Medicines & Healthcare products Regulatory Agency

Public Assessment Report

National Procedure

Spevigo 450 mg concentrate for solution for infusion

Spesolimab

PLGB 14598/0238

Boehringer Ingelheim International GmbH

LAY SUMMARY

Spevigo 450 mg concentrate for solution for infusion
Spesolimab

This is a summary of the Public Assessment Report (PAR) for Spevigo 450 mg concentrate for solution for infusion. It explains how this product was assessed and its authorisation recommended, as well as its conditions of use. It is not intended to provide practical advice on how to use this product.

This product will be referred to as Spevigo in this lay summary for ease of reading.

This product has been authorised by MHRA for Great Britain (consisting of England, Scotland and Wales). In coming to its decision, MHRA has relied on a European Commission (EC) decision on 09 December 2022 (EMEA/H/C/005874/0000), in accordance with the advice from the Committee for Medicinal Products for Human Use (CHMP). This is known as the EC Decision Reliance Procedure.

This application was approved under Regulation 50 of the Human Medicines Regulation 2012, as amended (previously Article 8.3 of Directive 2001/83/EC, as amended).

For practical information about using Spevigo, patients should read the Patient Information Leaflet (PIL) or contact their doctor or pharmacist.

What is Spevigo and what is it used for?
This application is a full-dossier application. This means that the results of pharmaceutical, non-clinical and clinical tests have been submitted to show that this medicine is suitable for treating the specified indication.

Spevigo is used alone in adults to treat flares of a rare inflammatory skin disease called generalised pustular psoriasis (GPP). During a flare, patients may experience painful skin blisters that develop suddenly over large areas of the skin. These blisters, also called pustules, are filled with pus. The skin may become red, itchy, dry, cracked or scaly. Patients may also experience more general signs and symptoms, such as fever, headache, extreme tiredness, or a burning sensation of the skin. Spevigo improves skin clearance and reduces symptoms of GPP during a flare.

How does Spevigo work?
Spevigo contains the active substance spesolimab. Spesolimab belongs to a group of medicines called interleukin (IL) inhibitors. This medicine works by blocking the activity of a protein called IL36R, which is involved in inflammation.

How is Spevigo used?
The pharmaceutical form of this medicine is a concentrate for solution for infusion and the route of administration is intravenous (into a vein).

The recommended dose is 900 mg (2 vials of 450 mg/7.5 mL).

The patient’s doctor or nurse will give the patient this medicine by infusion (drip) into a vein. It will be given over a period of 90 minutes, up to a maximum of 180 minutes if the infusion is slowed down or stopped temporarily.

If the patient still experiences flare symptoms, their doctor can decide to give the patient a second dose of Spevigo one week after the first.

For further information on how Spevigo is used, refer to the PIL and Summary of Product Characteristics (SmPC) available on the Medicines and Healthcare products Regulatory Agency (MHRA) website.

This medicine can only be obtained with a prescription.

The patient should ask the administering healthcare practitioner if they have any questions concerning their medicine.

What benefits of Spevigo have been shown in studies?
A main study was conducted to evaluate the efficacy and safety of Spevigo. The study involved 53 adults with generalised pustular psoriasis flare-ups of moderate to severe intensity. The study showed that Spevigo was more effective than placebo (a dummy treatment) at improving skin clearance and reducing symptoms of GPP during a flare. After one week, 54% (19 out of 35) of patients who received a single dose of Spevigo had no visible pustules compared with 6% (1 out of 18) of patients who were given placebo, as measured using the GPPGA pustulation subscore (a measure of the severity of the pustules).

What are the possible side effects of Spevigo?
For the full list of all side effects reported with this medicine, see Section 4 of the PIL or the SmPC available on the MHRA website.

If a patient gets any side effects, they should talk to their doctor, pharmacist or nurse. This includes any possible side effects not listed in the product information or the PIL that comes with the medicine. Patients can also report suspected side effects themselves, or a report can be made on their behalf by someone else who cares for them, directly via the Yellow Card scheme at https://yellowcard.mhra.gov.uk or search for 'MHRA Yellow Card' online. By reporting side effects, patients can help provide more information on the safety of this medicine.

The most common side effects with Spevigo (which may affect more than 1 in 10 people) are:

- Infections - Patients should tell their doctor as soon as possible if they notice any signs or symptoms of an infection. Please refer to the PIL for further information.
- Redness, swelling, hardening, warmth or pain at the injection site.

Why was Spevigo approved?
MHRA decided that the benefits are greater than the risks and recommended that this medicine can be approved for use.

Spevigo has been authorised with a conditional marketing authorisation (CMA). CMAs are intended for medicinal products that address an unmet medical need, such as a lack of alternative therapy for a serious and life-threatening disease. CMAs may be granted where comprehensive clinical data is not yet complete, but it is judged that such data will become available soon.

What measures are being taken to ensure the safe and effective use of Spevigo?
As for all newly-authorised medicines, a Risk Management Plan (RMP) has been developed for Spevigo. The RMP details the important risks of Spevigo, how these risks can be minimised, any uncertainties about Spevigo (missing information), and how more information will be obtained about the important risks and uncertainties.

The following safety concerns have been recognised for Spevigo:
Important identified risks:

- None

Important potential risks:

- Serious or opportunistic infections
- Systemic hypersensitivity reaction
- Malignancy
- Peripheral neuropathy

Missing information:

- Pregnant or breast-feeding women

The Marketing Authorisation Holder will conduct a post-authorisation safety study to further characterise the safety of spesolimab for flare treatment in patients with GPP.

The information included in the SmPC and the PIL is compiled based on the available quality, non-clinical and clinical data, and includes appropriate precautions to be followed by healthcare professionals and patients. Side effects of Spevigo are continuously monitored and reviewed including all reports of suspected side-effects from patients, their carers, and healthcare professionals.

An RMP and a summary of the pharmacovigilance system have been provided with this application and are satisfactory.

Other information about Spevigo
A marketing authorisation was granted in Great Britain on 27 July 2023.

The full PAR for Spevigo follows this summary.

This summary was last updated in September 2023.

TABLE OF CONTENTS

I. INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the Medicines and Healthcare products Regulatory Agency (MHRA) considered that the application Spevigo 450 mg concentrate for solution for infusion (PLGB 14598/0238) could be approved.

The product is approved for the following indication:
For the treatment of flares in adult patients with generalised pustular psoriasis (GPP) as monotherapy.

The active substance, spesolimab, is a humanised antagonistic monoclonal immunoglobulin G1 (IgG1) antibody blocking human IL36R signalling. Binding of spesolimab to IL36R prevents the subsequent activation of IL36R by cognate ligands (IL36 α, β and γ) and downstream activation of pro-inflammatory pathways.

This product has been authorised by MHRA for Great Britain (consisting of England, Scotland and Wales). In coming to its decision, MHRA has relied on a European Commission (EC) decision on 09 December 2022 (EMEA/H/C/005874/0000), in accordance with the advice from the Committee for Medicinal Products for Human Use (CHMP).
For the scientific discussion of the quality, non-clinical and clinical assessment conducted by the European Medicines Agency (EMA), please refer to the European Public Assessment Report, available on the EMA website.

This application was approved under Regulation 50 of the Human Medicines Regulation 2012, as amended (previously Article 8.3 of Directive 2001/83/EC, as amended).

Spevigo 450 mg concentrate for solution for infusion has been authorised as a conditional marketing authorisation (CMA). CMAs are granted in the interest of public health and are intended for medicinal products that fulfil an unmet medical need and the benefit of immediate availability outweighs the risk posed from less comprehensive data than normally required. Unmet medical needs include, for example, treatment or diagnosis of serious and life-threatening diseases where no satisfactory treatment methods are available. CMAs may be granted where comprehensive clinical data is not yet complete, but it is judged that such data will become available soon. Adequate evidence of safety and efficacy to enable the MHRA to conclude that the benefits are greater than the risks is required, and has been provided for Spevigo 450 mg concentrate for solution for infusion. The CMA for Spevigo 450 mg concentrate for solution for infusion, including the provision of any new information, will be reviewed every year and this report will be updated as necessary.

This application was evaluated for fulfilment of orphan designation criteria and was examined by the Commission on Human Medicines (CHM). The applicant withdrew the application for orphan designation.

In line with the legal requirements for children's medicines, the application included a licensing authority decision on the agreement of a paediatric investigation plan (PIP) MHRA-100264-PIP01-21-M01.

At the time of the submission of the application the PIP was not yet completed as some measures were deferred.

The MHRA has been assured that acceptable standards of Good Manufacturing Practice (GMP) are in place for this product at all sites responsible for the manufacture, assembly and batch release.

A Risk Management Plan (RMP) and a summary of the pharmacovigilance system have been provided with this application and are satisfactory.

A marketing authorisation was granted on 27 July 2023.

II. PRODUCT INFORMATION

SUMMARY OF PRODUCT CHARACTERISTICS (SmPC)

The SmPC is in line with current guidelines and is satisfactory.

PATIENT INFORMATION LEAFLET

The PIL is in line with current guidelines and is satisfactory.

LABEL

The labelling is in line with current guidelines and is satisfactory.

III. QUALITY ASPECTS

MHRA considered that the quality data submitted for this application is satisfactory.

The grant of a marketing authorisation was recommended.

IV. NON-CLINICAL ASPECTS

MHRA considered that the non-clinical data submitted for this application is satisfactory.

The grant of a marketing authorisation was recommended.

V. CLINICAL ASPECTS

MHRA considered that the clinical data submitted for this application is satisfactory.

The grant of a marketing authorisation was recommended.

VI. RISK MANAGEMENT PLAN (RMP)

The applicant has submitted an RMP, in accordance with the requirements of Regulation 182 of The Human Medicines Regulation 2012, as amended. In addition to routine pharmacovigilance and risk minimisation measures, the following additional pharmacovigilance measures have been proposed:

Important identified risks
None

Important potential risks

Serious or opportunistic infections	
Evidence for linking the risk to the medicine	No increased occurrence observed in clinical trials with spesolimab.
Risk factors and risk groups	Increased age, impaired immune function, comorbidities, and duration of exposure to and number of concomitant immunosuppressive therapies.
Risk minimisation measures	Routine risk minimisation measures: EU-SmPC sections 4.3, 4.4 PL section 2 Prescription only medicine, administration in a healthcare setting by physicians experienced in the management of patients with inflammatory skin diseases Additional risk minimisation measures: None
Additional pharmacovigilance activities	Additional pharmacovigilance activities: PASS 1368-0128 See section II.C of this summary for an overview of the post-authorisation development plan.
Systemic hypersensitivity reaction	
Evidence for linking the risk to the medicine	General risk from proteins to cause hypersensitivity reactions. As the antibody is humanised, the risk for hypersensitivity reactions (including DRESS) in patients treated with spesolimab is considered low. Hypersensitivity events observed in trial 1368-0013 were not related to spesolimab treatment.
Risk factors and risk groups	Risk groups or risk factors are unknown. Potential intrinsic risk for spesolimab to induce a T-cell humoral immune response.
Risk minimisation measures	Routine risk minimisation measures: EU-SmPC sections 4.3, 4.4 PL section 2 Prescription only medicine, administration in a healthcare setting by physicians experienced in the management of patients with inflammatory skin diseases Additional risk minimisation measures: None

Additional pharmacovigilance activities	Additional pharmacovigilance activities: PASS 1368-0128 See section II.C of this summary for an overview of the post-authorisation development plan.
Malignancy	
Evidence for linking the risk to the medicine	Clinical data on malignancy associated with IL-36R inhibition is limited by duration and number of treated individuals. In related mechanisms, meta-analyses of cancer incidence among patients with immune suppression therapy (e.g. TNFs, methotrexate) did not yield clear correlation between tumour incidence and therapies not intended to completely ablate immune function.
Risk factors and risk groups	Tumour location, genetic susceptibility, alcohol consumption, smoking, obesity, increased age, race, family history, exposure to chemicals or UV (e.g. PUVA treatment for psoriasis) or other substances, chronic inflammation, immunosuppression, infectious agents, radiation
Risk minimisation measures	Routine risk minimisation measures: Prescription only medicine, administration in a healthcare setting by physicians experienced in the management of patients with inflammatory skin diseases Additional risk minimisation measures: None
Additional pharmacovigilance activities	Additional pharmacovigilance activities: PASS 1368-0128 See section II.C of this summary for an overview of the post-authorisation development plan.
Peripheral neuropathy	
Evidence for linking the risk to the medicine	In preclinical toxicity studies with a surrogate antibody, no histopathological changes were noted in the nervous system. Cases of peripheral neuropathy reported in clinical trials were not assessed as related to spesolimab.
Risk factors and risk groups	Risk factors and risk groups are unknown.
Risk minimisation measures	Routine risk minimisation measures: EU-SmPC section 4.4 PL section 2 Prescription only medicine, administration in a

	healthcare setting by physicians experienced in the management of patients with inflammatory skin diseases Additional risk minimisation measures: None
Additional pharmacovigilance activities	Additional pharmacovigilance activities: PASS 1368-0128 See section II.C of this summary for an overview of the post-authorisation development plan.

Missing information	
Pregnant or breast-feeding women	
Risk minimisation measures	Routine risk minimisation measures: EU-SmPC section 4.6 PL section 2 Prescription only medicine, administration in a healthcare setting by physicians experienced in the management of patients with inflammatory skin diseases Additional risk minimisation measures: None

This is acceptable.

VII. USER CONSULTATION

A full colour mock-up of the Patient Information Leaflet (PIL) has been provided with the application, in accordance with legal requirements.

The PIL has been evaluated via a user consultation study in accordance with legal requirements. The results show that the PIL meets the criteria for readability as set out in the Guideline on the readability of the label and package leaflet of medicinal products for human use.

VIII. OVERALL CONCLUSION, BENEFIT/RISK AND RECOMMENDATION

The quality of the product is acceptable. The non-clinical and clinical data submitted have shown the positive benefit/risk of the product in the treatment of flares in adult patients with generalised pustular psoriasis (GPP).

Spevigo has been authorised with the condition to perform further studies and/or to provide additional measures to minimise the risk. The Marketing Authorisation Holder shall complete, within the stated timeframe, the following measures:

Description	**Due date**
In order to confirm the efficacy and safety of spesolimab in the treatment of flares in adult patients with generalised pustular psoriasis (GPP), the MAH should conduct and submit the final results of study 1368-0120, an open-label trial in the treatment of recurrent flares in adult patients with generalised pustular psoriasis, conducted according to an agreed protocol.	31/08/2028

The Summaries of Product Characteristics (SmPCs), Patient Information Leaflet (PIL) and labelling are satisfactory.

IX. TABLE OF CONTENT OF THE PAR UPDATE

Steps taken after the initial procedure with an influence on the Public Assessment Report (non-safety variations of clinical significance).

Please note that only non-safety variations of clinical significance are recorded below and in the annexes to this PAR. The assessment of safety variations, where significant changes are made, are recorded on the MHRA website or European Medicines Agency (EMA) website. Minor changes to the marketing authorisation are recorded in the current SmPCs and/or PIL available on the MHRA website.

Application type	**Scope**	**Product information affected**	**Date of grant**	**Outcome**	**Assessment report attached Y/N**