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1. ABSTRACT

Name of company: Boehringer Ingelheim			
Name of finished medicinal product: Spesolimab I.V. Infusion			
Name of active ingredient: Spesolimab			
Report date:	**Study number:**	**Version/Revision:**	**Version/Revision date:**
28 August 2026	1368.93	Version 1.0	NA
Title of study:	Post-marketing Surveillance of Spesolimab I.V. Infusion in improvement of Generalized Pustular Psoriasis (GPP) with acute symptoms in Japan		
Keywords:	Spesolimab I.V. Infusion, Japan, PMS, Generalized Pustular Psoriasis (GPP) with acute symptoms		
Rationale and background:	This post-marketing surveillance (PMS) plan was proposed as an additional pharmacovigilance plan of the Japanese risk management plan (RMP). In Japan, post-approval execution of PMS is requested by the Japanese Pharmaceuticals and Medical Devices Act (J-PMD Act) to collect and accumulate safety and effectiveness data for re-examination. Re-examination period is defined by J-PMD Act. Eight years after approval for new indication of new compound, results of PMS need to be submitted as a part of re-examination dossier to the Japanese regulatory authority, the Ministry of Health, Labour and Welfare (MHLW). Collected data from PMS is included in the Japanese periodic safety reports and submitted to Pharmaceuticals and Medical Devices Agency (PMDA) on designated dates until the end of re-examination period. The Effisayil™ 1 (1368.0013) trial was multi-center, double-blind, randomized, placebo-controlled, Phase II study to evaluate efficacy, safety and tolerability of a single intravenous dose of spesolimab in patients with GPP presenting with an acute flare of moderate to severe intensity. As the number of Japanese patients treated with spesolimab in Effisayil™ 1 study was only 2 (total: 51), confirmation of the safety profile of spesolimab treatment for acute phase GPP patients in the real-world clinical setting was required.		
Research question and objectives:	To evaluate the frequency of adverse drug reactions (ADRs) (including safety concerns: Serious infections, Serious hypersensitivity) of Spesolimab I.V. Infusion and to understand GPP disease activities in the real-world setting in GPP patients with acute symptoms.		

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Study design:	Non-interventional cohort study with new data collection (NISnd) (Observational) Patients newly initiated Spesolimab I.V. Infusion were enrolled and followed up to 28 weeks after the first dose of Spesolimab I.V. Infusion unless there was an inevitable incident (death, move to other hospital etc.). The patients who were retreated with spesolimab up to 28 weeks after the first dose of this drug were followed by the investigators up to 8 weeks after the retreatment. The maximum observation period was 36 weeks after the first dose of this drug.		
Setting:	Sites (mainly hospitals) at which Spesolimab I.V. Infusion were available for prescription throughout entire country were selected according to the number of GPP patients with acute symptoms. Planned number of sites: Approximately 70 Sites A medical representative of Sales Division (GPSP Operating function) explained the objectives and design of this study to the investigators at study sites and exchanged a written contract with the head of the study site (e.g., hospital director). This study was conducted in 34 sites in Japan. Study period: March 2023 – October 2025 Enrolment period: March 2023 – February 2025		
Subjects and study size, including dropouts:	<u>Inclusion criteria</u> - GPP patients with acute symptoms who were administered Spesolimab I.V. Infusion in Japan - Patients who had never been treated with Spesolimab I.V. Infusion before enrolment <u>Exclusion criteria</u> None <u>Patient disposition</u> In this PMS, a total of 52 patients were registered. Case report forms (CRFs) were collected and fixed from all 52 patients.		

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Variables and data sources:	Outcomes: Primary outcome: Frequency of ADRs Secondary outcome: None Further outcomes: Other safety outcomes were; - Frequency of safety specifications (Serious infections, Serious hypersensitivity) - Frequency of serious adverse events (AEs) - Frequency of AEs leading to death - Frequency of AEs leading to treatment discontinuation Other effectiveness outcome was; - Japanese Dermatological Association (JDA) GPP Severity Score Others: characteristics associated with ADRs Demographics, baseline characteristics, labs and vitals as baseline, previous/concomitant medications etc. Data sources Patients' data were collected by electronic CRF on Electronic Data Capture system		

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Results:	In this PMS, a total of 52 patients were registered. CRFs were collected and fixed for all 52 patients. All 52 patients were included in the safety set. Of these, 51 patients were included in the effectiveness set. One patient was excluded from the effectiveness set because of "No effectiveness outcomes". <u>Baseline characteristics</u> In the safety set (N = 52 patients), 51.92% (27 patients) of patients were men. The mean (± SD) age was 61.3 ±15.8 years. A total of 40.38% (21 patients) were aged 65 and above. The mean time from GPP diagnosis to first administration of spesolimab was 1024.1 ± 2394.9 days. The mean duration of acute symptoms prior to the first administration of spesolimab was 8.8 ± 12.1 days. A medical history was reported in 28.85% (15 patients). Concomitant diseases were reported in 67.31% (35 patients). Among these patients, psoriasis vulgaris and psoriatic arthritis were reported as concomitant diseases in 2 patients (3.85%) and 1 patient (1.92%), respectively. Previous medications were used in 50.00% (26 patients). Previous medications for GPP were reported in 42.31% (22 patients). During the observation period, concomitant medications were used in 86.54% (45 patients). Concomitant medications for GPP were used in 71.15% (37 patients). Concomitant therapies were reported in 7.69% (4 patients). The mean observation period was 199.7 ± 66.6 days. An additional dose of spesolimab for persistent acute symptoms was administered in 46.15% (24 patients). Re-administration due to recurrent acute symptoms was reported in 2 patients (3.85%). The mean time to re-administration from the first administration was 66.0 ± 66.5 days. The mean total dose was 1367.3 ± 487.8 mg. In the effectiveness set (N = 51 patients), the mean JDA GPP severity score at baseline was 10.3 ± 3.6 (49 patients). Based on the JDA GPP severity score, patients were classified as mild in 13.73% (7 patients), moderate in 35.29% (18 patients), and severe in 47.06% (24 patients). <u>Primary outcome</u> ADRs were reported in 7 of 52 patients (13.46%). ADRs were observed in 3 of 52 patients (5.77%) at <7 days and in 4 of 52 patients (7.69%) at 7 to <28 days after administration of spesolimab, whereas no ADRs were		

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	observed at ≥28 days. No ADRs were observed in the 2 patients who received the re-administration of spesolimab. No statistically significant factors associated with the occurrence of ADRs were identified in the logistic regression analysis of subgroups. <u>Further outcomes</u> In the safety specification items, serious infections were reported as AEs in 7 of 52 patients (13.46%) and as ADRs in 2 of 52 patients (3.85%). Serious hypersensitivity was reported as AEs in 2 of 52 patients (3.85%) and as ADRs in 1 of 52 patients (1.92%). Among patients who received re-administration of spesolimab, a serious infection was reported as an AE in 1 of 2 patients (50.00%), while no serious hypersensitivity was reported as AEs. No ADRs categorized into safety specification items were reported in these patients. Furthermore, no AEs or ADRs categorized into safety specification items were reported after the first re-administration. In the safety set (N = 52 patients), serious AEs were reported in 8 of 52 patients (15.38%). An AE leading to death was reported in 1 patient (1.92%). No AEs leading to treatment discontinuation were reported. Serious ADRs were reported in 2 of 52 patients (3.85%). No ADRs leading to death or treatment discontinuation were reported. In the effectiveness set (N = 51 patients), the mean (± SD) JDA GPP severity score was 10.3 ± 3.6 at baseline (49 patients) and 4.8 ± 3.3 at the last observation (35 patients). The mean change from baseline to the last observation was −6.0 ± 4.4 (34 patients). For patients who received re-administration, the mean JDA GPP severity score was 3.5 ± 2.1 at re-administration (2 patients), and no evaluable data were available at the last observation after re-administration. The cross-tabulation of JDA GPP severity classification showed a trend toward improvement across all severity categories, including mild, moderate, and severe. For patients who received re-administration, no results were available in the cross-tabulation of JDA GPP severity classification due to the absence of evaluable patients.		
Discussion:	There was no notable difference in the safety profile between the results of this PMS study and those described in the Japanese package insert and the 1368.0013 trial. This study did not indicate any changes in the benefit-risk balance of Spesolimab I.V. Infusion.		

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Names and affiliations of principal investigators:	[redacted]		