Spevigo®
(spesolimab-sbzo) injection

FOR PATIENTS WITH GENERALIZED PUSTULAR PSORIASIS (GPP)[1]

Treat GPP with Confidence

SPEVIGO is the only FDA-approved treatment for GPP[1,2]

SPEVIGO is 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 (88 lb).

SPEVIGO is contraindicated in patients with severe or life-threatening hypersensitivity to spesolimab-sbzo or to any of the excipients in SPEVIGO. Reported hypersensitivity reactions have included drug reaction with eosinophilia and systemic symptoms (DRESS) and anaphylaxis.

Please see below and throughout for Important Safety Information.

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

Infections: SPEVIGO may increase the risk of infections. In patients with a chronic infection or a history of recurrent infection, consider the potential risks and expected clinical benefits of treatment prior to prescribing SPEVIGO. Treatment with SPEVIGO is not recommended in patients with any clinically important active infection until the infection resolves or is adequately treated. Instruct patients to seek medical advice if signs or symptoms of clinically important infection occur during or after treatment with SPEVIGO. If a patient develops a clinically important active infection, discontinue SPEVIGO therapy until the infection resolves or is adequately treated.

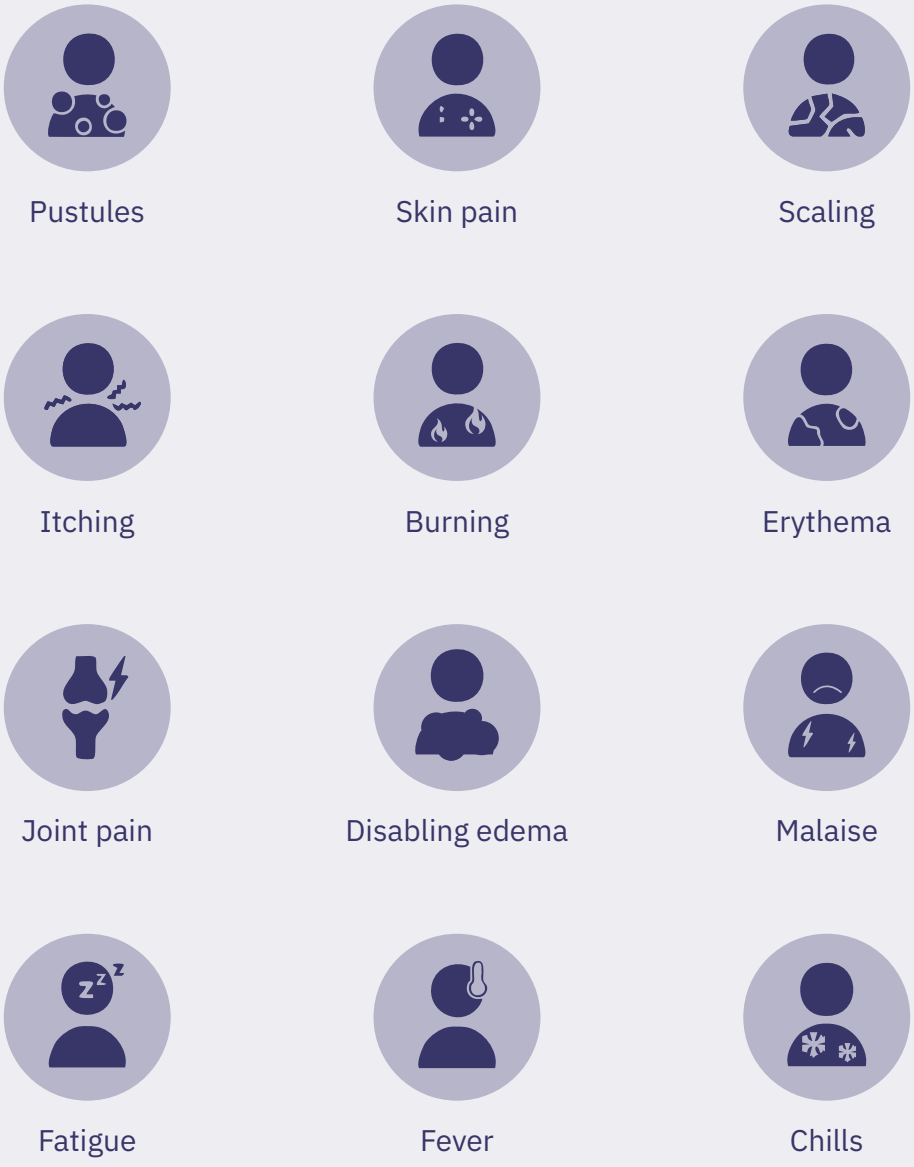
Risk of Tuberculosis: Evaluate patients for tuberculosis (TB) infection prior to initiating treatment with SPEVIGO. Avoid use of SPEVIGO in patients with active TB infection. Consider initiating anti-TB therapy prior to initiating SPEVIGO in patients with latent TB or a history of TB in whom an adequate course of treatment cannot be confirmed. Monitor patients for signs and symptoms of active TB during and after SPEVIGO treatment.

Please see additional SPEVIGO Important Safety Information on the following pages and the Prescribing Information, including Medication Guide.

GPP is chronic, heterogeneous, and unpredictable[3,4]

Generalized Pustular Psoriasis (GPP) is a serious, chronic, and persistent inflammatory skin disease with recurring flares that can impose a substantial burden on patients, even between flares.[5,6] Following a flare, GPP symptoms may continue.[6]*

Patients may exhibit skin symptoms and inflammatory symptoms under the skin[4,7,8]



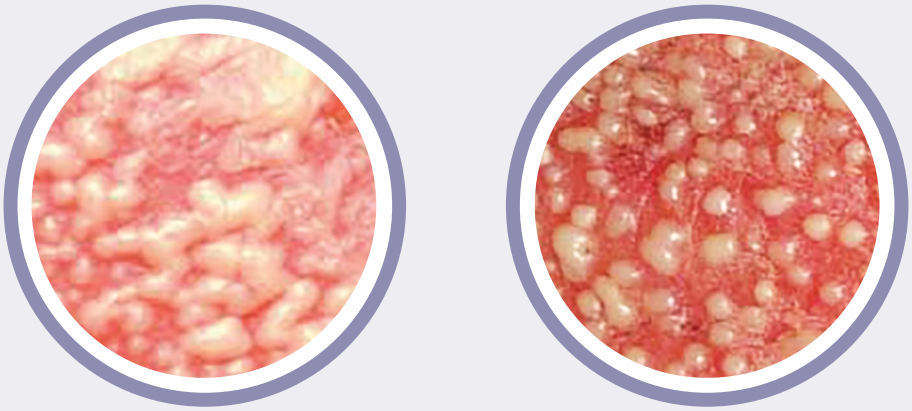
*Survey of dermatologists in the CorEvitas (previously Corrona) Psoriasis Registry (a collaboration with the National Psoriasis Foundation) who had treated adult patients (aged ≥18 years) with GPP within the past 5 years (N=29).[6]

GPP, generalized pustular psoriasis.

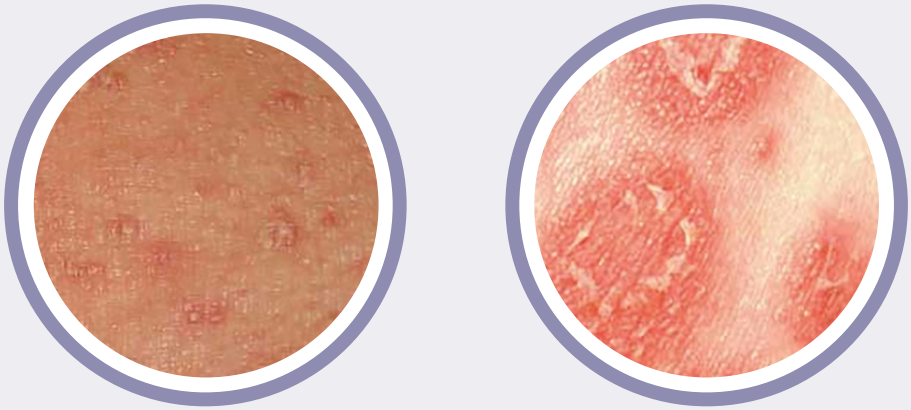
Please see SPEVIGO Prescribing Information, including Medication Guide.

GPP flare frequency, severity, and duration vary between patients and between flares[4]

GPP during a flare[9]



GPP between flares[9]



Skin biopsy is not required for the diagnosis of GPP, and it may delay treatment of this potentially life-threatening condition[10]

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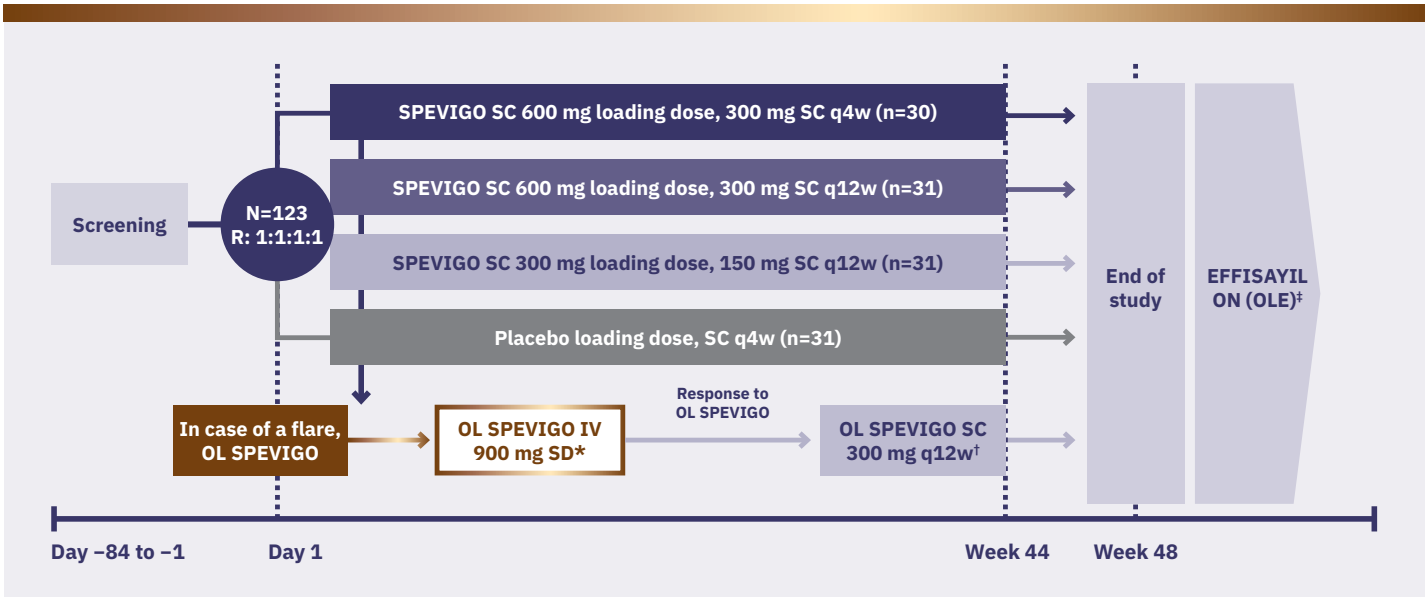
GPP, generalized pustular psoriasis.

Effisayil® 2 is the first placebo-controlled study in patients with GPP that focuses on treatment with Spevigo® SC when not experiencing a GPP flare[11,12]



While a 600 mg LD of SPEVIGO followed by 300 mg q12w dosage and a 300 mg LD of SPEVIGO followed by 150 mg q12w dosage were studied in Study EFFISAYIL 2, these dosages are not approved.[1]

Primary endpoint

Time to GPP flare, up to Week 48. GPP flare is defined as an increase of ≥2 in GPPPGA total score from baseline and a GPPPGA pustulation subscore ≥2.[1] Intake of open-label intravenous SPEVIGO or other investigator-prescribed medication for GPP worsening will be considered as an event.[11]

*An optional second dose of SPEVIGO 900 mg IV could be administered to patients with persistent flare symptoms at Day 8.[11]
†Patients receiving OL SPEVIGO 300 mg SC q12w have the option to escalate to 300 mg SC q4w.[11]
‡Patients will be given the opportunity to enter an OLE trial (EFFISAYIL ON, 1368-0025) if they have completed the treatment period in this study up to Week 48 (ie, no premature discontinuation of trial treatment), agree to participate in the OLE trial, and meet the trial eligibility criteria.[11]

GPP, generalized pustular psoriasis; GPPPGA, Generalized Pustular Psoriasis Physician Global Assessment; IV, intravenous; LD, loading dose; OL, open label; OLE, open-label extension; q4w, every 4 weeks; q12w, every 12 weeks; R, randomization; SC, subcutaneous; SD, single dose.

IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS (continued)

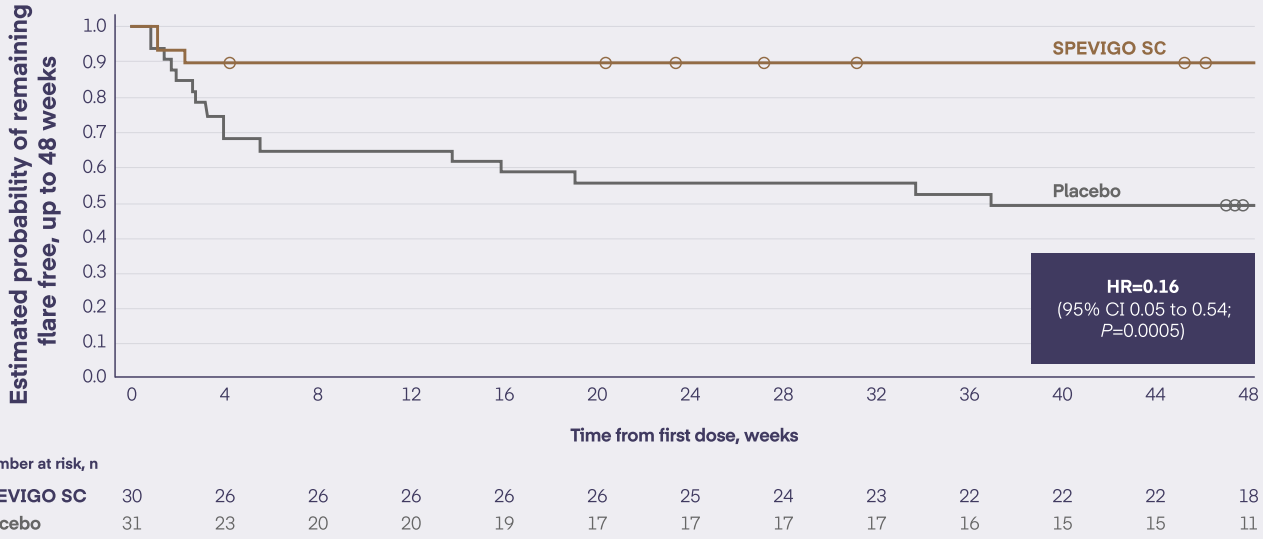
Hypersensitivity and Infusion-Related Reactions:

- Serious hypersensitivity reactions, including anaphylaxis and delayed reactions such as drug reaction with eosinophilia and systemic symptoms (DRESS), have been reported during and following administration of SPEVIGO. These reactions can occur with the first dose or subsequent doses.
- SPEVIGO is contraindicated in patients with severe or life-threatening hypersensitivity to spesolimab-sbzo or to any of the excipients in SPEVIGO. If a patient develops signs of anaphylaxis or other serious hypersensitivity, discontinue SPEVIGO immediately and initiate appropriate treatment.
- If a patient develops mild or moderate hypersensitivity during an intravenous infusion or other infusion-related reactions, stop SPEVIGO infusion and consider appropriate medical therapy (eg, systemic antihistamines and/or corticosteroids). Upon resolution of the reaction, the infusion may be restarted at a slower infusion rate with gradual increase to complete the infusion.

Please see SPEVIGO Prescribing Information, including Medication Guide.

Over 48 weeks of observation, SPEVIGO SC significantly reduced the relative risk of GPP flares by 84% vs placebo[11]

Time to first GPP flare, up to 48 weeks[11]



Number at risk, n

SPEVIGO SC	30	26	26	26	26	26	25	24	23	22	22	22	18
Placebo	31	23	20	20	19	17	17	17	17	16	15	15	11

No flares occurred in patients treated with SPEVIGO 300 mg SC after Week 4 through 48 weeks. Three patients experienced a GPP flare in the first 4 weeks after one dose of SPEVIGO SC.[11]

GPP flare is defined by an increase of ≥2 in GPPPGA total score from baseline and a GPPPGA pustulation subscore ≥2.[1]

While a 600 mg LD of SPEVIGO followed by 300 mg q12w dosage and 300 mg LD of SPEVIGO followed by 150 mg q12w dosage were studied in EFFISAYIL 2, these dosages are not approved. The recommended dosage of SPEVIGO for treatment of GPP when not experiencing a flare is subcutaneous LD of 600 mg followed by 300 mg subcutaneously, administered every 4 weeks.[1]

SPEVIGO SC was administered with a 600 mg subcutaneous loading dose followed by 300 mg subcutaneously every 4 weeks.[11]

CI, confidence interval; GPP, generalized pustular psoriasis; HR, hazard ratio; LD, loading dose; SC, subcutaneous; q12w, every 12 weeks.

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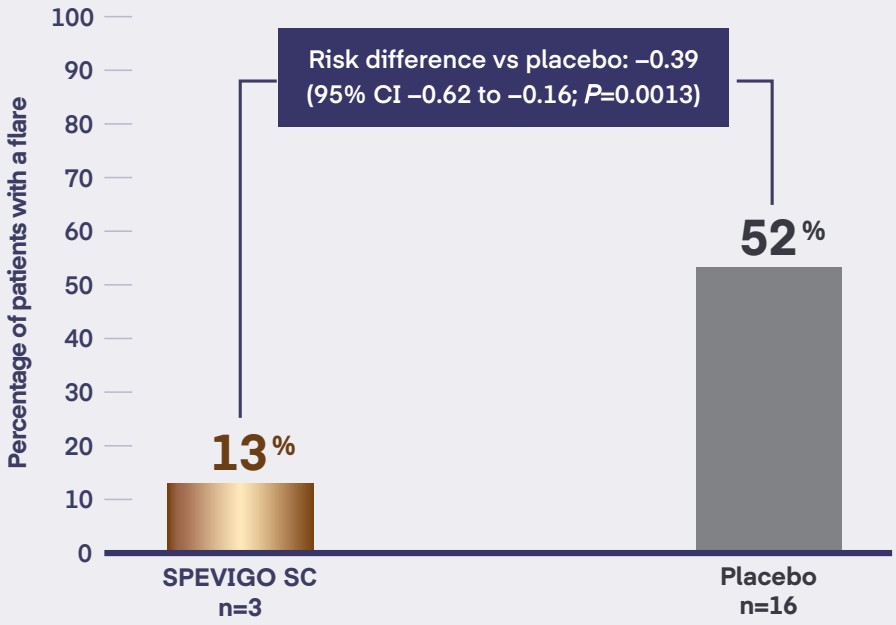
In the Spevigo® SC treatment arm, 87% of patients remained flare free over 48 weeks[11]*

Effisayil® 2 evaluated the occurrence of at least 1 GPP flare up to Week 48 as a key secondary endpoint[11]



Using a 1-sided α of 0.0063 (adjusted for multiplicity), SPEVIGO SC showed statistically significant improvement over placebo[11]

SPEVIGO SC was administered with a 600 mg subcutaneous loading dose followed by 300 mg subcutaneously every 4 weeks.[1]

*Measured as a binary outcome (flare or no flare) and defined as a GPPPGA pustulation subscore of ≥2 and an increase in the GPPPGA score of ≥2.[1,11]

CI, confidence interval; GPP, generalized pustular psoriasis; SC, subcutaneous.

IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS (continued)
Vaccinations: Prior to initiating SPEVIGO for treatment of GPP, complete all age-appropriate vaccinations according to current immunization guidelines. Avoid use of live vaccines in patients during and for at least 16 weeks after treatment with SPEVIGO. No specific studies have been conducted in SPEVIGO-treated patients who have recently received live viral or live bacterial vaccines.

ADVERSE REACTIONS
Intravenous SPEVIGO for Treatment of GPP Flare (Study Effisayil-1): Most common adverse reactions reported in ≥5% of patients treated with SPEVIGO in the clinical trial were asthenia and fatigue, headache, nausea, pruritus and prurigo, infusion site hematoma and bruising, and urinary tract infection (UTI).

Please see SPEVIGO Prescribing Information, including Medication Guide.

Adverse reactions with SPEVIGO SC for treatment of GPP when not experiencing a flare[1]

Regarding the exposure-adjusted incidence rates for subjects on randomized treatment prior to receiving rescue treatment for flare or completing the trial without a flare[1]

Adverse reaction, rate per 100 patient-years	SPEVIGO SC†	Placebo
Injection site reaction*	**31.6**	**12.7**
Urinary tract infection	18.0	0
Pruritus	8.8	0
Arthralgia	13.3	6.0

There were 3 subjects who discontinued subcutaneous SPEVIGO in the subcutaneous SPEVIGO cohort due to treatment-emergent adverse events (TEAEs) of psoriasis compared to no subjects in the placebo cohort who discontinued placebo for any TEAE.[1]

The safety analysis included all patients who were randomly assigned and received at least one treatment dose.[11]

*Injection site reactions included erythema, pain, swelling, induration, urticaria, and warmth at the injection site.[1]
†SPEVIGO SC was administered with a 600 mg subcutaneous loading dose followed by 300 mg subcutaneously every 4 weeks.[1]

GPP, generalized pustular psoriasis; SC, subcutaneous; TEAE, treatment-emergent adverse event.

IMPORTANT SAFETY INFORMATION (continued)

ADVERSE REACTIONS (continued)

Specific Adverse Reactions

- **Infections:** The most frequent adverse reactions that occurred in subjects treated with intravenous SPEVIGO were infections. During the 1-week placebo-controlled period in Study Effisayil-1, infections were reported in 14% of subjects treated with SPEVIGO compared with 6% of subjects treated with placebo. Serious infection (UTI) was reported in 1 subject (3%) in the SPEVIGO group and no subjects in the placebo group. Infections observed through Week 1 in Study Effisayil-1 in subjects treated with SPEVIGO were mild (29%) to moderate (71%).
- **Drug Reaction With Eosinophilia and Systemic Symptoms (DRESS):** Two cases of DRESS were reported in Study Effisayil-1 in subjects with GPP who were treated with intravenous SPEVIGO. RegiSCAR DRESS validation scoring (with the following categories: "no," "possible," "probable," or "definite" DRESS) was applied to the reported cases. Reported cases were assessed as "no DRESS" and "possible DRESS."

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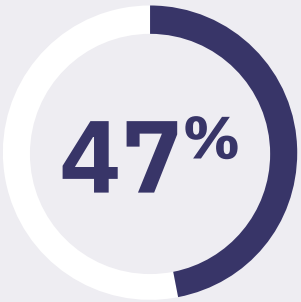
GPP may have a serious impact on patients even when they are not flaring[5]

In Effisayil® 2, 48% (n=15/31) of patients in the placebo group did not experience a GPP flare throughout the 48-week trial.[12]*

IN A POST HOC ANALYSIS, EVALUATING DISEASE BURDEN IN UNTREATED GPP PATIENTS,
GPP negatively impacted patients, even in the absence of a flare[12]



of non-flaring patients experienced **moderate pain and symptoms†‡**

of non-flaring patients experienced **severe pain†**

of non-flaring patients experienced **severe symptoms‡**

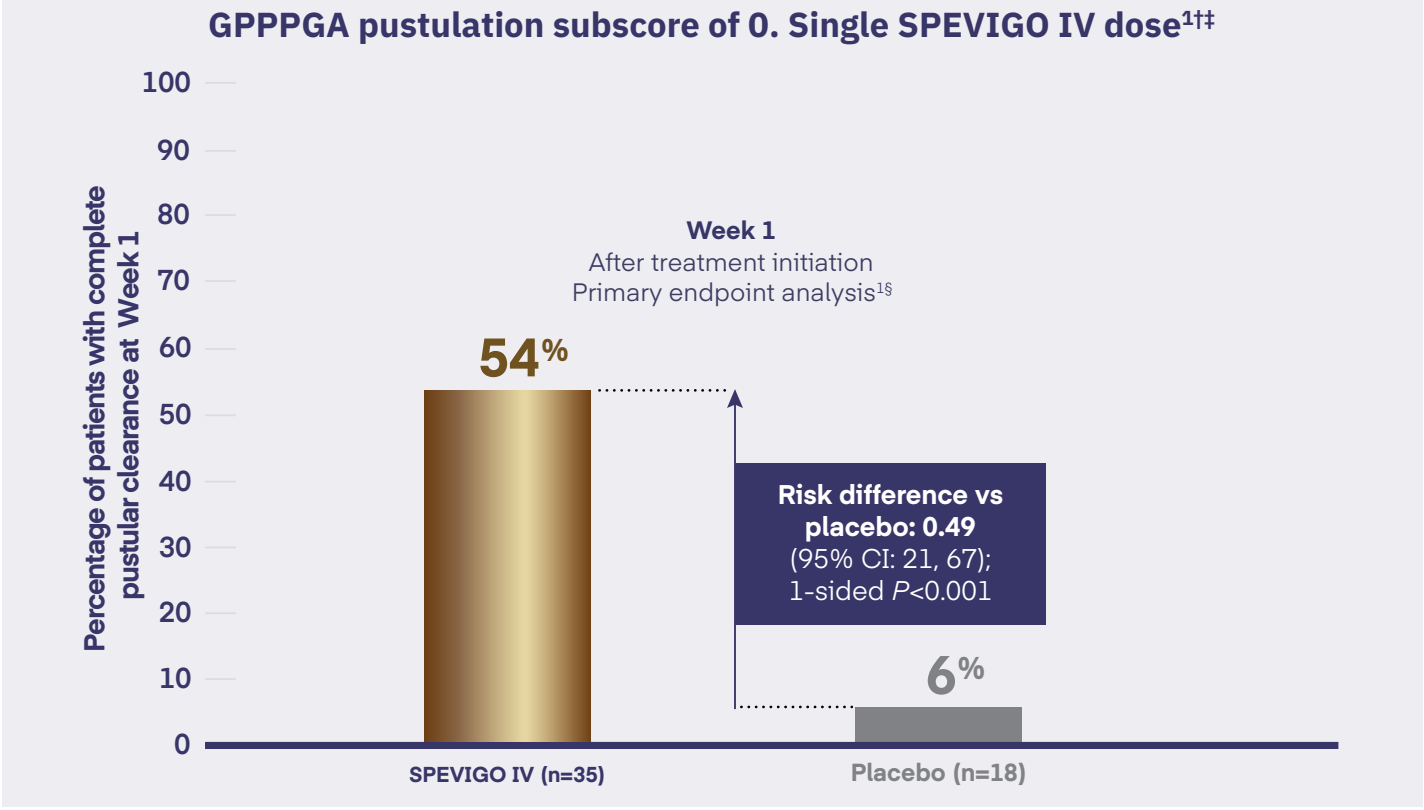
Post hoc analyses, even those based on observations from clinical trials, are not intended to be compared with results from prespecified analyses of controlled clinical trials. Differences in patient populations, outcome definitions, and methods of collecting data make it inappropriate to compare this analysis to controlled clinical trial outcome data. Data from a post hoc analysis should be viewed as relevant supplementary information. No information from this post hoc analysis should be in any way construed as making any claim about the efficacy, safety, or appropriateness of any specific therapy.

*GPP flare was defined as an increase in the GPPPGA total score of ≥2 from baseline and GPPPGA pustulation subscore of ≥2.[1]
†Patient-reported severity of pain was evaluated using the Pain VAS score (continuous scale 0-100; 0-4=no pain, 5-44=mild pain, 45-74=moderate pain, 75-100=severe pain).[12]
‡Patient-reported severity of GPP symptoms was evaluated using the PSS score (range 0-16; 0-3=no symptoms, 4-7=mild symptoms, 8-11=moderate symptoms, 12-15=severe symptoms, 16=very severe symptoms).[12]

GPP, generalized pustular psoriasis; GPPPGA, Generalized Pustular Psoriasis Physician Global Assessment; PSS, Psoriasis Symptom Scale; VAS, visual analog scale.

Please see SPEVIGO Prescribing Information, including Medication Guide.

With Spevigo® IV, 54% of patients achieved rapid and complete pustular clearance* at Week 1[1]



Effisayil® 1 was a multicenter, randomized, double-blind, placebo-controlled trial of SPEVIGO IV in patients with a GPP flare[1,13]

Primary endpoint

Proportion of patients with a GPPPGA pustulation subscore of 0 (no visible pustules) at Week 1 after treatment.[1]

Patients were randomized 2:1 to receive either a single 900 mg IV dose of SPEVIGO IV (n=35) or placebo (n=18) on Day 1.[13] At Week 1, patients in either treatment arm with persistent flare symptoms could receive a single dose of OL SPEVIGO IV.[1] Persistent flare was defined as ≥2 GPPPGA total score and ≥2 GPPPGA pustulation subscore.[13] Other therapies for GPP could be offered in case of disease worsening per the physician's discretion.[13] Patients must have discontinued biologics, retinoids, methotrexate, and/or cyclosporine before receiving their first dose of SPEVIGO IV or placebo.[13] After Day 8, patients with flare recurrence (defined as ≥2-point increase in GPPPGA total score and GPPPGA pustulation subscore after achieving clinical response [GPPPGA total score of 0 or 1]) could receive a 900 mg IV OL dose of SPEVIGO.[13] The key secondary endpoint was the proportion of patients with GPPPGA total score of 0 or 1 at Week 1.[13]

*Pustular clearance was defined as GPPPGA pustulation subscore of 0 (no visible pustules).[1]
†SPEVIGO IV was administered as a single 900 mg dose by intravenous infusion.[1]
‡Missing values or any use of other medication for GPP within the first week of the trial were regarded as nonresponse for the analysis of the endpoint.[13]
§54% of patients achieved the primary endpoint of pustular clearance at Week 1.[13]

CI, confidence interval; GPP, generalized pustular psoriasis; GPPPGA, Generalized Pustular Psoriasis Physician Global Assessment; IV, intravenous; OL, open label.

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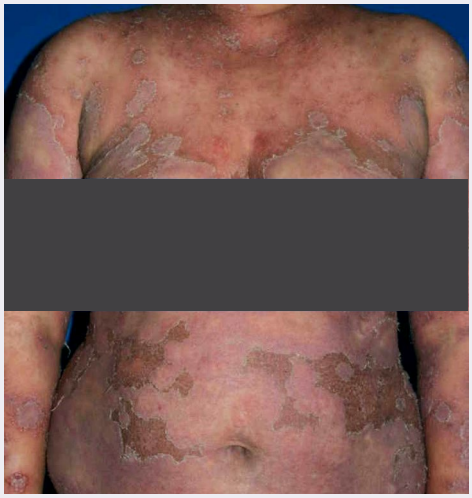
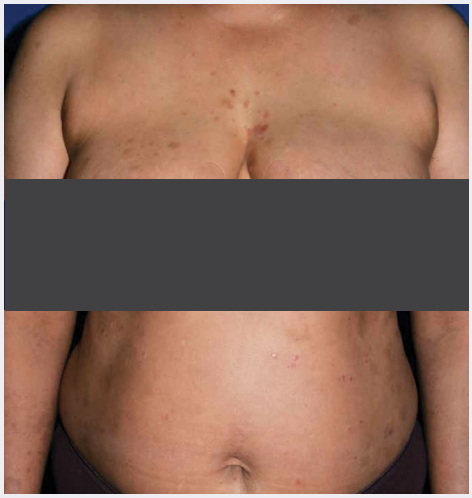
A patient from the Effisayil® 1 clinical trial[14]





Day 1

(Baseline, before **SPEVIGO IV**)

GPPPGA Pustulation Subscore (baseline): 3
GPPPGA Total Score (baseline): 3

Week 4

(4 weeks after **SPEVIGO IV**)

GPPPGA Pustulation Subscore: 0
GPPPGA Total Score: 1

GPPPGA, Generalized Pustular Psoriasis Physician Global Assessment; IV, intravenous.

IMPORTANT SAFETY INFORMATION (continued)

ADVERSE REACTIONS (continued)

Subcutaneous SPEVIGO for Treatment of GPP When Not Experiencing a Flare (Study Effisayil-2): Regarding the exposure-adjusted incidence rates for subjects on randomized treatment prior to receiving rescue treatment for flare or completing trial without a flare, the rate per 100-patient years for injection site reaction (including erythema, pain, swelling, induration, urticaria, and warmth at the injection site) was 31.6 for the subcutaneous SPEVIGO cohort (600 mg loading dose followed by 300 mg every 4 weeks) vs 12.7 for the placebo cohort. The rate per 100-patient years for UTI was 18 for SPEVIGO vs 0 for placebo. The rate per 100-patient years for pruritus was 8.8 for SPEVIGO vs 0 for placebo. The rate per 100-patient years for arthralgia was 13.3 for SPEVIGO vs 6 for the placebo cohort. There were 3 subjects who discontinued subcutaneous SPEVIGO due to treatment-emergent adverse events of psoriasis compared to no subjects in the placebo cohort who discontinued placebo for any treatment-emergent adverse event.

Safety in Study Effisayil-2 After Flare: In Effisayil-2, subjects who experienced a GPP flare and received at least one dose of an open-label single intravenous 900 mg dose of SPEVIGO were treated with open-label subcutaneous SPEVIGO 300 mg. These subjects (n=19) received subcutaneous dosing at every 12 weeks, which could have been increased to every 4 weeks based on GPPPGA total score or pustulation subscore increased by ≥1 from any previous open-label maintenance visit. The reported safety profile of open-label subcutaneous SPEVIGO use after treatment of GPP flare with open-label intravenous SPEVIGO use was consistent with the safety profiles of use of SPEVIGO from Trial Effisayil-1 and randomized controlled data from Trial Effisayil-2.

Clinical Development of Spesolimab-sbzo

- **Guillain-Barre Syndrome (GBS):** Among approximately 835 subjects exposed to spesolimab-sbzo during clinical development, GBS was reported in 3 subjects who received various doses of spesolimab-sbzo via various methods of administration in clinical trials for unapproved indications.

Please see SPEVIGO Prescribing Information, including Medication Guide.

Adverse reactions with Spevigo® IV for treatment of GPP flares[1]*

Selected adverse reactions occurring in ≥1% of the SPEVIGO IV group and more frequently than the placebo group through Week 1 in subjects with GPP flare (Study EFFISAYIL 1)[1]

Adverse reaction, n (%)	SPEVIGO IV† (n=35)	Placebo (n=18)
Asthenia and fatigue	3 (9)	1 (6)
Headache	3 (9)	1 (6)
Nausea	2 (6)	0
Pruritus and prurigo	2 (6)	0
Infusion site hematoma and bruising	2 (6)	0
Urinary tract infection	2 (6)	0
Bacteremia	1 (3)	0
Bacteriuria	1 (3)	0
Cellulitis	1 (3)	0
Herpes dermatitis and oral herpes	1 (3)	0
Upper respiratory tract infection	1 (3)	0
Dyspnea	1 (3)	0
Eye edema	1 (3)	0
Urticaria	1 (3)	0

In EFFISAYIL 1, additional adverse reactions that occurred through Week 12 in subjects treated with 1 single dose of randomized SPEVIGO were mild to moderate infections, including: device-related infection (3%), subcutaneous abscess (3%), furuncle (3%), and influenza (3%).[1]

*All AEs occurring between the start of treatment and the end of residual effect period (16 weeks after the placebo dose or last dose of SPEVIGO).[1] AEs were coded using the Medical Dictionary for Regulatory Activities 23.1. AE severity was graded according to the RCTC v2.0. Pustular psoriasis was excluded as an AE from this safety analysis. Data set at Week 12 included patients randomized to SPEVIGO who received up to 3 doses of SPEVIGO and patients randomized to the placebo group who received OL SPEVIGO at or after Day 8. All AEs in the residual effect period are included. SAEs—SPEVIGO IV at Week 1: Drug reaction with eosinophilia and systemic symptoms, urinary tract infection, drug-induced hepatic injury (considered to be a systemic symptom of drug reaction with eosinophilia and systemic symptoms) and arthritis; SPEVIGO IV at Week 12: Drug reaction with eosinophilia and systemic symptoms, urinary tract infection, drug-induced hepatic injury (considered to be a systemic symptom of drug reaction with eosinophilia and systemic symptoms), arthritis, worsening of chronic plaque psoriasis; influenza and squamous cell carcinoma of skin.[13]

†SPEVIGO IV was administered as a single 900 mg dose by intravenous infusion.[1]

AE, adverse event; IV, intravenous; OL, open label; RCTC, Rheumatology Common Toxicity Criteria; SAEs, serious adverse events.

IMPORTANT SAFETY INFORMATION (continued)

SPECIFIC POPULATIONS

Pediatric Use: The safety and effectiveness of SPEVIGO for the treatment of GPP have been established in pediatric patients 12 years of age and older and weighing at least 40 kg. Use of SPEVIGO for this indication is supported by data from a randomized, placebo-controlled study, which included 6 pediatric subjects 14 to 17 years of age with a history of GPP treated with subcutaneous SPEVIGO (Study Effisayil-2), and evidence from an adequate and well-controlled study of intravenous SPEVIGO in adults with GPP (Study Effisayil-1), with additional pharmacokinetic analyses showing similar drug exposure levels in adults and pediatric subjects 12 years of age and older and weighing 40 kg or more. The safety and effectiveness of SPEVIGO in pediatric patients younger than 12 years of age or in pediatric patients weighing less than 40 kg have not been established.

Please see SPEVIGO Prescribing Information, including Medication Guide.

Spevigo® (spesolimab-sbzo) injection

References

1. SPEVIGO. Prescribing Information. LEO Pharma Inc. **2.** Elewski B, Lebwohl MG. Management of chronic generalized pustular psoriasis: a review and expert opinion. *J Psoriasis Psoriatic Arthritis*. 2025;10(2):58–66. doi:10.1177/24755303251318976 **3.** Lebwohl MG, Medeiros RA, Mackey RH, et al. The disease burden of generalized pustular psoriasis: real-world evidence from CorEvitas' Psoriasis Registry. *J Psoriasis Psoriatic Arthritis*. 2022;7(2):71-78. doi:10.1177/24755303221079814 **4.** Choon SE, Navarini AA, Pinter A. Clinical course and characteristics of generalized pustular psoriasis. *Am J Clin Dermatol*. 2022;23(Suppl 1):21-29. doi:10.1007/s40257-021-00654-z **5.** Reisner DV, Johnsson FD, Kotowsky N, et al. Impact of generalized pustular psoriasis from the perspective of people living with the condition: results of an online survey. *Am J Clin Dermatol*. 2022;23(Suppl 1):S65-S71. doi:10.1007/s40257-021-00663-y **6.** Strober B, Kotowsky N, Medeiros R, et al. Unmet medical needs in the treatment and management of generalized pustular psoriasis flares: results from a survey of Corrona registry dermatologists. *Dermatol Ther (Heidelb).* 2021;11(2):529-541. doi:10.1007/s13555-021-00493-0 **7.** Rivera-Díaz R, Daudén E, Carrascosa JM, de la Cueva P, Puig L. Generalized pustular psoriasis: a review on clinical characteristics, diagnosis, and treatment. *Dermatol Ther (Heidelb).* 2023;13(3):673-688. doi:10.1007/s13555-022-00881-0 **8.** Benjegerdes KE, Hyde K, Kivelevitch D, Mansouri B. Pustular psoriasis: pathophysiology and current treatment perspectives. *Psoriasis (Auckl).* 2016;6:131-144. doi:10.2147/PTT.S98954 **9.** Burden AD, Bachelez H, Choon SE, et al. The Generalized Pustular Psoriasis Physician Global Assessment (GPPGA) score: online assessment and validation study of a specific measure of GPP disease activity. *Br J Dermatol.* 2023;189(1):138-140. doi:10.1093/bjd/ljad071 **10.** Armstrong AW, Elston CA, Elewski BE, et al; for the Medical Board of the National Psoriasis Foundation. Generalized pustular psoriasis: a consensus statement from the National Psoriasis Foundation. *J Am Acad Dermatol*. 2024;90(4):727-730. doi:10.1016/j.jaad.2023.09.080 **11.** Morita A, Strober B, Burden AD, et al. Efficacy and safety of subcutaneous spesolimab for the prevention of generalised pustular psoriasis flares (Effisayil 2): an international, multicentre, randomised, placebo-controlled trial. *Lancet*. 2023;402(10412):1541-1551. doi:10.1016/S0140-6736(23)01378-8 **12.** Strober B, Mostaghimi A, Anadkat MJ, et al. Measuring GPPGA, pain, symptom, and quality of life index scores in untreated generalized pustular psoriasis: results from the placebo group of the Effisayil 2 trial. Poster presented at Winter Clinical Dermatology Conference; January 12-17, 2024; Honolulu, HI. **13.** Bachelez H, Choon SE, Marrakchi S, et al., for the Effisayil 1 Trial Investigators. Trial of spesolimab for generalized pustular psoriasis. *N Engl J Med*. 2021;385(26):2431-2440. doi:10.1056/NEJMoa2111563 **14.** Data on file. LEO Pharma Inc.

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