

**Office of Biostatistics and Epidemiology/Division of Epidemiology
Pharmacovigilance Review Memorandum**

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Subject: Pharmacovigilance Plan Review

Sponsor: Octapharma

Product: Cutaquig® (Immune Globulin Subcutaneous
[Human])

Proposed Indication: Replacement therapy for primary
immunodeficiency in adults, including common
variable immunodeficiency, X-linked
agammaglobulinemia, congenital
agammaglobulinemia, Wiskott-Aldrich syndrome,
and severe combined immunodeficiencies

Submission Type/Number: BLA 125668/0

Submission Date: December 29, 2017

Action Due Date: December 28, 2018

1. Objective of the Review

The purpose of this review memo is to assess the adequacy of the sponsor's pharmacovigilance plan (PVP) for the proposed indications and determine if any additional post-marketing studies or risk evaluation and mitigation strategy (REMS) are required for Cutaquig@.

2. Product Information

Product information includes product description, proposed indication, and dosing regimen.

2.1 Product description

Cutaquig is a newly developed human immunoglobulin for subcutaneous administration (IGSC). It is a sterile solution of human normal immunoglobulin containing 16.5% (165 mg/mL) protein, of which at least 96% is human immunoglobulin G (IgG). Cutaquig is made from a pool of at least (b) (4) donations of human (b) (4) plasma. The production process of Cutaquig is based on the manufacturing process of Octagam (currently licensed intravenous immunoglobulin [IGIV] manufactured by Octapharma) including (b) (4) in which a commercially available (b) (4) is used for the (b) (4) (b) (4). Cutaquig is available in vial sizes of 6 mL, 10 mL, 12 mL, 20 mL, 24 mL, and 48 mL.

2.2 Proposed indication

Cutaquig is indicated for replacement therapy for primary immunodeficiency (PI) in adults. It includes, but is not limited to, common variable immunodeficiency (CVID), X-linked agammaglobulinemia, congenital agammaglobulinemia, Wiskott-Aldrich syndrome, and severe combined immunodeficiencies (SCID).

2.3 Proposed dosing regimen

The dose regimen should achieve a trough level of IgG (measured before the next infusion) of at least 5 to 6 g/L and aim to be within the reference interval of serum IgG for age. The initial weekly dose = previous IGIV dose (in grams) x (b) (4) / number of weeks between IGIV doses. Cutaquig can be administered at regular intervals from daily up to weekly. The dose should be adjusted based on the patient's pharmacokinetics, the desired IgG trough level, and clinical response.

3. Pertinent Regulatory History

Cutaquig was first approved in Canada on 15-Feb-2018. It had not been marketed as of 30-Jun-2018.

4. Materials Reviewed

Materials reviewed in support of this assessment include the following:

4.1 Pertinent sections of the licensing application in the Electronic Document Room (EDR)

- Section 1.14 Proposed Labeling, BLA 125668/0
- Section 1.16 Risk Management Plan (RMP), BLA 125668/0.24
- Section 5.3.5.2 Clinical Study Reports: SCGAM-01, BLA 125668/0
- Section 5.3.5.2 Clinical Study Reports: SCGAM-04, BLA 125668/0.29
- Section 5.3.6 120 days Safety Update, BLA 125668/0.20

4.2 Input from the clinical reviewer

The clinical review team raised no new safety concerns that require additional post-marking studies or a risk evaluation and mitigation strategy for Cutaquig.

5. Clinical Safety Database

The clinical experience with Cutaquig comes from three interventional studies (SCGAM-01, SCGAM-03, and SCGAM-04). A summary of each study and the pertinent safety issues are in Table 1.

Table 1: Overview of Clinical Studies Contributing to the Safety Assessment of Cutaquig

Study ID Study Period	Design Phase	No. of Patients (Age)	Indication	Dose Regimen	Number of Infusions	Safety Results (No. of ADRs/ Infusion)	Status
SCGAM-01* Jun-2014 to Oct-2017	Prospective, open-label, non- controlled, multicenter Phase III	N=61 N=23 (2 to <16 yrs) N=38 (16 to ≤75 yrs)	PI	<i>Cutaquig</i> as prescribed	3,497	472 AEs 5 SAEs 13 ADRs (0.004)	Ongoing
SCGAM-03 (Follow-up to SCGAM-01) May-2016 to May-2018	Prospective, open-label, non- controlled, multicenter Phase III	N=19	PI	<i>Cutaquig</i> as prescribed	800	110 AEs 6 SAEs 1 ADR	Ongoing
SCGAM-04 Feb-2017 to Jan-2018	Prospective, open-label, non- controlled, multicenter Phase III	N=25 (18 to ≤ 65 yrs)	PI	<i>Cutaquig</i> as prescribed	775	59 AEs no SAEs 3 ADRs (0.004)	Completed

PI = primary immunodeficiency; SAE = serious adverse event (any causality); ADR = adverse drug reaction (causally related)

*By 31 May 2018, 63 subjects, including 25 subjects < 16 years, were enrolled in study SCGAM-01. Of them, 54

subjects completed the study and 3 pediatric subjects are ongoing.

5.1 Study SCGAM-01 (ongoing)

Study SCGAM-01 is a prospective, open-label, non-controlled, and multi-center Phase III study to evaluate the pharmacokinetics, efficacy, tolerability, and safety of Cutaquig in patients with primary immunodeficiency diseases. The primary objectives of this study are 1) to assess the efficacy of Cutaquig in preventing serious bacterial infections (SBIs) compared with historical control data and 2) to evaluate the pharmacokinetic (PK) characteristics of Cutaquig and to compare the area under the curve (AUC) with that of IGIVs. Secondary objectives are to evaluate the PK profile, tolerability, and safety of Cutaquig, to assess the dosing conversion factor when switching patients from IGIV treatment, to develop guidance and recommendations to support further adjustments of dosing based on the total IgG trough level, and to assess the effect of Cutaquig on Quality of Life measures. It is planned to include between 50 and 64 patients with PI. For the pharmacokinetic sub-study, at least 20 patients with complete PK profiles should be analyzed. The study comprises a 12-week wash-in and wash-out period followed by a 12-month efficacy period. Cutaquig is given weekly (± 2 days) at 1.5 times the previous IGIV dose adjusted for weekly dosing.

This study started on 17-Jun-2014. By 27-Oct-2017, the data lock point of the report, 61 patients including 23 children (younger than 16 years of age) were enrolled in the study. The 61 patients in the safety analysis set received 3,497 infusions in the study, with a mean of 57.33 infusions administered per patient. The average dose of Cutaquig used per patient was 0.175 g/kg.

Table 2 shows summary of adverse events (AEs) including infections, excluding infections, or infections only in Study SCGAM-01 by type of adverse event.

Table 2: Summary of Adverse Events in Study SCGAM-01 (patients: N=61, infusions: N=3497)

Type of Adverse Event	Number (%) of Patients with AE	Number of AEs (AEs/Infusion)
AEs including infections and excluding infusion site reactions		
TEAE	57 (93.4%)	472 (0.1349)
SAE	4 (6.6%)	5 (0.0014)
Severe AE	3 (4.9%)	4 (0.0011)
Related AE	11 (18.0%)	14 (0.0040)
Temporally associated AE	51 (83.6%)	268 (0.0766)
Related temporally associated AE	10 (16.4%)	13 (0.0037)
AEs excluding infections and infusion site reactions		
TEAE	49 (80.3%)	233 (0.0666)
SAE	4 (6.6%)	4 (0.0011)
Severe AE	3 (4.9%)	3 (0.0009)
Related AE	11 (18.0%)	14 (0.0040)
Temporally associated AE	42 (68.9%)	135 (0.0386)
Related temporally associated AE	10 (16.4%)	13 (0.0037)
Infections only		

TEAE	54 (88.5%)	239 (0.0683)
SAE	1 (1.6%)	1 (0.0003)
Severe AE	1 (1.6%)	1 (0.0003)
Temporally associated AE	44 (72.1%)	133 (0.0380)

TEAE = treatment-emergent adverse event; SAE = serious adverse event; Related AE = causally related AE considered by investigator; Temporally associated AE = AE with an onset during the infusion or within 72 hours after the end of the infusion.

Source: modified from Table 19 in Clinical Study Report for Study SCGAM-01, BLA 125644/0, Page 75-76

Of the 61 patients in the safety analysis set, 57 patients (93.4%) experienced at least one AE, including infection, during the course of the study. If infections are excluded, 49 patients (80.3%) experienced 233 events. In total, 472 AEs were recorded throughout the study, of which approximately half were infections (239 events). Eleven patients (18.0%) had 14 events that the investigator considered to be related to Cutaquig.

When analyzed by intensity and excluding infections, 28 patients experienced AEs considered mild, 18 moderate, and 3 were severe.

There were 5 serious adverse events (SAEs) (i.e., thyroid tumor, worsening of seizure, acute appendicitis, severe persistent asthma, and acute bronchiolitis); all were considered unrelated to study medication by the sponsor. One patient reported an unrelated infection of severe intensity (respiratory syncytial virus bronchiolitis), and all other infections were considered non-serious and unrelated. There were no SAEs or treatment-emergent adverse events (TEAEs) leading to death, withdrawal, or other significant AEs.

The most commonly reported TEAEs by system organ class (SOC) were infections and infestations (83.6%) followed by gastrointestinal disorders (34.4%) and injury (27.9%). The most commonly reported TEAEs by preferred term (PT) were infections and infestations, specifically sinusitis (24.6%), nasopharyngitis (23.0%), and upper respiratory tract infection (21.3%).

Fifty-one patients (83.6%) had 268 temporally associated AEs (i.e., with an onset during the infusion or within 72 hours after the end of the infusion): infections and infestations (70.5%), gastrointestinal disorders (26.2%), musculoskeletal and connective tissue disorders (19.7%), and injury (18.0%). Thirteen (13) temporally associated AEs in 10 patients were considered drug-related (details in Appendix).

The AE rate per patient was 3.82 for AEs excluding infections and 3.92 for infection AEs alone. For each infusion, there were 0.0386 temporally associated AEs, 0.0037 related temporally associated AEs, and 0.0380 temporally associated infection AEs. Over the primary study period, the estimated proportion of infusions with at least one temporally associated AE (excluding infections) was 0.0288 for each patient, with an upper one-sided 95% confidence limit of 0.0370.

Overall 75.4% of patients experienced infusion site reactions. In three-quarters (76.7%) of infusions, there was no infusion site reaction (ISR), in one-fifth (20.8%) a mild reaction, in 2.4%

a moderate ISR, and a severe ISR was observed in only 2 infusions. The incidence of local reactions decreased over time: there was a local reaction in approximately 38% of infusions over the first 4 infusions, which decreased to 14% over the last 4 infusions. The most common types of ISR were erythema, redness, swelling, and pruritus.

Review of laboratory results showed clinically significant changes from baseline laboratory results in only a small number of patients. Ten patients had positive results for viral markers (HBsAg, Parvovirus-B19 viral load, and HAV viral load) during the study, but only one, a positive result for HBsAg at the end of study visit, was considered to be clinically significant. This patient was retested approximately 1 month later and both HBsAg and HBV viral load were negative, excluding the possibility of active HBV infection. All other positive findings were graded as non-clinically significant by the investigator as the findings were observed in screening tests. There were no findings of note on physical examination or in the vital signs data.

5.2 Study SCGAM-03 (Follow-up to SCGAM-01, ongoing)

This prospective, open-label, non-controlled, single-arm, and multicenter clinical Phase III study is aimed to monitor the long-term safety, tolerability, and efficacy of Cutaquig in patients with PI who have completed study SCGAM-01. All patients from the main study who completed the trial according to the protocol are offered participation in this extension study, if they have previously tolerated Cutaquig well. Re-screening will be performed, if the last visit of study SCGAM-01 (Week 65) is not identical to the first visit for study SCGAM-03. The maximum delay between completing study SCGAM-01 (i.e., last infusion of Cutaquig) and commencing first treatment in the extension study SCGAM-03 is 5 weeks. De novo patients will be allowed to participate in Canada.

The study started on 23-May-2016. By 31-May-2018, 19 patients were enrolled in the USA, of who 18 received treatment. One hundred and ten (110) AEs were recorded, 1 of them (cellulitis of abdominal wall) was considered related to Cutaquig treatment. Six serious AEs (subdural hematoma after head injury, C3-4 disc replacement, laminectomy for degenerative joint disease with spondylosis, spinal stenosis with spondylolisthesis, and 2 episodes of status asthmaticus in one patient) were reported; none of them were assessed as related to Cutaquig by the Investigator or by Octapharma. One patient withdrew from the study based on the patient's and investigator's decision (no clinical details).

Reviewer's comments: This study (SCGAM-03) began in 2016 and was ongoing at the time of the BLA submission. Limited safety data were provided in the most recent 120 days Safety Update received by the FDA on 24-Jul-2018. The data lock point (DLP) date for the 120 days Safety Update is 31-May-2018. No long-term follow-up data were available

5.3 Study SCGAM-04 (completed)

Study SCGAM-04 was a prospective, open-label, non-controlled, single-arm, multicenter Phase 3 clinical study to evaluate the efficacy of Cutaquig in preventing SBIs compared with historical control data, as well as, the tolerability and safety of Cutaquig.

The study was initiated in February 2017 and completed in Jan 2018. The study comprised an 8-week wash-in and washout period followed by a 6-month efficacy follow-up period. Twenty-five (25) adult patients with PI were enrolled at 5 study sites in Russia. The 25 patients in the safety analysis set received 775 infusions in the study, with the number of infusions administered per patient ranging from 7 to 32. The average dose of Cutaquig used per patient was 0.11 g/kg.

Table 3 shows summary of adverse events including infections, excluding infections, or infections only in Study SCGAM-04 by type of AE.

Table 3: Summary of Adverse Events in Study SCGAM-04 (patient: N=25, infusions: N=775)

Type of AE	Number (%) of Patients with AE	Number of AEs (AEs/Infusion)
AEs including infections and excluding infusion site reactions		
TEAE	18 (72%)	59 (0.0761)
SAE	0	0
Severe AE	0	0
Related AE	3 (12%)	3 (0.0039)
Temporally associated AE	14 (56%)	28 (0.0361)
Related temporally associated AE	3 (12%)	3 (0.0039)
AEs excluding infections and infusion site reactions		
TEAE	11 (44%)	26 (0.0335)
SAE	0	0
Severe AE	0	0
Related AE	3 (12%)	3 (0.0039)
Temporally associated AE	7 (28%)	12 (0.0155)
Related temporally associated AE	3 (12%)	3 (0.0039)
Infections only		
TEAE	16 (64%)	34 (0.0439)
SAE	0	0
Severe AE	0	0
Temporally associated AE	11 (44%)	17 (0.0219)

TEAE = treatment-emergent adverse event; SAE = serious adverse event; Related AE = causally related AE considered by investigator; Temporally associated AE = AE with an onset during the infusion or within 72 hours after the end of the infusion.

Source: modified Table 12 in Clinical Study Report for Study SCGAM-04, BLA 125644/0.29, Page 50

Of the 25 patients in the safety analysis set, 18 patients (72%) experienced at least one AE, including infection, during the course of the study. If infections are excluded, 11 patients (44%) experienced 26 events. In total, 59 AEs were recorded throughout the study, of which 34 were infections. Three patients (12%) had 3 events (musculoskeletal discomfort, dizziness, and headache) that the investigator considered to be related to Cutaquig.

When analyzed by intensity and excluding infections, 8 patients experienced events of mild intensity and 5 patients experienced events of moderate intensity; no severe AEs were reported. All infection AEs were non-serious and unrelated to Cutaquig, as per the sponsor.

There were no SAEs or TEAEs leading to death, withdrawal, or other significant AEs. One patient withdrew from the study based on the patient's decision.

The most commonly reported TEAEs by SOC were infections and infestations (52%) followed by general disorders (i.e., 3 conditions aggravated, 1 chest pain, and 1 asthenia) (16%). The most commonly reported TEAEs by PT were respiratory tract infection (24%), bronchitis (16%), and condition aggravated (12%).

Fourteen patients (56%) had 28 temporally associated AEs: respiratory tract infection (6 [24%]), condition aggravated (2 [8%]), and bronchitis (4 [16%]). Three of the temporally associated AEs (musculoskeletal discomfort, dizziness, and headache) were considered drug-related.

The AE rate per patient was 1.04 for AEs excluding infections and 1.36 for infection AEs alone. For each infusion, there were 0.0155 temporally associated AEs (that occurred within 72 hours of infusion), 0.0039 related temporally associated AEs, and 0.0219 temporally associated infection AEs. Over the primary study period the ratio of infusions with at least one temporally associated AE (excluding infections) was 0.55 per patient, with an upper one-sided 95% confidence limit of 1.19.

Fifteen patients (60%) experienced infusion site reactions. In 659 (85%) of the 775 infusions, there was no ISR, in 102 (13.2%) a mild reaction, and in 17 (2.2%) a moderate reaction. No severe ISRs were reported. The most common types of ISR were manifested as erythema, pruritus, and contact dermatitis.

The laboratory results did not indicate any safety concerns. All viral tests remained negative throughout the study. There were no findings of note on physical examination or in the vital signs data.

5.4 New safety data from 120 days Safety Update

Per request by the FDA (FDA Information request dated March 14, 2018), the sponsor also provided new safety information in 120 days Safety Update, which included data covering the period from 27-Oct-2017 (DLP for SCGAM-01) to 28-Jun-2018 from three clinical studies: SCGAM-01, SCGAM-03, and SCGAM-04.

5.4.1 Related AEs

New clinical findings included in the 120 days Safety Update for the time period 27-Oct-2017 to 28-Jun-2018 are listed below:

In the SCGAM-01, one (1) new related AE of Intermittent Headache, which occurred after 27-Oct-2017, was assessed by investigator as possibly related to Cutaquig.

In SCGAM-03 and SCGAM-04, all related AEs have been discussed in the Sections of 5.2 and 5.3.

There were a total of 18 related temporally associated AEs, excluding ISR, that were reported during the entire study period from 3 clinical studies (Appendix). Most of the AEs (15 out of 18) were considered mild in severity; the remaining 3 AEs were of moderate severity. Fifteen (15) AEs stated that the patient recovered within 1 day, the outcomes for the remaining 3 AEs were unknown. None resulted in a change in the dose of the study drug.

5.4.2 Serious AEs

In the SCGAM-01, one (1) new serious AE of Acute Arthritis, which occurred after 27-Oct-2017, was assessed by investigator as unrelated to Cutaquig.

All SAEs were assessed as unrelated to Cutaquig by the Investigator and Octapharma.

Reviewer's Assessment:

Data from these three safety studies showed that Cutaquig was well tolerated in the indicated patient population and no new safety signals, relative to what is already known from clinical trials and other IGSC, were observed. Most AEs were non-serious infections or infestations. All related AEs were well-known events following IgG treatment and labeled in the proposed package insert, and most were of mild or moderate intensity. The rate of infusion site reaction was relatively high per patient but low per infusion. The most common types of ISR were erythema, redness, swelling, and pruritus. The safety profile of Cutaquig appears qualitatively similar to that of other IGSC products licensed in the U.S.

There were a total of 106 patients treated with Cutaquig who received more than 5072 infusions. Given the study's relatively small sample size, it is unlikely that rare events would be captured.

6. Pharmacovigilance Plan Review

Based on data from previous clinical trials, post-marketing data, and published literatures, the sponsor delineated the important identified risks, important potential risks, and the important missing information (see Table 4 below):

Table 4: Summary of Safety Concerns as Proposed by the Sponsor

Important identified risk(s)	<ul style="list-style-type: none"> • Hypersensitivity reactions, including anaphylactic reactions • Thromboembolic events • Aseptic meningitis • Renal dysfunction/failure • Hemolysis
Important potential risk(s)	<ul style="list-style-type: none"> • Transfusion-related acute lung injury (TRALI) • Suspected transmission of pathogen infection
Missing information	<ul style="list-style-type: none"> • Safety in pregnant or breastfeeding women

The sponsor has proposed to use routine pharmacovigilance to monitor post-marketing safety of Cutaquig. There are no ongoing or planned additional pharmacovigilance studies. The proposed post-marketing pharmacovigilance actions for the identified safety concerns and missing information are summarized in Table 5.

Table 5: Summary of Pharmacovigilance Activities by Safety Concern Proposed by the Sponsor

Safety Concern	Risk Minimization Measures	Pharmacovigilance Actions
Aseptic meningitis	Routine risk communication: Summary of Product Characteristics (SmPC) section 4.4 Package Leaflet (PL) sections 2 and 4	Routine pharmacovigilance activities beyond adverse reactions reporting and signal detection: Medical Dictionary for Drug Regulatory Affairs (MedDRA) queries are used to review cases from the Drug Safety Database at the time of the quarterly signal analysis, the cumulative yearly review of adverse reactions and at Periodic Safety Update Report (PSUR)/Periodic Benefit Risk Evaluation Report (PBRER) intervals. Additional pharmacovigilance activities: None
Hemolysis	Routine risk communication: SmPC section 4.8 PL sections 2 and 4	
Hypersensitivity, including anaphylactic reactions	Routine risk communication: SmPC sections 4.3, 4.4, and 4.8 PL sections 2 and 4	
Thromboembolic events	Routine risk communication: SmPC sections 4.4 and 4.8 PL sections 2 and 4	
Renal dysfunction/failure	Routine risk communication: SmPC section 4.8 PL section 4	
Transfusion-Related Acute Lung Injury (TRALI)	Routine risk communication: SmPC section 4.8 PL section 4	
Suspected transmission of pathogen infection	Routine risk communication: SmPC sections 4.4 and 4.8 PL section 2	

Safety in pregnant or breastfeeding women	Routine risk communication: SmPC section 4.6 PL section 2
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Source: BLA 125688/0.24, Section 1.16 Risk Management Plan, Table 16, Page 28-29

Reviewer's Assessment:

The sponsor's proposed post-marketing pharmacovigilance activities are adequate for all safety concerns noted in Table 4. No new safety signals have been identified that would justify further studies or a REMS.

7. Post Licensure Safety Review

There are no post-licensure materials for review because the product has not been marketed in any country at DLP of BLA submission.

8. Integrated Risk Assessment

- The sponsor's proposed PVP adequately defines and describes the identified risks, potential risks, and important missing information.
- The sponsor's proposed PVP, which includes routine PV surveillance and adverse event reporting as required by FDA regulation, is acceptable.
- DE review of the pre-licensure safety data and the post-marketing safety reports from other IGSC products has not identified any safety concern that would warrant a post-marketing study or risk evaluation and mitigation strategy.

9. DE Recommendations

The Sponsor's proposed routine PV surveillance plan is adequate. No additional pharmacovigilance actions are needed at this time.

Appendix

Table: All cumulative related AEs (excluding infusion site reactions) from Studies SCGAM-01, SCGAM-03 and SCGAM-04

Subject ID	Age	Start Date	Verbatim	LLT	Infusional AE *	Investig.	Severity	AE Latency**	AE Outcome
(b) (6)	37	19-OCT-2015	Feverishness	Fever	Yes	Possible	Mild	0,1	Recovered/resolved
	43	25-JAN-2016	Positive direct coombs test	Direct Coombs test positive	Yes	Possible	Moderate	0	Recovered/resolved
	16	18-AUG-2015	High level of free hemoglobin	Free hemoglobin present	Yes	Possible	Mild	0	Recovered/resolved
	7	19-JAN-2016	Temperature increased	Body temperature increased	Yes	Possible	Mild	0,45	Recovered/resolved
	7	19-JAN-2016	Vomiting	Vomiting	Yes	Possible	Mild	0,45	Recovered/resolved
	34	24-FEB-2015	Abdominal swelling	Swelling abdomen	Yes	Probable	Moderate	0,22	Recovered/resolved
	55	13-APR-2016	Headache	Headache	Yes	Probable	Mild	0,14	Recovered/resolved
	55	18-APR-2016	Headache	Headache	Yes	Probable	Mild	0,15	Recovered/resolved
	12	11-MAY-2015	Myalgia	Myalgia	Yes	Probable	Moderate	0,15	Recovered/resolved
	63	19-SEP-2016	Stomach cramping during infusion	Stomach cramps	Yes	Possible	Mild	0	Recovered/resolved
	7	25-MAY-2017	Intermittent headache	Intermittent headache	Yes	Possible	Mild	0	Recovered/resolved
	71	18-MAY-2017	Decreased haptoglobin	Haptoglobin decreased	Yes	Possible	Mild	1,49	Unknown
	71	18-MAY-2017	Increased plasma hemoglobin	Hemoglobin increased	Yes	Possible	Mild	1,49	Unknown
	49	17-JAN-2017	Increased plasma free hemoglobin	Free hemoglobin present	No	Probable	Mild	7,21	Unknown

(b) (6) Scgam-03	62	24-JUN-2017	Cellulitis of abdominal wall	Cellulitis of abdominal wall	Yes	Possible	Mild	1,07	Recovered resolved
Scgam-04	>18	2017	Musculoskeletal discomfort	Musculoskeletal discomfort	Yes	Possible	Mild	<72 hours	Recovered resolved
Scgam-04	>18	2017	Dizziness	Dizziness	Yes	Possible	Mild	<72 hours	Recovered resolved
Scgam-04	>18	2017	Headache	Headache	Yes	Possible	Mild	<72 hours	Recovered resolved

* during or within 72 hrs. after end of infusion

** Days since Begin Last Administration 24-Jul-2018

Source: Table 2, 120 days Safety Update, BLA 125644/0.20, page 20