PRODUCT MONOGRAPH

INCLUDING PATIENT MEDICATION INFORMATION

[Pr]**Spevigo®**

spesolimab for injection

Concentrate for solution for intravenous infusion

450 mg/7.5 mL (60 mg/mL)

Interleukin-36 Inhibitor

ATC code: L04AC22

Boehringer Ingelheim (Canada) Ltd.
5180 South Service Road
Burlington, Ontario
L7L 5H4
www.boehringer-ingelheim.ca

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PART I: HEALTH PROFESSIONAL INFORMATION

1 INDICATIONS

Spevigo (spesolimab for injection) is indicated for the treatment of flares in adult patients with generalized pustular psoriasis (GPP).

1.1 Pediatrics (<18 years of age)

The safety and efficacy of Spevigo in children below the age of 18 years have not been established. No data are available in this population.

1.2 Geriatrics (≥65 years of age)

No dose adjustment is required. There is limited information in patients 65 years and older.

2 CONTRAINDICATIONS

Spevigo is contraindicated in patients with severe or life-threatening hypersensitivity to this drug or to any ingredient in the formulation, including any non-medicinal ingredient, or component of the container. For a complete listing, see 6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING.

4 DOSAGE AND ADMINISTRATION

4.1 Dosing Considerations

Treatment with Spevigo should be initiated by physicians experienced in the management of patients with inflammatory skin diseases.

4.2 Recommended Dose and Dosage Adjustment

The recommended dose of Spevigo is a single dose of 900 mg (2 x 450 mg/7.5 ml vials) administered as an intravenous infusion. If flare symptoms persist, an additional 900 mg dose may be administered 1 week after the initial dose.

Pediatrics (<18 years of age)

The safety and efficacy of Spevigo in pediatric patients have not been established. No data are available in this population.

Geriatrics (≥65 years of age)

No dose adjustment is required. There is limited information in patients aged 65 years and older.

Renal or Hepatic Impairment

Spevigo has not been studied in these patient populations. These conditions are generally not expected to have any clinically relevant impact on the pharmacokinetics of monoclonal antibodies and no dose adjustments are considered necessary.

4.3 Reconstitution

Parenteral Products:

Instructions for Dilution

Spevigo must be diluted before use.

The vial should be visually inspected before use. Spevigo is a colourless to slightly brownish-yellow, clear to slightly opalescent solution. If the solution is cloudy, discoloured, or contains large or coloured particulates, the vial should be discarded.

Preparation

- Use aseptic technique to prepare the solution for infusion.
- Draw and discard 15 mL from a 100 mL container of sterile 0.9% sodium chloride solution.
- Slowly replace with 15 mL of Spevigo (complete content from two vials of 450 mg/7.5 mL).
- Mix gently before use.
- The diluted Spevigo solution for infusion should be used immediately.

Spevigo is for single-use only and does not contain preservatives.

4.4 Administration

- Do not mix Spevigo with other medicinal products.
- Administer Spevigo as a continuous intravenous infusion through an intravenous line containing a sterile, non-pyrogenic, low protein binding in-line filter (pore size of 0.2 micron) over 90 minutes.
- If the infusion is slowed or temporarily stopped, the total infusion time (including stop time) should not exceed 180 minutes (see 7 WARNINGS AND PRECAUTIONS).
- A pre-existing intravenous line may be used for administration of Spevigo. The line must be flushed with sterile 0.9% sodium chloride solution prior to and at the end of infusion. No other infusion should be administered in parallel via the same intravenous access.
- No incompatibilities have been observed between Spevigo and infusion sets composed of polyvinylchloride (PVC), polyethylene (PE), polypropylene (PP), polybutadiene and polyurethane (PUR), and in-line filter membranes composed of polyethersulfone (PES, neutral and positively charged) and positively charged polyamide (PA).

5 OVERDOSAGE

There is no clinical experience with overdoses of Spevigo.

The highest dose of Spevigo administered in clinical trials was 1200 mg. Adverse events observed in subjects receiving single or repeated doses up to 1200 mg were consistent with the known safety profile of Spevigo.

In the event of overdose, it is recommended that the patient be monitored for any signs or symptoms of adverse reactions and symptomatic treatment be instituted as appropriate.

For management of a suspected drug overdose, contact your regional poison control centre.

6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

Table 1 - Dosage Forms, Strengths, Composition and Packaging

Route of Administration	Dosage Form / Strength / Composition	Non-medicinal Ingredients
Intravenous infusion	Concentrate for Solution for Infusion 450 mg/7.5 mL (60 mg/mL)	Arginine hydrochloride, glacial acetic acid, polysorbate 20, sodium acetate trihydrate, sucrose, water for injection

Spevigo is supplied in a 10 mL clear glass vial with a coated rubber stopper containing 7.5 mL concentrate. Each pack has two vials.

The vial stopper is not manufactured with natural rubber latex.

Excipients

This medicinal product contains less than 1 mmol sodium (23 mg) per 900 mg dose, essentially 'sodium free'.

7 WARNINGS AND PRECAUTIONS

General

Limited safety data are available for re-treatment with spesolimab for a subsequent new flare.

Traceability

In order to improve traceability of biological medicinal products, the trade name and the batch number of the administered product should be clearly recorded in the patient file.

Infections

Spevigo may increase the risk of infections. Higher rates of infections such as urinary tract infections and upper respiratory infections were observed in patients receiving Spevigo compared with placebo (see 8 ADVERSE REACTIONS).

In patients with a chronic infection or a history of recurrent infection, the potential risks and expected clinical benefits of treatment should be considered prior to prescribing Spevigo. Treatment with Spevigo should not be initiated in patients with any clinically important active infection until the infection resolves or is adequately treated. Patients should be instructed to seek medical advice if signs or symptoms of clinically important infection occur after treatment with Spevigo.

Pre-treatment evaluation for tuberculosis

Patients should be evaluated for tuberculosis (TB) infection prior to initiating treatment with Spevigo. Spevigo should not be administered to patients with active TB infection.

Anti-TB therapy should be considered prior to initiating Spevigo in patients with latent TB or a history of TB in whom an adequate course of treatment cannot be confirmed. After Spevigo treatment, patients should be monitored for signs and symptoms of active TB.

Hypersensitivity and infusion-related reactions

Hypersensitivity and infusion-related reactions may occur with monoclonal antibodies such as Spevigo. Hypersensitivity may include immediate reactions such as anaphylaxis and delayed reactions such as drug reaction with eosinophilia and systemic symptoms (DRESS).

If a patient develops signs of anaphylaxis or other serious hypersensitivity, Spevigo should be discontinued immediately, and appropriate treatment should be initiated (see 2 CONTRAINDICATIONS).

If a patient develops mild or moderate infusion-related reactions, Spevigo should be stopped and appropriate medical therapy should be considered (e.g., 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 (see 4 DOSAGE AND ADMINISTRATION).

Immunizations

No specific studies have been conducted in patients who have recently received live viral or live bacterial vaccines. Live vaccines should not be given concurrently with Spevigo. The interval between live vaccinations and initiation of Spevigo therapy should be at least 4 weeks. Live vaccines should not be administered for at least 16 weeks after treatment with Spevigo.

Neurologic

Peripheral neuropathy

The potential for peripheral neuropathy with Spevigo is unknown. Cases of peripheral neuropathy have been reported in clinical trials with spesolimab. Physicians should be vigilant for symptoms potentially indicative of new-onset peripheral neuropathy.

Driving and Operating Machinery

Spevigo has no or negligible influence on the ability to drive and use machines.

Reproductive Health: Female and Male Potential

- **Fertility**

There are no data available on the effect of Spevigo on human fertility. No specific non-clinical animal study on fertility has been conducted with spesolimab (see 16 NON-CLINICAL TOXICOLOGY).

7.1 Special Populations

7.1.1 Pregnant Women

There are limited data from the use of Spevigo in pregnant women. Non-clinical animal reproductive and developmental toxicology studies were not conducted with spesolimab due to lack of pharmacologic activity in non-human species (see 16 NON-CLINICAL TOXICOLOGY). Human IgG are known to cross the human placental barrier. As a precautionary measure, it is recommended to avoid the use of Spevigo in pregnancy.

7.1.2 Breast-feeding

It is unknown whether Spevigo is excreted in human milk. There are no data on the effects on the breastfed infant, or the effects on milk production. Spesolimab is a monoclonal antibody and is expected to be present in human milk. A risk to newborns/infants cannot be excluded.

7.1.3 Pediatrics (<18 years of age)

The safety and efficacy of Spevigo in pediatric patients have not been established. No data are available in this population.

7.1.4 Geriatrics (≥65 years of age)

No dose adjustment is required. There is limited information in patients aged 65 years and older.

8 ADVERSE REACTIONS

8.1 Adverse Reaction Overview

The most frequent adverse reactions associated with Spevigo were infections. During the 1-week placebo-controlled period in EFFISAYIL-1, infections were reported in 17.1% of patients treated with Spevigo compared with 5.6% of patients treated with placebo. Serious infection (urinary tract infection) was reported in 1 patient (2.9%) in the Spevigo group and no patients in the placebo group. Infections observed in clinical trials with spesolimab were generally mild to moderate with no distinct pattern regarding pathogen or type of infection.

In EFFISAYIL-1, local tolerability was assessed after the Day 1 and the Day 8 infusions, based on 6 symptoms (swelling, induration, heat, redness, pain, other) and 3 grades of intensity (mild, moderate, severe). In the placebo group, 1 patient (5.6%) had symptoms (heat of moderate intensity) on Day 1 and no patient had symptoms on Day 8. In the Spevigo group, 6 patients (17.1%) had mild to moderate symptoms on Day 1 and no patient had symptoms on Day 8. No severe symptoms were reported in any treatment group.

8.2 Clinical Trial Adverse Reactions

Clinical trials are conducted under very specific conditions. The adverse reaction rates observed in the clinical trials therefore, may not reflect the rates observed in practice and should not be compared to the rates in the clinical trials of another drug. Adverse reaction information from clinical trials may be useful in identifying and approximating rates of adverse drug reactions in real-world use.

Spevigo was studied in a randomized, double-blind, placebo-controlled trial (EFFISAYIL-1) comparing a single intravenous 900 mg dose of Spevigo (n=35) with placebo (n=18) in patients with GPP experiencing an acute flare [see 14 CLINICAL TRIALS].

Table 2 summarizes the adverse reactions that occurred at a rate of at least 1% and at a higher rate in the Spevigo group than in the placebo group through Week 1.

Table 2 – Selected Adverse Reactions Occurring in ≥1% of the Spevigo Group and More Frequently than in the Placebo Group through Week 1

Adverse Reaction	**Spevigo N=35 n (%)**	**Placebo N=18 n (%)**
Asthenia and fatigue	3 (9)	1(6)
Headache	3 (9)	1 (6)
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

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. After Week 1 to Week 12, subjects in either treatment group whose GPP flare reoccurred after achieving a clinical response were eligible to receive a single open-label rescue intravenous dose of 900 mg of Spevigo, with a maximum of 3 total doses of Spevigo throughout the study. Six subjects received a single open-label rescue dose of Spevigo. Thirty-six subjects received 1 dose of Spevigo, 13 subjects received 2 doses of Spevigo, and 2 subjects received 3 doses of Spevigo throughout the study.

In Study 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: device-related infection (3%), subcutaneous abscess (3%), furuncle (3%), and influenza (3%).

Additional adverse reactions that occurred through Week 17 in subjects treated with a single dose of open-label Spevigo at Week 1 (second dose and first dose for subjects in the Spevigo and placebo groups, respectively) were mild to moderate infections: otitis externa (7%), vulvovaginal candidiasis (4%), vulvovaginal mycotic infection (4%), and latent tuberculosis (4%), diarrhea (11%), and gastritis (4%). No new adverse reactions were identified for up to 16 weeks in subjects treated with a single dose of open-label rescue Spevigo from Week 1 to Week 12 (range 1-3 total doses).

9 DRUG INTERACTIONS

9.2 Drug Interactions Overview

No interaction studies have been performed.

Live vaccines should not be given concurrently with Spevigo (see 7 WARNINGS AND PRECAUTIONS).

9.4 Drug-Drug Interactions

No formal drug interactions studies have been conducted with Spevigo.

9.5 Drug-Food Interactions

Interactions with food have not been established.

9.6 Drug-Herb Interactions

Interactions with herbal products have not been established.

9.7 Drug-Laboratory Test Interactions

Interactions with laboratory tests have not been established.

10 CLINICAL PHARMACOLOGY

10.1 Mechanism of Action

Spesolimab is a humanized antagonistic monoclonal immunoglobulin G1 (IgG1) antibody that blocks interleukin-36 (IL-36) signalling by binding to IL-36 receptor (IL-36R). Binding of spesolimab to IL-36R prevents the subsequent activation of IL-36R by cognate ligands (IL-36 α, β and γ) and downstream activation of pro-inflammatory and pro-fibrotic pathways.

There is evidence that suggests the link between IL36R signalling and skin inflammation but the precise mechanism of how the decrease in IL-36R signalling in the skin of GPP patients is linked to the treatment is not clear.

10.2 Pharmacodynamics

The pharmacodynamic effect of Spevigo in treatment of GPP has not been fully characterized.

10.3 Pharmacokinetics

A population pharmacokinetic (PK) model was developed based on data collected from healthy subjects, patients with GPP and patients with other diseases. After a single intravenous dose of 900 mg Spevigo, the population PK model-estimated $AUC^{0-\infty}$ (95% CI) and C_{max} (95% CI) in a typical anti-drug antibody (ADA)-negative patient with GPP were 4750 (4510, 4970) mcg·day/mL and 238 (218, 256) mcg/mL, respectively.

Distribution:

Based on the population PK analysis, the typical volume of distribution at steady state was 6.4 L.

Metabolism:

The metabolic pathway of spesolimab has not been characterized. As a humanized IgG1 monoclonal antibody, spesolimab is expected to be degraded into small peptides and amino acids via catabolic pathways in a manner similar to endogenous IgG.

Elimination:

Spesolimab AUC increased approximately dose-proportionally within the dose range of 0.3 to 20 mg/kg with clearance (CL) and terminal half-life independent of dose.

At dose range 0.3-20 mg/kg, in a typical GPP patient weighing 70 kg without ADA formation, spesolimab CL (95% CI) was 0.184 (0.175, 0.194) L/day. The terminal-half-life was 25.5 (24.4, 26.3) days.

Special Populations and Conditions

Pediatric population: The pharmacokinetics of spesolimab in pediatric patients has not yet been studied.

Age, Gender and Race: Based on population pharmacokinetic analyses, age, gender and race did not have an effect on the pharmacokinetics of spesolimab.

Hepatic and renal insufficiency: As a monoclonal antibody, spesolimab is not expected to

undergo hepatic or renal elimination. No formal study of the effect of hepatic or renal impairment on the pharmacokinetics of spesolimab was conducted.

Body weight: Spesolimab concentrations were lower in subjects with higher body weight. The clinical impact of body weight on spesolimab plasma concentrations is not yet clear.

11 STORAGE, STABILITY AND DISPOSAL

Spevigo sterile concentrate is for single-use only and does not contain preservatives.

Store in a refrigerator at 2°C - 8°C in original carton to protect from light. Do not freeze.

Prior to use, the unopened vial may be stored at room temperature (15°C-30°C) for up to 24 hours in the original package to protect from light.

For storage conditions after dilution of the medicinal product, see 12 SPECIAL HANDLING INSTRUCTIONS.

12 SPECIAL HANDLING INSTRUCTIONS

The diluted Spevigo solution for infusion should be used immediately. If not used immediately, the diluted drug product may be stored for up to 4 hours at 2-8°C. The diluted solution for infusion should be stored protected from light from the time of preparation to start of administration.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

PART II: SCIENTIFIC INFORMATION

13 PHARMACEUTICAL INFORMATION

Drug Substance

Proper name: Spesolimab

Chemical name: Not applicable. Spesolimab is an immunoglobulin.

Molecular mass: 146 kDA

Structural formula: Spesolimab is a humanized monoclonal IgG1 antibody (mAb) against human IL-36R. The spesolimab molecule is composed of two heterodimers. Each heterodimer is composed of a heavy chain (449 amino acids) and a light chain (215 amino acids). The four polypeptide chains of the antibody are linked together by disulfide bonds. Each heavy polypeptide chain contains one consensus sequence for N-linked glycosylation.

Physicochemical properties: spesolimab is a colourless to slightly brownish-yellow, clear to slightly opalescent solution.

14 CLINICAL TRIALS

14.1 Clinical Trials by Indication

Treatment of Flares in patients with generalized pustular psoriasis

Table 3 - Summary of patient demographics for clinical trials in treatment of flares in patients with generalized pustular psoriasis

Study #	Study design	Dosage, route of administration and duration	Study subjects (n)	Mean age (Range)	Sex
EFFISAYIL-1 (Study 1368-0013)	Randomised, double-blind, placebo-controlled, in adults with flares of GPP Post week 1-week 12: open label	900 mg, intravenous infusion, single dose with optional second dose at day 8 (follow up to 12 weeks)	Spevigo:35 Placebo:18	43 years (21 to 69)	Male: 32% Female:68%

A randomised, double-blind, placebo-controlled study (EFFISAYIL-1) was conducted to evaluate the clinical efficacy and safety of Spevigo in adult patients with flares of Generalized Pustular Psoriasis (GPP), regardless of IL36RN mutation status. Patients were randomised if they had a flare of GPP of moderate-to-severe intensity, as defined by a Generalized Pustular Psoriasis Physician Global Assessment (GPPGA) total score (which ranges from 0 [clear] to 4 [severe]) of at least 3 (moderate), presence of fresh pustules (new appearance or worsening of pustules),

GPPGA pustulation sub score of at least 2 (mild), and at least 5% of body surface area (BSA) covered with erythema and the presence of pustules. Patients were required to discontinue systemic and topical therapy for GPP prior to receiving study drug.

The primary endpoint of the study was the proportion of patients with a GPPGA pustulation subscore of 0 (indicating no visible pustules) at Week 1. The key secondary endpoint of the study was the proportion of patients with a GPPGA total score of 0 or 1 (clear or almost clear skin) at Week 1. Additional secondary endpoint at Week 4 was the proportion of patients with a 75% reduction in the Psoriasis Area and Severity Index for Generalized Pustular Psoriasis (GPPASI 75).

A total of 53 patients were randomised to receive a single intravenous dose of 900 mg - Spevigo (n= 35) or placebo (n=18). Patients in either treatment arm who still experienced flare symptoms at Week 1 were eligible to receive a single intravenous dose of open-label 900 mg Spevigo, resulting in 12 patients (34%) in the Spevigo arm receiving a second dose of Spevigo and 15 patients (83%) in the placebo arm receiving one dose of Spevigo on Day 8. In addition, 6 patients (4 Spevigo arm; 2 placebo arm) received rescue treatment with a single 900 mg dose of intravenous Spevigo for reoccurrence of a flare after Week 1.

The study population consisted of 32% men and 68% women. The mean age was 43 (range: 21 to 69) years; 55% of patients were Asian and 45% were Caucasian. Most patients included in the study had a GPPGA pustulation sub score of 3 (43%) or 4 (36%), and patients had a GPPGA total score of 3 (81%) or 4 (19%). A total of 13 of 53 (24.5%) patients had been previously treated with biologic therapy for GPP.

Study results

The study met the pre-specified objectives at Week 1 for both GPPGA pustulation sub score of 0 (indicating no visible pustules) and GPPGA total score of 0 or 1 (clear or almost clear skin). Results are shown in Table 4.

Table 4 - GPPGA Pustulation Sub Score and GPPGA Total Score at Week 1

	Spevigo 900 mg IV	Placebo
Number of Patients analysed	35	18
Patients achieving a GPPGA pustulation sub score of 0, n (%)	19 (54.3)	1 (5.6)
Risk difference versus placebo, % (95% CI)	48.7 (21.5, 67.2)	
p-value*	0.0004	
Patients achieving a GPPGA total score of 0 or 1, n (%)	15 (42.9)	2 (11.1)
Risk difference versus placebo, % (95% CI)	31.7 (2.2, 52.7)	
p-value*	0.0118	

GPPGA = Generalized Pustular Psoriasis Physician Global Assessment; IV = intravenous
*One-sided p-value

14.3 Immunogenicity

As with all therapeutic proteins, there is the potential for immunogenicity. The detection of antibody formation is highly dependent on the sensitivity and specificity of the assay.

In patients with GPP treated with Spevigo in EFFISAYIL-1 (study 1368-0013), anti-drug antibodies (ADA) formed with a median onset of 2.3 weeks. Following administration of IV Spevigo 900 mg, 24% (12 out of 50) of patients had a maximum ADA titer greater than 4000 and were neutralizing antibody (Nab)-positive by end of the trial (Weeks 12 to 17).

Females appeared to have higher immunogenicity response; the percentage of patients with ADA titer greater than 4000 was 30% in females, and 12% in males, respectively.

In most patients with ADA titer values greater than 4000, plasma spesolimab concentrations were significantly reduced. In patients with ADA titers below 4000, no apparent impact on spesolimab pharmacokinetics was observed.

In the presence of ADA, efficacy was observed upon re-treatment of recurring flares with Spevigo in open label extension trial. There was no apparent correlation between the presence of ADA to Spevigo and hypersensitivity reactions.

15 MICROBIOLOGY

No microbiological information is required for this drug product.

16 NON-CLINICAL TOXICOLOGY

Animal toxicology studies have not been conducted with spesolimab due to a lack of pharmacologic activity in non-human species. The repeat-dose, reproductive, and developmental toxicology studies were conducted in mice using a surrogate, mouse specific anti-IL36R monoclonal antibody (BI 674304).

General Toxicology:

In the pivotal repeat-dose toxicology study, mice were administered BI 674304 by intravenous injection twice per week for 26 weeks at doses of 0 (vehicle), 10, or 50 mg/kg. Additional groups of mice administered vehicle or high-dose BI 674304 were observed for a 4-week recovery period following dosing. There were ten unscheduled deaths during the course of the study (3, 2 and 5 mice from the control, 10 and 50 mg/kg groups, respectively). The cause of mortality/moribundity was determined in 3 of the 10 mice; 1) euthanasia due to an abrasion on the tail that led to ulceration and infection, which impaired dosing (50 mg/kg), 2) euthanasia due to systemic bacterial infection (50 mg/kg) and 3) malignant lymphoma, a type of cancer that occurs naturally in this strain of mouse (10 mg/kg). The cause of mortality/moribundity in the other 7 animals could not be determined. The mortalities were not considered related to the administration of BI 674304 as they occurred across all dose groups, including the control. No adverse changes in body weight, food consumption or clinical observations were noted at this dose. No adverse effects on clinical pathology parameters including haematology, immunophenotyping, clinical chemistry and histopathology, including lymphoid tissues, have been observed.

Carcinogenicity:

Carcinogenicity and mutagenicity studies have not been conducted with spesolimab or BI 674304.

Genotoxicity:

Genotoxicity studies have not been conducted with spesolimab or BI 674304.

Reproductive and Developmental Toxicology:

Pre-clinical studies conducted in mice using a surrogate antibody directed towards murine IL-36R do not indicate direct or indirect harmful effects with respect to pregnancy, embryonic/fetal development or fertility, at intravenous doses up to 50 mg/kg twice weekly. Serum concentrations of BI 674304 were low in the females of these studies. The reproductive and developmental data should be interpreted with caution.

Table 5 - Reproductive Toxicology

Study Type	Species	No. of animals/group	Doses (mg/kg/twice weekly IV)	Findings
Fertility and early embryonic development study	Mice	22m 22f	0, 10, 50 2-4 weeks prior to cohabitation, during cohabitation, and/or gestation	NOAEL = 50 mg/kg. BI 674304 was neither a teratogen nor embryotoxic. BI 674304 did not affect fertility of the adult mice nor the development of the pups exposed via the treated mother.
Embryo fetal development study	Mice	25f	0, 10, 50 GD 6, 9, 12, and 15	A higher number of resorptions was observed but was within the historical control range and therefore an effect of BI 674304 was considered to be equivocal.
Pre- and postnatal development study	Mice	22f	0, 10, 50 GD 6 to LD 18	NOAEL = 50 mg/kg. BI 674304 did not affect pregnancy or delivery; or morphological, functional and immunological developmental parameters of offspring.

GD, gestation day; LD, lactation day

PATIENT MEDICATION INFORMATION

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

PrSpevigo®

Spesolimab for Injection

Read this carefully before you start taking **Spevigo** and each time you get a refill. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about **Spevigo**.

What is Spevigo used for?

Spevigo is a prescription medicine used in adults to treat:

painful skin blisters (also called pustules) developing suddenly over large areas of your skin.

These episodes are also known as a flare, and are related to a rare, inflammatory, skin disease called generalized pustular psoriasis (GPP). **Spevigo** helps to clear your skin and reduces your symptoms such as burning, itching, pain, redness and fatigue during a flare.

How does Spevigo work?

Spevigo contains the active substance spesolimab. Spesolimab is a monoclonal antibody belonging to a group of medicines called interleukin (IL) inhibitors. Monoclonal antibodies are proteins that recognize and bind specifically to certain proteins in the body. **Spevigo** works by blocking the activity of a protein called IL-36R, which can cause pustules, painful inflammation on the skin and fibrosis (scarring).

What are the ingredients in Spevigo?

Medicinal ingredient: spesolimab

Non-medicinal ingredients: arginine hydrochloride, glacial acetic acid, polysorbate 20, sodium acetate trihydrate, sucrose, water for injection.

Spevigo comes in the following dosage forms:

Spevigo is available as single use vials, 450 mg/vial (60 mg/mL).
Each pack has two vials.
The vial stopper does not contain natural rubber latex.

Do not use Spevigo if:

You are allergic to spesolimab or any of the other ingredients of this medicine. See **What are the ingredients in Spevigo?**

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take Spevigo. Talk about any health conditions or problems you may have, including if you:

- have an infection that does not go away or that keeps coming back;
- have tuberculosis (TB) or have been in close contact with someone with TB;
- have recently received or are scheduled to receive an immunization (vaccine). You should not receive live vaccines for at least 16 weeks after treatment with **Spevigo**;
- are pregnant or plan to become pregnant. It is not known if **Spevigo** can harm your unborn baby;
- are breastfeeding or plan to breastfeed. It is not known if **Spevigo** passes into your breast milk;
- experience symptoms like new-onset weakness in your arms or legs or numbness (loss of sensation), tingling or burning sensation in any part of your body. These might be signs of peripheral neuropathy.

Talk to your healthcare professional right away if you have any of the signs or symptoms of an allergic reaction, including:

- difficulty breathing or swallowing;
- swelling of the face, lips, tongue or throat;
- severe itching of the skin, with a red rash or raised bumps that is different from your GPP symptoms;
- feel faint.

You can also have allergic reactions days or weeks after receiving **Spevigo**. Call your doctor immediately if you develop any widespread skin rash not previously experienced, fever, and/or facial swelling 2-8 weeks after receiving the medication.

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements, or alternative medicines.

How to take Spevigo:

- Your healthcare provider will give you **Spevigo** through a needle placed in your vein (intravenous infusion) over 90 minutes.
- **Spevigo** is usually given one time. Your healthcare provider will decide if you should receive an additional treatment after 1 week.

Usual dose:

The usual dose is a single dose of 900 mg (2 x 450 mg/7.5 mL vials) administered as an intravenous infusion.

If your flare persists, an additional 900 mg dose may be administered 1 week after the initial dose.

Overdose:

If you think you, or a person you are caring for, have taken too much **Spevigo**, contact a healthcare professional, hospital emergency department, or regional poison control centre immediately, even if there are no symptoms.

What are possible side effects from using Spevigo?

These are not all the possible side effects you may have when taking **Spevigo**. If you experience any side effects not listed here, tell your healthcare professional.

- urinary tract infections;
- upper respiratory tract infections;
- itching;
- feeling tired;
- redness, swelling, hardening, warmth, or pain at the injection site.

Serious side effects and what to do about them			
Symptom / effect	**Talk to your healthcare professional**		**Stop taking drug and get immediate medical help**
	Only if severe	**In all cases**	
COMMON			
Urinary tract infections: burning when you urinate, urinating more often than normal		✓	
Upper respiratory tract infections: fevers, chills or sweats, cough, shortness of breath		✓	
Allergic (hypersensitivity) reactions and infusion reactions: feeling faint, swelling of your face, eyelids, lips, mouth, tongue or throat, chest tightness, skin rash		✓	
Serious allergic reactions that may occur days to weeks after receiving Spevigo: skin rash that is different than the rash from GPP, fever, swollen lymph nodes, facial swelling, mouth sores		✓	

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, tell your healthcare professional.

Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada.html) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:

Store in a refrigerator at 2°C to 8°C in original carton to protect from light. Do not freeze.

If you want more information about Spevigo:

- Talk to your healthcare professional.
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website: (https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html; the manufacturer's website (www.boehringer-ingelheim.ca), or by calling 1-800-263-5103, extension 84633.

This leaflet was prepared by Boehringer Ingelheim (Canada) Ltd.

The information in this leaflet is current up to the time of the last revision date shown below, but more current information may be available from the manufacturer.

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