiology, histopathology, response to therapies, epidemiology and genetics.[2] 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).[3] 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.

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.

The role of the interleukin-36 pathway in GPP is supported by the finding of loss-of-function mutations in the interleukin-36 receptor antagonist gene (IL36RN) and associated genes (CARD14, AP1S3, SERPINA3, and MPO) and by the overexpression of interleukin-36 cytokines in GPP skin lesions.[4-8]

Benefit Considerations

Some Certificates of Coverage allow for coverage of experimental/investigational/unproven treatments for life-threatening illnesses when certain conditions are met. The member specific benefit plan document must be consulted to make coverage decisions for this service. Some states mandate benefit coverage for off-label use of medications for some diagnoses or under some circumstances when certain conditions are met. Where such mandates apply, they supersede language in the benefit document or in the medical or drug policy. Benefit coverage for an otherwise unproven service for the treatment of serious rare diseases may occur when certain conditions are met. Refer to the Policy and Procedure addressing the treatment of serious rare diseases.

Clinical Evidence

Proven

Generalized Pustular Psoriasis Flares

A phase 2, multicenter, randomized, double blind, placebo-controlled trial (Study Effisayil-1) 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 body surface 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 spesolimab-sbzo 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.

A randomized, double-blind, placebo-controlled study (Study Effisayil-2) evaluated the efficacy and safety of spesolimab-sbzo for subcutaneous administration in adults and pediatric subjects (12 years of age and older and weighing at least 40 kg) with a history of at least two GPP flares of moderate-to-severe intensity in the past.[1] Patients were randomized to one of four treatment arms, including three different regimens for Spevigo and one placebo arm. The primary endpoint was the time to the first GPP flare up to week 48. For the recommended dosage regimen, the percentage of patients with a GPP flare was 10% with Spevigo vs. 52% with placebo (risk difference -39, 95% CI: -62, -16). The most common adverse reactions with Spevigo use for treatment of GPP in patients not experiencing a flare were injection site reaction, urinary tract infection, arthralgia, and pruritus.

Unproven

Plaque Psoriasis

Generalized pustular psoriasis (GPP) is a rare neutrophilic skin disease and is distinct from plaque psoriasis. Key exclusion criteria in a phase 2 trial (Effisayil™ 1) evaluating spesolimab-sbzo for the treatment of GPP flares were plaque psoriasis without pustules or with pustules restricted to psoriatic plaques.[2]

U.S. Food and Drug Administration (FDA)

This section is to be used for informational purposes only. FDA approval alone is not a basis for coverage.

Spevigo is a humanized anti–interleukin-36 receptor monoclonal antibody indicated for the treatment of generalized pustular psoriasis (GPP) in adults and pediatric patients 12 years of age and older and weighing at least 40 kg.[1]

References

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Policy History/Revision Information

Date	Summary of Changes
10/01/2024	**Related Policies** • Added reference link to the Medical Benefit Drug Policy titled *Provider Administered Drugs – Site of Care* **Supporting Information** • Archived previous policy version 2024D0119D

Instructions for Use

This Medical Benefit Drug Policy provides assistance in interpreting UnitedHealthcare standard benefit plans. When deciding coverage, the member specific benefit plan document must be referenced as the terms of the member specific benefit plan may differ from the standard plan. In the event of a conflict, the member specific benefit plan document governs. Before using this policy, please check the member specific benefit plan document and any applicable federal or state mandates. UnitedHealthcare reserves the right to modify its Policies and Guidelines as necessary. This Medical Benefit Drug Policy is provided for informational purposes. It does not constitute medical advice.

This Medical Benefit Drug Policy may also be applied to Medicare Advantage plans in certain instances. In the absence of a Medicare National Coverage Determination (NCD), Local Coverage Determination (LCD), or other Medicare coverage guidance, CMS allows a Medicare Advantage Organization (MAO) to create its own coverage determinations, using objective evidence-based rationale relying on authoritative evidence (Medicare IOM Pub. No. 100-16, Ch. 4, §90.5).

UnitedHealthcare may also use tools developed by third parties, such as the InterQual® criteria, to assist us in administering health benefits. UnitedHealthcare Medical Benefit Drug Policies are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice.