Original Effective Date: 02/25/2023
Current Effective Date: 07/04/2024
Last P&T Approval/Version: 04/24/2024
Next Review Due By: 10/2024
Policy Number: C24676-A

Spevigo (spesolimab-sbzo)

PRODUCTS AFFECTED

Spevigo (spesolimab-sbzo)

COVERAGE POLICY

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Coverage Guideline must be read in its entirety to determine coverage eligibility, if any. This Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide Molina Healthcare complete medical rationale when requesting any exceptions to these guidelines.

Documentation Requirements:
Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

DIAGNOSIS:
Generalized Pustular Psoriasis

REQUIRED MEDICAL INFORMATION:
This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. If a drug within this policy receives an updated FDA label within the last 180 days, medical necessity for the member will be reviewed using the updated FDA label information along with state and federal requirements, benefit being administered and formulary preferencing. Coverage will be determined on a case-by case basis until the criteria can be updated through Molina Healthcare, Inc. clinical governance. Additional information may be required on a case-by-case basis to allow for adequate review. When the requested drug product for coverage is dosed by weight, body surface area or other member specific measurement, this data element is required as part of the medical necessity review. The Pharmacy and Therapeutics Committee has determined that the drug benefit shall be a mandatory generic and that generic drugs will be dispensed whenever available.

A. ACUTE TREATMENT OF GENERALIZED PUSTULAR PSORIASIS FLARE (IV ONLY):
   1. Documented diagnosis of generalized pustular psoriasis (GPP) flare
      AND
   2. Prescriber attests that other pustular and skin conditions have been ruled out (e.g., Synovitis–acne–pustulosis–hyperostosis–osteitis syndrome, Primary erythrodermic psoriasis vulgaris,

Plaque psoriasis without pustules, Plaque psoriasis with plaque limited pustules, Drug induced generalized exanthematous pustulosis, etc.)
AND

3. Prescriber attests, or clinical reviewer has found, the member is not experiencing a life- threatening flare of GPP or requires intensive care treatment
AND
4. FOR MEMBERS ON BACKGROUND TREATMENT WITH ORAL RETINOIDS, METHOTREXATE, OR CYCLOSPORINE: Prescriber attests this will be stopped before receiving spesolimab
AND
5. Documentation of moderate to severe intensity flare
AND
6. Prescriber attests, or clinical reviewer has found, a second dose will be given only if member continues to have significant pustulation and erythema compared to pre-treatment baseline OR member has worsening pustulation and/or erythema after some initial improvement
AND
7. Prescriber attests, or clinical reviewer has found, treatment plan for no more than 2 total doses, no more than 1 week apart
AND
8. Documentation member weighs at least 40kg
AND
9. Prescriber attests member does not have an active infection, including clinically important localized infections
AND
10. (a) Prescriber attests, or clinical reviewer has found, member has had a negative TB screening* or TB test (if indicated)** result within the last 12 months
*MOLINA REVIEWER NOTE: TB SCREENING assesses patient for future or ongoing TB exposure or risk and includes reviewing if they have been exposed to tuberculosis, if they have resided or traveled to areas of endemic tuberculosis, if patient resides or works in a congregate setting (e.g., correctional facilities, long-term care facilities, homeless shelters), etc.
**MOLINA REVIEWER NOTE: TB SKIN TEST (TST, PPD) AND TB BLOOD TEST (QuantiFERON TB Gold, T-Spot) are not required or recommended in those without risk factors for tuberculosis
OR
(b) For members who have a positive test for latent TB, provider documents member has completed a treatment course (a negative chest x-ray is also required every 12 months) OR that member has been cleared by an infectious disease specialist to begin treatment

B. CHRONIC TREATMENT OF GENERALIZED PUSTULAR PSORIASIS (SQ ONLY):

1. Documented diagnosis of generalized pustular psoriasis (GPP)
AND
2. Documentation member has experienced at least one GPP flare in the past
AND
3. Documentation of prescriber baseline disease activity evaluation and goals for treatment to be used to evaluate efficacy of therapy at renewal (e.g., time in remission, number of flares, etc.)
AND
4. Documentation member is NOT currently experiencing a flare (i.e., skin is clear or almost clear [normal or post inflammatory hyperpigmentation, faint diffuse pink or slight red skin only, no or discrete pustules, no scaling or crusting or it is superficial)]
AND
5. Documentation member weighs at least 40kg
AND
6. Prescriber attests member does not have an active infection, including clinically important localized infections
AND
7. (a) Prescriber attests, or clinical reviewer has found, member has had a negative TB screening* or

TB test (if indicated)** result within the last 12 months
*MOLINA REVIEWER NOTE: TB SCREENING assesses patient for future or ongoing TB exposure or risk and includes reviewing if they have been exposed to tuberculosis, if they have resided or traveled to areas of endemic tuberculosis, if patient resides or works in a congregate setting (e.g., correctional facilities, long-term care facilities, homeless shelters), etc.
**MOLINA REVIEWER NOTE: TB SKIN TEST (TST, PPD) AND TB BLOOD TEST (QuantiFERON TB Gold, T-Spot) are not required or recommended in those without risk factors for tuberculosis
OR
(b) For members who have a positive test for latent TB, provider documents member has completed a treatment course (a negative chest x-ray is also required every 12 months) OR that member has been cleared by an infectious disease specialist to begin treatment

CONTINUATION OF THERAPY:

A. ACUTE TREATMENT OF GENERALIZED PUSTULAR PSORIASIS FLARE: N/A

B. CHRONIC TREATMENT OF GENERALIZED PUSTULAR PSORIASIS:
   1. Adherence to therapy at least 85% of the time as verified by the prescriber or member medication fill history OR adherence less than 85% of the time due to the need for surgery or treatment of an infection, causing temporary discontinuation
      AND
   2. Prescriber attests to or clinical reviewer has found no evidence of intolerable adverse effects or drug toxicity
      AND
   3. Documentation of positive clinical response as demonstrated by low disease activity (e.g., maintained remission, decrease number of flares, etc.)
      AND
   4. (a) Prescriber attests, or clinical reviewer has found, member has had a negative TB screening* or TB test (if indicated)** result within the last 12 months for initial and continuation of therapy
      *MOLINA REVIEWER NOTE: TB SCREENING assesses patient for future or ongoing TB exposure or risk and includes reviewing if they have been exposed to tuberculosis, if they have resided or traveled to areas of endemic tuberculosis, if patient resides or works in a congregate setting (e.g., correctional facilities, long-term care facilities, homeless shelters), etc.
      **MOLINA REVIEWER NOTE: TB SKIN TEST (TST, PPD) AND TB BLOOD TEST (QuantiFERON TB Gold, T-Spot) are not required or recommended in those without risk factors for tuberculosis
      OR
      (b) For members who have a positive test for latent TB, provider documents member has completed a treatment course (a negative chest x-ray is also required every 12 months) OR that member has been cleared by an infectious disease specialist to begin treatment

DURATION OF APPROVAL:
Initial authorization: Acute treatment - 12 weeks (2 doses); Chronic treatment – 6 months, Continuation of Therapy: Acute treatment - N/A; Chronic treatment – 12 months

PRESCRIBER REQUIREMENTS:
Prescribed by or in consultation with a board-certified dermatologist [If prescribed in consultation, consultation notes must be submitted with initial request]

AGE RESTRICTIONS:
12 years of age and older

QUANTITY:
<u>IV for Treatment of GPP Flare:</u>

Initial dose: 900mg once
If flare symptoms persist, may administer an additional 900 mg dose one week after initial dose
MAXIMUM QUANTITY: Two 900 mg doses per flare

SQ for Chronic Prevention of GPP Flare:
600mg (four 150mg injections) once, followed by 300mg (two 150mg injections) 4 weeks later and every 4 weeks thereafter
After IV use after a flare, initiate or reinitiate Spevigo SQ 300mg every 4 weeks, 4 weeks after IV dose (no loading dose required)

PLACE OF ADMINISTRATION:
The recommendation is that infused medications in this policy will be for pharmacy or medical benefit coverage administered in a place of service that is a non-inpatient hospital facility-based location.

The recommendation is that injectable medications in this policy will be for pharmacy benefit coverage and patient self-administered.

DRUG INFORMATION

ROUTE OF ADMINISTRATION:
Intravenous, Subcutaneous

DRUG CLASS:
Antipsoriatics - Systemic

FDA-APPROVED USES:
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

COMPENDIAL APPROVED OFF-LABELED USES:
None

APPENDIX

APPENDIX:
None

BACKGROUND AND OTHER CONSIDERATIONS

BACKGROUND:
Spesolimab is a monoclonal antibody that inhibits IL-36 signaling by specifically binding to IL36R protein. This prevents activation of IL36R and overactive signaling of pro-inflammatory pathways. Spesolimab is approved for the treatment of a rare form of psoriasis called generalized pustular psoriasis. This is the first FDA approved drug for this condition.

Generalized pustular psoriasis is a skin condition characterized by widespread sterile pustules. It can occur in patients with other forms of psoriasis or on its own. It has sudden onset, and its often accompanied by fever, fatigue and weakness. Patients may also have leukocytosis, low albumin, and other signs of systemic inflammation. Serious complications may also arise that require intensive care treatment including sepsis and hepatic, respiratory or renal dysfunction. Some triggers have been identified and those include infection, exposure to and withdrawal from medications, especially antibiotics and steroids, hormonal fluctuations, and pregnancy although for many patients a trigger may not be

identified. The time course of flares seems to vary based on case reports, but even with treatment, flares may persist for 6 months to 2 years with lessening severity over time. Current recommended treatments include oral retinoids, like acitretin, methotrexate and cyclosporine. Internationally some biologic immunomodulators used for plaque psoriasis have been approved for use for GPP based on small, non-randomized trials.

Genetic mutations have been found that increase the risk of developing GPP. IL36RN is a gene that encodes for proteins that regulate inflammation, particularly in the skin. Mutations in the IL36RN gene reduce the amount of a protein in the skin needed to control the inflammatory signaling pathway, so without this control, these pro-inflammatory pathways are overly active.

Spesolimab was approved based on a phase 2, international, multicenter, randomized, double blind, placebo-controlled trial that investigated the safety and efficacy of spesolimab in patients with a GPP flare (Effisayil-1). Patients were included if they were 18-75 years of age and had GPP defined by the European Rare and Severe Psoriasis Expert Network (ERASPEN). Genetic testing was performed to look for mutations in IL36RN and other GPP associated genes, but patients were enrolled without regard to their mutation status. Patients were enrolled if their flare was determined to be moderate to severe intensity and covered at least 5% body surface area with erythema and pustules. Intensity was determined by the Generalized Pustular Psoriasis Physician Global Assessment total score rating severity of pustules, erythema and scaling. This is a 5 point scale from 0 which is clear skin to 4 which is severe disease. They also used a pustulation subscore which is also a 5 point scale ranging from 0 which is no visible pustules to 4 which is severe pustulation. Patients were excluded if they had other types of skin eruptions, or the pustules were limited to psoriatic plaques. Patients were excluded if they had a life-threatening flare of GPP or required intensive care treatment. Patients were allowed to be on maintenance medication with retinoids, methotrexate, or cyclosporine leading up to the trial, but were excluded if they required dose increase of their maintenance med immediately prior to randomization. And maintenance medications were required to be discontinued for the trial. The primary end point of the trial was a GPPGA pustulation subscore of 0, so no visible pustules, at the end of week 1. A key secondary endpoint evaluated GPPGA total score of 0 or 1 which is clear or almost clear skin at the end of week 1. Additional secondary endpoints were measured at week 4 and 12 and included psoriasis, pain and fatigue assessments.
The study enrolled 53 patients who”were’randomized 2 to 1 to receive Spesolimab or placebo. At the end of week 1, 54% of patients in the spesolimab group achieved a GPPGA pustulation subscore of 0 compared to 6% in the placebo group. This difference was found to be statistically significant. For the secondary end point at week 1, 43% of patients in the spesolimab group achieved a GPPGA total score of 0 or 1 compared to 11% in the placebo group and this was also found to be statistically significant. Because of the potential for GPP flares to be severe and life- threatening due to widespread systemic inflammation in addition to the cutaneous manifestations, the control period was 1 week and both active and placebo arms were offered an open-label dose on day 8 of the trial if they met criteria (GPPGA total score 2 or higher, pustulation subscore 2 or higher, or GPPGA total score increase by 2 or more after achieving 0 to 1 previously). After week 1, 83% of patients in the placebo arm received spesolimab. Because of this, the placebo comparator for secondary endpoints at week 4 and for the 12 week endpoint was lost. Of these patients, 73% reached a pustulation subscore of 0 one week after treatment (15 of 18 patients in the placebo arm). In the spesolimab group 34%, received an open label dose on day 8. Of these who received 2 doses, 42% achieved a pustulation subscore of 0 at week 2 (12 patients received 2 doses; 5 had subscore 0 at week 2). Maintenance of the pustulation subscore of 0 at week 12 ranged from 40% to 65% depending on the group being reported on (4 groups: Spesolimab all, Spesolimab single dose only, Spesolimab 2 doses, Placebo randomized + spesolimab day 8). Secondary endpoints at week

12 were all improved in the spesolimab randomized group.
There was no analysis provided based on IL36RN mutation. But it was reported that 5 patients in the Spesolimab group and 2 in the placebo group were found to have this mutation.
Safety was also evaluated during this trial. At the end of week 1, 66% of patients in the spesolimab group and 56% in the placebo group experienced an adverse event. Even though fever can occur as part of the GPP flare, fever was included in the adverse event review as fever due to the study drug could not be ruled out. At week 12 at the end of the study, 82% of patients who received at least 1 dose of spesolimab had an adverse event, and 12% were classified as serious. There were no deaths, 47% of patients reported infections. There was no consistency found in type of infection or pathogen. Two patients in the trial who received spesolimab had symptoms reported as DRESS – drug reaction with eosinophilia and systemic symptoms. DRESS is a severe adverse drug reaction characterized by extensive skin rash, organ involvement, lymphadenopathy, eosinophilia and lymphocytosis. One patient had a life-threatening reaction of drug induced hepatic injury. An external case assessment was done for both patients. In case 1, the patient's presentation was not found to be consistent with DRESS. Patient 2 was found to have possible DRESS by the external case assessment.

There is currently a 5-year open label extension trial that patients were offered enrollment in to studying a SC formulation for prevention of flares. From this trial, 39 patients of the 53 were enrolled in the extension trial.

In March 2024, Spevigo received FDA approval for a subcutaneous dosage form of spesolimab for the treatment of GPP when not experiencing a flare. This was based on a randomized, double-blind, placebo-controlled trial (Effisayil-2). The study was designed to evaluate the efficacy and safety of Spevigo 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. Subjects were randomized if they had a GPPPGA total score of 0 or 1 at screening (clear or almost clear skin). These subjects must have had a history of flaring while on concomitant treatment for GPP or a history of flaring upon dose reduction or discontinuation of these concomitant medications. Patients were able to receive IV Spevigo if they experienced a flare during the trial. The primary endpoint was time to first GPP flare and a key secondary endpoint was occurrence of at least one flare through week 48 of the trial. Spesolimab was found to be superior to placebo in GPP flare prevention, significantly reducing the risk of a GPP flare and flare occurrence over 48 weeks.

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:
All other uses of Spevigo (spesolimab-sbzo) are considered experimental/investigational and therefore, will follow Molina's Off- Label policy. Contraindications to Spevigo (spesolimab-sbzo) include: Severe or life-threatening hypersensitivity to spesolimab-sbzo or to any of the excipients in Spevigo, concurrent use of live vaccines.

OTHER SPECIAL CONSIDERATIONS:
If required, the 600 mg subcutaneous loading dose of Spevigo is to be administered by a healthcare professional. For subsequent 300 mg doses, if the healthcare professional determines that it is appropriate, a patient 12 years of age and older may self-inject or the caregiver may administer Spevigo after proper training in subcutaneous injection technique. In pediatric patients 12 to 17 years of age, administer Spevigo under the supervision of an adult.

CODING/BILLING INFORMATION

Note: 1) This list of codes may not be all-inclusive. 2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement

HCPCS CODE	DESCRIPTION
J1747	Injection, spesolimab-sbzo, 1 mg

AVAILABLE DOSAGE FORMS:
Spevigo SOLN 450MG/7.5ML single-dose vial
Spevigo INJ 150/1ML single-dose prefilled syringe

REFERENCES

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2. Bachelez, H., Choon, S., Marrakchi, S., Burden, A. D., Tsai, T., Morita, A., Lebwohl, M. G. (2021). Trial of spesolimab for generalized pustular psoriasis. New England Journal of Medicine, 385(26), 2431-2440. Doi:10.1056/nejmoa2111563
3. Supplement to: Bachelez, H., Choon, S., Marrakchi, S., Burden, A. D., Tsai, T., Morita, A., Lebwohl, M. G. (2021). Trial of spesolimab for generalized pustular psoriasis. New England Journal of Medicine, 385(26), 2431-2440. Doi:10.1056/nejmoa2111563
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6. Navarini, A., Burden, A., Capon, F., Mrowietz, U., Puig, L., Köks, S., Barker, J. (2017). European consensus statement on phenotypes of Pustular Psoriasis. Journal of the European Academy of Dermatology and Venereology, 31(11), 1792-1799. Doi:10.1111/jdv.14386
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8. Morita, A., Strober, B., A. David Burden, Siew Eng Choon, Anadkat, M. J., Slaheddine Marrakchi, … Lebwohl, M. (2023). Efficacy and safety of subcutaneous spesolimab for the prevention of generalized pustular psoriasis flares (Effisayil 2): an international, multicentre, randomized, placebo-controlled trial. The Lancet, 402(10412), 1541–1551. https://doi.org/10.1016/s0140-6736(23)01378-8

SUMMARY OF REVIEW/REVISIONS	DATE
REVISION- Notable revisions: Required Medical Information Continuation of Therapy Duration of Approval Age Restrictions Quantity Place of Administration Route of Administration FDA-Approved Uses Background Other Special Considerations References	Q2 2024
REVISION- Notable revisions: Required Medical Information Continuation of Therapy Duration of Approval Coding/Billing Information	Q4 2023
NEW CRITERIA CREATION	Q1 2023