Summary Table of Study Protocol

Title	Periodic Knowledge, Attitudes, and Behavior (KAB) Survey of Patients and/or Caregivers to Assess Understanding of the Risks with the BKEMV™ Risk Evaluation and Mitigation Strategy (REMS)
Protocol version identifier	20240214 Version 2.0
Date of last version of the protocol	18 October 2024
EU Post Authorization Study (PAS) Register No	
Active Substance	Eculizumab-aeeb
Medicinal Product	BKEMV
Device	N/A
Product Reference	N/A
Procedure Number	N/A
Joint PASS	No

Research Question and Objectives	The objectives of the Patient KAB Survey are to conduct a survey with patients who are at least 18 years of age who have been dispensed and caregivers of patients of all ages who have been dispensed at least 1 dose of BKEMV. The following key message domains for patients have been developed based on the goal of the REMS as reviewed and approved by the FDA (refer to Section 3.2.6 of the BKEMV REMS Supporting Document). For a complete list of the key message questions encompassing the domains, as outlined below, Section 4. Patients should understand that receiving treatment with BKEMV increases the chance of getting serious meningococcal infections, which may quickly become life-threatening and cause death if not recognized and treated early (Key Message Domain 1). Patients should understand the need to be vaccinated against meningococcal infection and receive antibacterial drug prophylaxis if needed (Key Message Domain 2). Patients should be able to recognize the signs and symptoms of meningococcal infection and the need for immediate medical evaluation (Key Message Domain 3). The survey will begin with screening questions followed by key message questions. Additionally, the survey will collect data about patient and/or caregiver awareness, reading, and use of the BKEMV educational materials followed by the collection of demographic information.
Country(ies) of Study	United States

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Marketing Authorization Holder

Marketing authorization holder(s)	Amgen Inc.
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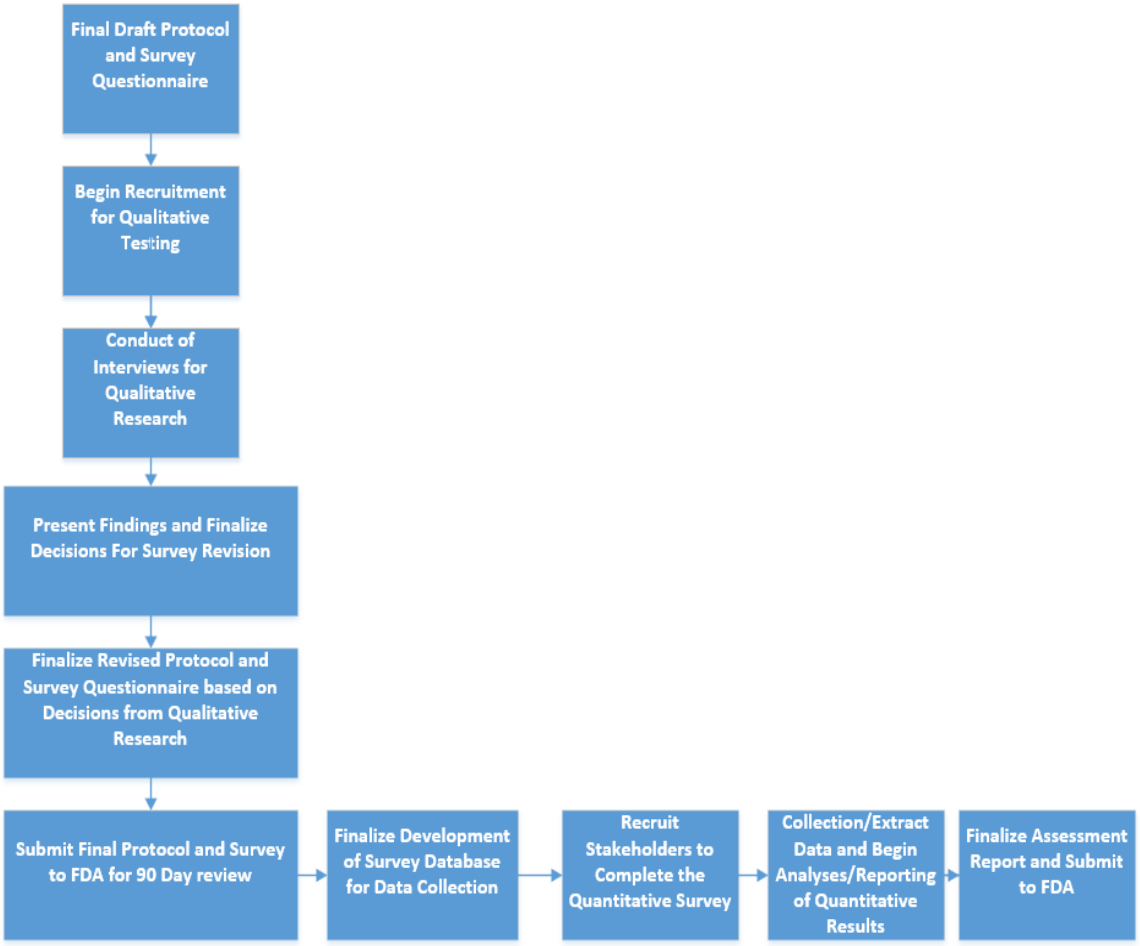
This protocol was developed, reviewed, and approved in accordance with Amgen's standard operating procedures.

Protocol Version	Date of Protocol	Page Header Date
Original, Version 1.0	11 July 2024	11 July 2024
Amendment 1, Version 2.0	18 October 2024	18 October 2024

Confidentiality Notice

Study Design Schema

Wave 1 KAB Survey Projected Timeline



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2. List of Abbreviations

Abbreviation	Definition
ADE	Adverse Device Effect
AE	Adverse Event
aHUS	Atypical Hemolytic Uremic Syndrome
Amgen	Amgen Inc.
CAPTCHA	Completely Automated Public Turing Test to Tell Computers and Humans Apart
CATI	Computer-Assisted Telephone Interviewing
CFR	Code of Federal Regulations
CI	Confidence Interval
DCT	Data Collection Tool
FDA	Food and Drug Administration
FDCA	Food, Drug, and Cosmetic Act
GCP	Good Clinical Practice
HCP	Healthcare Provider/Professional
HIPAA	Health Insurance Portability and Accountability Act
HIV	Human Immunodeficiency Virus
ICH	International Council for Harmonisation
IEC	Independent Ethics Committee
IRB	Institutional Review Board
KAB	Knowledge, Attitudes, and Behavior
N/A	Not Applicable
OSF	Other Safety Findings
Patient and/or Caregiver	Participant

Abbreviation	Definition
PI	Prescribing Information
PNH	Paroxysmal Nocturnal Hemoglobinuria
QC	Quality Control
QR	Qualitative Research
REMS	Risk Evaluation and Mitigation Strategy
SAS	Statistical Analysis System
SCC	Survey Coordinating Center
SERRM	Safety, Epidemiology, Registries & Risk Management
SOP	Standard Operating Procedures
TL	Tables and Listings
UAT	User Acceptance Testing
UBC	United BioSource LLC
URL	Uniform Resource Locator
US	United States

3. Responsible Parties

Name, Degree(s)	Job Title	Affiliation	Address
PPD , JD	Assoc Director | REMS Planning & Implementation Lead	Amgen Inc.	One Amgen Center Drive, Thousand Oaks, CA 91320
PPD BS/BA	Associate Director Knowledge, Attitudes, and Behavior Programs	United BioSource LLC	933 Canyon Road, Morgantown, WV 26508

4. Abstract

Title: BKEMV™ Periodic Knowledge, Attitudes, and Behavior (KAB) Survey of Patients and/or Caregivers to Assess Understanding of the Risks with the BKEMV Risk Evaluation and Mitigation Strategies (REMS)

Study Rationale & Background: The BKEMV REMS was approved by the United States (US) Food and Drug Administration (FDA) on 28 May 2024. In accordance with section 505-1 of Federal Food, Drug, and Cosmetic Act (FDCA), the FDA determined that a Risk Evaluation and Mitigation Strategy (REMS) is necessary for BKEMV to mitigate the risk of serious meningococcal infections and to educate healthcare providers/professionals (HCPs) and patients and/or caregivers regarding:

a. the need to ensure that patients are vaccinated against meningococcal infections,

b. the need to ensure that patients are aware of early signs and symptoms of meningococcal infections and the need for immediate medical evaluation; and,

c. the need to ensure that prescribers are aware of early signs and symptoms of meningococcal infections and the need for immediate medical evaluation.

The specific objectives to be achieved by the BKEMV REMS include the assessment of patients' and/or caregivers' knowledge of the following key message domains:

1. BKEMV increases your chance of getting serious and life-threatening meningococcal infections.

2. These serious meningococcal infections may quickly become life-threatening and cause death if not recognized and treated early.

3. Complete or update meningococcal vaccine(s) at least 2 weeks before your first dose of BKEMV or as soon as possible if you have not already received these vaccines.

4. If you have not completed or are not up to date with meningococcal vaccines at least 2 weeks before your first dose of BKEMV and BKEMV therapy must be started right away, take antibiotics as directed by your healthcare provider.

5. Call your healthcare provider or get emergency medical care right away if you get any of these signs or symptoms of a serious meningococcal infection:
   a) fever
   b) fever with or without a rash
   c) fever with high heart rate
   d) headache with nausea or vomiting
   e) stiff neck or stiff back
   f) confusion
   g) muscle aches with flu-like symptoms
   h) sensitivity of eyes to light

6. Carry the Patient Safety Card with you at all times during treatment and for 3 months after your last dose of BKEMV.

7. Show the Patient Safety Card to any healthcare provider that treats you.

The survey will begin with screening questions followed by key message questions. The survey will also collect data about patient awareness, reading, and use of the BKEMV educational materials followed by the collection of demographic information.

A component of the BKEMV REMS Assessment Plan is the conduct of a quantitative evaluation survey with patients and/or caregivers, to assess awareness of the REMS materials, knowledge of the risks associated with BKEMV, and knowledge of the requirements of the BKEMV REMS. Throughout this protocol, the quantitative evaluation survey will, hereinafter, be referred to as the "Patient Knowledge Attitudes, and Behavior (KAB) Survey." Findings from the Patient KAB Survey, together with other REMS evaluation metrics, will be used to assess the BKEMV REMS and determine whether changes need to be made to the REMS processes or educational materials to make them more effective in achieving the intended goal. Also hereinafter, a patient and/or caregiver may be referred to as "participant."

This protocol provides the procedures to be followed with patients who have been dispensed and caregivers of patients of all ages who have been dispensed at least 1 dose of BKEMV, for inclusion in the BKEMV REMS Assessment Reports to be submitted to the FDA at 12 months post the approval of the REMS, and annually thereafter. This noninterventional study is part of the BKEMV REMS Assessment and is a commitment to the FDA.

Research Question(s) & Objective(s): The above key message domains identify the most critical information for stakeholders to know about the risk and safe use behaviors to mitigate the risks with BKEMV. The objectives of the Patient KAB Survey are to conduct a survey with patients who have been dispensed and caregivers of patients of all ages who have been dispensed at least 1 dose of BKEMV to assess their awareness and understanding of the risk of serious meningococcal infections associated with the use of BKEMV, the BKEMV REMS requirements, and the REMS goals and materials. The key message questions have been grouped into the following key message domains:

- Key Message Domain 1: Patients should understand that receiving treatment with BKEMV increases the chance of getting serious meningococcal infections, which may quickly become life-threatening and cause death if not recognized and treated early.
    - BKEMV increases your chance of getting serious and life-threatening meningococcal infections.
    - These serious meningococcal infections may quickly become life-threatening and cause death if not recognized and treated early.
- Key Message Domain 2: Patients should understand the need to be vaccinated against meningococcal infection and receive antibacterial drug prophylaxis if needed.
    - Complete or update meningococcal vaccine(s) at least 2 weeks before your first dose of BKEMV or as soon as possible if you have not already received these vaccines.
    - If you have not completed or are not up to date with meningococcal vaccines at least 2 weeks before your first dose of BKEMV and BKEMV therapy must be started right away, take antibiotics as directed by your healthcare provider.
- Key Message Domain 3: Patients should be able to recognize the signs and symptoms of meningococcal infection and the need for immediate medical evaluation.
    - Call your healthcare provider or get emergency medical care right away if you get any of these signs or symptoms of a serious meningococcal infection:

a) fever
b) fever with or without a rash
c) fever with high heart rate
d) headache with nausea or vomiting
e) stiff neck or stiff back
f) confusion
g) muscle aches with flu-like symptoms
h) sensitivity of eyes to light

- Carry the Patient Safety Card with you at all times during treatment and for 3 months after your last dose of BKEMV.
- Show the Patient Safety Card to any healthcare provider that treats you.

The survey questions associated with each key message domain have been developed as described above. A select number of questions will be pre-tested through qualitative research (QR) and finalized prior to implementation of the Wave 1 Patient KAB Survey.

Study Design: This is a US-based, observational, cross-sectional survey of patients who have been dispensed and caregivers of patients of all ages who have been dispensed at least 1 dose of BKEMV. The survey can be self-administered by respondents via secure internet and telephone modalities utilizing a validated United BioSource LLC (UBC) Pathways® Knowledge Survey System for data collection that is secure for receiving and storing survey data.

To ensure maximum participation in the survey, all patients who have been dispensed identified at a designated interval, prior to survey launch, will receive a Pre-Notification Letter explaining the purpose and details of the upcoming survey. After the Pre-Notification Letter has been sent, upon launch of the survey, the targeted population will be sent an Invitation Letter. Throughout the survey wave, reminder letters will be distributed to non-responders. Because patients are not enrolled in the REMS, no telephone numbers are available; therefore, outbound calling cannot be performed.

Population: Respondents must meet all the following inclusion criteria to be eligible for inclusion in the study:

- Patients of 18 years of age who have been dispensed at least 1 dose of BKEMV will be permitted to participate.
- Caregivers of patients of all ages who have been dispensed at least 1 dose of BKEMV will be permitted to participate.
- Individuals who have participated in QR will be permitted to participate.[1]

Respondents meeting any of the following exclusion criteria will not be included in the study:

1. Because of the time in which this qualitative evaluation took place compared to when the quantitative survey is to be conducted(Table 1) and because the population targeted for the qualitative research were not patients being treated with BKEMV, allowing those who participated in QR to also participate in the quantitative survey creates no inherent risk in influencing the outcome of whether or not patients and/or caregivers who will be targeted during the quantitative survey are aware of the REMS objectives.

- Respondents who do not agree to participate in the survey.
- Respondents who are currently working for and/or whose immediate family members who are currently working for or consultants to Amgen, UBC, or the FDA.
- Respondents who report having a conflict of interest.
- Respondents who have previously participated may be eligible to participate in future surveys. This eligibility criteria will be dependent upon the number of patients who have been dispensed at least 1 dose of BKEMV, prior to launch of subsequent survey waves.

Variables: The Patient KAB Survey will document each patient and/or caregivers' knowledge and assess the attitudes and behaviors of the important information as presented in the key domain messages communicated through the BKEMV REMS. Key message questions will be pre-tested via QR and submitted for FDA review on or before 28 November 2024.

The Patient KAB Survey will also collect demographic characteristics for patients and/or caregivers who complete all survey questions.

These include:

- Type of respondent (patient versus caregiver)
- Patient age
- Education Level
- Length of time being treated with BKEMV
- Past Completer versus Current Completer – if it is decided that prior survey completers are permitted to participate this analysis will be introduced. This decision will occur prior to Wave 2 and subsequent waves thereafter.
- Geographic location
- Survey completion status

Data Sources: The survey will be administered via a secure web-based internet connection, which will allow respondents who choose to participate to do so at a time and location that is convenient for them.

The structured survey comprises key message questions or statements written in several formats, which include specific key message domains:

- Questions or statements with a defined list of possible answers from which the respondent is required to choose one answer (i.e., multiple-choice).
- Questions or statements with a defined list of possible answers from which the respondent is required to choose one or more answers (e.g., "Select all that apply").

- Questions or statements with response options of “yes” or “true,” “no” or “false,” and “I don’t know” that require the respondent to indicate agreement or disagreement.

All answers for key message questions permitting multiple responses will be tallied to provide a broad picture of respondent’s knowledge, attitudes, and behavior.

The desired response for key message questions is generally “true” or “yes” indicating knowledge of the objectives of the BKEMV REMS. However, some questions are formatted to have the respondent disagree with the statement as written (“false” or “no”) to avoid having the same affirmative answer for all desired responses. Whenever possible within a key domain message, there will be an equal balance of questions with a “true” or “yes” and “false” or “no.”

The recruitment list for survey participation will be compiled via the Specialty Pharmacy. This list will include patients who have been dispensed at least 1 dose of BKEMV. The respondent characteristics that are captured in this dataset to be used for survey execution include the patient’s first name, last name and mailing address.

Study Size: The survey will target the completion of at least 153 completed surveys in Wave 1.

Data Analysis: Statistical analyses will be primarily descriptive in nature. Survey administration data will be summarized using descriptive statistics.

In the primary analysis, descriptive analyses will be performed for each key message domain question. For each question/item, the number of individuals who selected each response will be reported. Additionally, the percentage and 95% confidence interval (CI) will be calculated for the correct response.

Milestones: The date of commercialization of BKEMV is not targeted to begin until March 2025. Data collection for Wave 1 is planned to begin on or about July 2025. The Wave 1 Patient KAB Survey assessment report will be submitted to the FDA by May 2026. The annual Assessment Reports will continue each year with data collection ending on 28 March and the final assessment report submitted by 28 May until notified otherwise by the FDA.

Milestones

Milestones	**Planned Date**[1]
Final Study Protocol and Survey	18 November 2024
Start of Data Collection	~July 2025
Wave 1 Assessment Report due to FDA	28 May 2026
Wave 2 Assessment Report due to FDA	28 May 2027
Wave 3 Assessment Report due to FDA	28 May 2028
End of Data Collection	TBD[2]

Final Assessment Report	TBD[2]

FDA = Food and Drug Administration
1. Dates are subject to change based on receipt of FDA feedback.
2. The Assessment Reports will continue until notified otherwise by the FDA.

Objectives	Endpoints
Primary	
To describe patient and/or caregiver knowledge of: • Patients should understand that receiving treatment with BKEMV increases the chance of getting serious meningococcal infections, which may quickly become life-threatening and cause death if not recognized and treated early (Key Message Domain 1). • Patients should understand the need to be vaccinated against meningococcal infection and receive antibacterial drug prophylaxis if needed (Key Message Domain 2). • Patients should be able to recognize the signs and symptoms of meningococcal infection and the need for immediate medical evaluation (Key Message Domain 3). See Appendix F for all question/options/answers to key message questions associated with each key message domain.	• The number of respondents who score 80% or greater in each key message domain
Secondary	
N/A	
Exploratory	
N/A	

N/A = not applicable

- Study Design/Type

This is a US-based, observational, cross-sectional survey of patients who have been dispensed and caregivers of patients of all ages who have been dispensed at least 1 dose of BKEMV. The survey can be self-administered by the respondents via secure internet and telephone modalities utilizing a validated UBC Pathways® Knowledge Survey System for data collection that is secure for receiving and storing survey data.

- Study Population or Data Resource

Patients who have been dispensed at least 1 dose of BKEMV. Caregivers of patients of all ages who have been dispensed at least 1 dose of BKEMV will also be permitted to participate.

- Summary of Respondent Eligibility Criteria

Respondents must meet all the following inclusion criteria to be eligible for inclusion in the study:

  - Patients who have been dispensed at least 1 dose of BKEMV.
  - Caregivers of patients of all ages who have been dispensed at least 1 dose of BKEMV.

Respondents meeting any of the following criteria will not be included in the study:

  - Respondents who do not agree to participate in the study.
  - Respondents who are currently working for and/or whose immediate family members are currently working for are consultants to Amgen, UBC, or the FDA.
  - Respondents who reported having a conflict of interest.

- Follow-up

  N/A

- Variables

The key message concepts, which will be evaluated in this KAB survey, include the following:

- BKEMV increases your chance of getting serious and life-threatening meningococcal infections.
- These serious meningococcal infections may quickly become life-threatening and cause death if not recognized and treated early.
- Complete or update meningococcal vaccine(s) at least 2 weeks before your first dose of BKEMV or as soon as possible if you have not already received these vaccines.
- If you have not completed or are not up to date with meningococcal vaccines at least 2 weeks before your first dose of BKEMV and BKEMV therapy must be started right away, take antibiotics as directed by your healthcare provider.
- Call your healthcare provider or get emergency medical care right away if you get any of these signs or symptoms of a serious meningococcal infection:
  a) fever
  b) fever with or without a rash
  c) fever with high heart rate
  d) headache with nausea or vomiting
  e) stiff neck or stiff back
  f) confusion
  g) muscle aches with flu-like symptoms
  h) sensitivity of eyes to light
- Carry the Patient Safety Card with you at all times during treatment and for 3 months after your last dose of BKEMV.
- Show the Patient Safety Card to any healthcare provider that treats you.

- Exposure Variable(s)

N/A

- Other Covariate(s)

N/A

- Study Sample Size

The goal for the Wave 1 Patient KAB Survey is a sample of at least 153 completed surveys. The survey enrollment window will remain open for the planned duration of the survey even if the target of 153 completed surveys is reached. Recruitment may exceed the minimum target sample size since the recruitment window will continue until the pre-specified survey end date, with a data cut-off no sooner than 60 days prior to submission of REMS assessments to the FDA.

As of 16 October 2024, the population of patients is estimated to be at 250 at the time of launch of the Wave 1 survey; therefore, no random sampling will be performed. To reduce the margin of error, all patients who have been dispensed at least 1 dose of BKEMV will receive an invitation for survey completion. Caregivers for patients under the age of 18 will be targeted to receive the invitation on behalf of this patient.

If the Patient KAB Survey sample size for Wave 1 is not achieved, the following measures will be considered to increase the response rate for future waves:

  - Increase survey field time to allow respondents additional time for survey completion.
  - Evaluate alternatives to increase survey participation (e.g., pre-registration).
  - Evaluate compensation.

- Data Analysis

Statistical analyses will be descriptive in nature. Counts and percentages will be calculated for each question/item in the questionnaire. Ninety-five percent (95%) CIs for the survey end points will be calculated to provide an estimate of precision; however no formal hypothesis will be tested. All CIs around the percentages will be exact binomial 2-sided 95% CIs calculated according to the method of Clopper-Pearson. Analyses will be performed at the respondent level; therefore, within-respondent variation is not relevant.

5. Amendments and Updates

None

6. Rationale and Background

The BKEMV™ (eculizumab-aeeb) Risk Evaluation and Mitigation Strategy (REMS) was approved by the United States (US) Food and Drug Administration (FDA) on 28 May 2024. In accordance with section 505-1 of Federal Food, Drug, and Cosmetic Act (FDCA), the FDA determined that a REMS is necessary for BKEMV mitigate the risk of serious meningococcal infections and to educate HCPs and patients and/or caregivers regarding the need to:

a. The need to ensure that patients are vaccinated against meningococcal infections,

b. The need to ensure that patients are aware of early signs and symptoms of meningococcal infections and the need for immediate medical evaluation; and,

c. The need to ensure that prescribers are aware of early signs and symptoms of meningococcal infections and the need for immediate medical evaluation.

The specific objectives to be achieved by the BKEMV REMS include the assessment of patients' and/or caregivers' knowledge of the following key message domains:

1. BKEMV increases your chance of getting serious and life-threatening meningococcal infections.

2. These serious meningococcal infections may quickly become life-threatening and cause death if not recognized and treated early.

3. Complete or update meningococcal vaccine(s) at least 2 weeks before your first dose of BKEMV or as soon as possible if you have not already received these vaccines.

4. If you have not completed or are not up to date with meningococcal vaccines at least 2 weeks before your first dose of BKEMV and BKEMV therapy must be started right away, take antibiotics as directed by your healthcare provider.

5. Call your healthcare provider or get emergency medical care right away if you get any of these signs or symptoms of a serious meningococcal infection:
   a) fever
   b) fever with or without a rash
   c) fever with high heart rate
   d) headache with nausea or vomiting
   e) stiff neck or stiff back
   f) confusion
   g) muscle aches with flu-like symptoms
   h) sensitivity of eyes to light

6. Carry the Patient Safety Card with you at all times during treatment and for 3 months after your last dose of BKEMV.

7. Show the Patient Safety Card to any healthcare provider that treats you.

A component of the BKEMV REMS Assessment Plan is the conduct of a quantitative evaluation survey with patients who have been dispensed and caregivers of patients of all ages who have been dispensed at least 1 dose of BKEMV, to assess awareness of the REMS materials, knowledge of the risks associated with BKEMV, and knowledge of the requirements of the BKEMV REMS.

Findings from the Patient KAB Survey, together with other REMS evaluation metrics, will be used to assess the BKEMV REMS and determine whether changes need to be made to the REMS processes and/or educational materials to make them more effective in achieving the intended goal.

6.1 Diseases and Therapeutic Area

BKEMV™ (eculizumab-aeeb) is indicated for the treatment of adults with PNH to reduce hemolysis and for the treatment of adult and pediatric patients with atypical hemolytic uremic syndrome (aHUS) to inhibit complement-mediated thrombotic microangiopathy. Eculizumab-aeeb binds to human C5 in the region of the protein that becomes C5b and blocks cleavage, thereby inhibiting the complement cascade and ultimately blocking terminal complement-mediated intravascular hemolysis.

The use of eculizumab products, complement inhibitors, increases a patient's susceptibility to serious, life threatening, or fatal meningococcal infections (septicemia and/or meningitis) in any serogroup, including non-groupable strains. Life-threatening and fatal meningococcal infections have occurred in both vaccinated and unvaccinated patients treated with complement inhibitors. There were no adverse events of meningococcal infections reported in the BKEMV clinical development program. The initiation of BKEMV treatment is contraindicated in patients with unresolved serious Neisseria meningitidis infection.

Risk groups or risk factors for meningococcal infections include:

- Genetic deficiency or therapeutic inhibition of terminal complement
- Lack of commercially available vaccine against certain meningococcus serogroup
- (Partial) resistance of meningococcal strain to prophylactic antibiotics
- Professionals who are exposed to environments of greater risk for meningococcal disease
- Research, industrial, and clinical laboratory personnel who are routinely exposed to Neisseria meningitidis
- Military personnel during recruit training (military personnel may be at increased risk of meningococcal infections when accommodated in close quarters)
- Day-care center workers
- Living on a college or university campus
- Travelling to endemic areas for meningococcal meningitis (e.g., India, Sub-Saharan Africa, pilgrimage to Saudi Arabia for Hajj)
    - Meningococcal infections may resolve with appropriate treatment. However, fatal outcomes have been reported in patients treated with eculizumab products. Vaccination does not eliminate the risk of serious meningococcal infections, despite development of antibodies following vaccination; therefore, patients should be closely monitored for early signs and symptoms of the disease.

6.2 Rationale

In accordance with Section 505 (1)(f)(3)(A) of the FDCA, the FDA determined that a REMS is necessary for BKEMV to ensure the benefits of the drug outweigh the potential risk of meningococcal infections.

A component of the BKEMV REMS Assessment Plan is the conduct of a quantitative evaluation survey with patients who have been dispensed and caregivers of patients of all ages who have been dispensed at least 1 dose of BKEMV to assess awareness of the REMS materials, knowledge of the risks associated with BKEMV, and knowledge of

the requirements of the BKEMV REMS.

Findings from the Patient KAB Survey, together with other REMS evaluation metrics, will be used to assess the BKEMV REMS and determine whether changes need to be made to the REMS processes or educational materials to make them more effective in achieving the intended goal.

This combined protocol/statistical analysis plan provides the procedures to be followed, for inclusion in the BKEMV REMS Assessment Reports. This noninterventional study is part of the BKEMV REMS Assessment and is a commitment to the FDA.

6.3 Feasibility and Futility Considerations

To effectively evaluate the Patient KAB Survey, Qualitative Research (QR) will be conducted on a subset of questions from the draft Wave 1 Patient KAB Survey. QR will be conducted with a general population of patients who are being treated for a blood disorder, excluding those with human immunodeficiency virus (HIV).

6.4 Statistical Inference (Estimation or Hypothesis[es])

Statistical analyses will be primarily descriptive in nature. Counts and percentages will be calculated for each question/item in the questionnaire. Ninety-five percent Confidence Intervals (CIs) for the survey end points will be calculated to provide an estimate of precision; however no formal hypothesis will be tested. All CIs around the percentages will be exact binomial 2-sided 95% CIs calculated according to the method of Clopper-Pearson. Analyses will be performed at the respondent level; therefore, within-respondent variation is not relevant.

7. Research Question and Objectives

The key message domain questions and statements in the survey address the goal and objectives of the BKEMV REMS and are written in several formats, which include:

- Questions or statements with a defined list of possible answers from which the respondent is required to choose one answer (i.e., multiple-choice).
- Questions or statements with a defined list of possible answers from which the respondent is required to choose 1 or more answers (i.e., Select all that apply).
- Questions or statements with response options of “yes” or “true,” or “false,” and “I don’t know” that require the respondent to indicate agreement or disagreement.

All answers for questions or statements will be tallied to provide a broad picture of the respondent’s knowledge, attitudes, and behavior.

The desired response for key message domain questions is generally “true” or “yes,” indicating knowledge of the objectives of the REMS. However, some questions are formatted to have the respondent disagree with the statement as written (“false”) to avoid having the same affirmative answer for all desired responses.

7.1 Primary

The objectives of the Patient KAB Survey are to conduct a survey with patients who have been dispensed and caregivers of patients of all ages who have been dispensed at least 1 dose of BKEMV to assess their awareness and understanding of the risks of BKEMV, the BKEMV REMS requirements, and the REMS goals and materials:

- Key Message Domain 1: Patients should understand that receiving treatment with BKEMV increases the chance of getting serious meningococcal infections, which

may quickly become life-threatening and cause death if not recognized and treated early.

- BKEMV increases your chance of getting serious and life-threatening meningococcal infections.
- These serious meningococcal infections may quickly become life-threatening and cause death if not recognized and treated early.

- Key Message Domain 2: Patients should understand the need to be vaccinated against meningococcal infection and receive antibacterial drug prophylaxis if needed.
  - Complete or update meningococcal vaccine(s) at least 2 weeks before your first dose of BKEMV or as soon as possible if you have not already received these vaccines.
  - If you have not completed or are not up to date with meningococcal vaccines at least 2 weeks before your first dose of BKEMV and BKEMV therapy must be started right away, take antibiotics as directed by your healthcare provider.
- Key Message Domain 3: Patients should be able to recognize the signs and symptoms of meningococcal infection and the need for immediate medical evaluation.
  - Call your healthcare provider or get emergency medical care right away if you get any of these signs or symptoms of a serious meningococcal infection:
    a) fever
    b) fever with or without a rash
    c) fever with high heart rate
    d) headache with nausea or vomiting
    e) stiff neck or stiff back
    f) confusion
    g) muscle aches with flu-like symptoms
    h) sensitivity of eyes to light
  - Carry the Patient Safety Card with you at all times during treatment and for 3 months after your last dose of BKEMV.
  - Show the Patient Safety Card to any healthcare provider that treats you.

7.2 Secondary

N/A

7.3 Exploratory

N/A

8. Research Methods

This is a US-based, observational, cross-sectional survey of patients, identified via the Specialty Pharmacy and who have been dispensed at least 1 dose of BKEMV. Caregivers of patients of all ages who have been dispensed at least 1 dose of BKEMV will also be permitted to participate. The survey can be self-administered by the respondents via secure

internet and telephone modalities utilizing a validated UBC Pathways® Knowledge Survey System for data collection that is secure for receiving and storing survey data.

All assessments described in this protocol are performed as part of normal clinical practice or standard practice guidelines for patients in the US.

8.1 Study Design

Comprehension Pre-Testing of the Survey (Qualitative Research)

To effectively evaluate the Patient KAB Survey, QR will be conducted on questions associated with the key message domains from the draft Wave 1 survey. QR will be conducted with a general population targeting 12 patients who have been diagnosed with a blood disorder excluding HIV. The conduct of QR will occur through 1:1 interviews with an experienced Moderator.

The purpose of QR of select survey questions is to identify potential terms, questions, or topics for clarification or revision based on respondent feedback. Furthermore, the research will assess comprehension among participants regarding the words and phrases used in select survey questions and response options.

QR will be carried out in a double-blinded manner. Therefore, during QR, respondents will not know the identity of Amgen and the product under study and Amgen will not know the respondents who participate in the study. If during the interview, a potential event/report is identified, it is possible that Amgen will receive information related to the respondent, should the respondent consent to follow-up. For more information about potential reporting see Section 10.

Feedback elicited from the QR interviews will be used to support the identification of terms, questions, or topics that require clarification or revision, based on areas of confusion or miscomprehension by interviewed participants.

Findings and recommendations from QR will be reviewed and incorporated as appropriate to update the select survey questions and response options being tested, prior to the implementation of the Wave 1 Patient KAB Survey. A copy of the Final Summary Report titled, Qualitative Research to Evaluate Healthcare Provider and Patient Knowledge, Attitudes, and Behavior (KAB) Surveys for BKEMV along with the QR moderator discussion guide used to conduct QR, redacted interview transcripts, and the findings presentation will be included in ANNEX 5 upon final submission of this document to the FDA (See Table 1 for an estimated submission date).

More information regarding QR can be found in the final Plan and Screener located in ANNEX 2.

8.2 Setting and Study Population

The Patient KAB Survey will be administered via the internet or telephone and patients and/or caregivers will be able to choose the method that is preferred. The UBC Pathways® Knowledge Survey System will be used for both methods of survey administration which has been validated and is secure for receiving and storing survey data. Details on data management are available in Section 8.6.

The projected timeline for program development, survey launch, recruitment, and reporting for Wave 1 is shown in Table 1 below.

Table 1: Projected Timeline for Wave 1 KAB Activities

Milestones	Planned Date[1]
Final Protocol and Survey for QR	~ 24 July 2024
QR	31 July 2024 – 30 October 2024
Protocol and Survey Revision Post QR	02 October 2024 – 29 November 2024
Protocol and Survey Submission to FDA – 90-day review	28 November 2024 – 26 February 2025
UBC Pathways® Knowledge Survey System Build	~31 March 2025 – 29 August 2025[2]
Distribution of Pre-Notification Letter	11 August 2025
UBC Pathways® Knowledge Survey System in Production (Survey Launch)	02 September 2025
Start of Data Collection Period	03 September 2025
Distribution of Initial Survey Invitation	04 September 2025
First Reminder Mailing (alternating modalities as applicable)	29 September 2025[3]
Second Reminder Mailing (alternating modalities as applicable)	27 October 2025[3]
Third Reminder Mailing (alternating modalities as applicable)	12 January 2026[3]
Fourth Reminder Mailing (alternating modalities as applicable)	23 February 2026[3]
End of Data Collection	29 March 2026
Data Processing and Report Development	30 March 2026 – 27 May 2026
Final Wave 1 Assessment Report to FDA	28 May 2026[4]

[1] Dates are subject to change based on receipt of FDA comments.
[2] UBC Pathways® Knowledge Survey System will begin building approximately 2 weeks following the completion of the FDA 90-day review cycle.
[3] Distribution of letter campaigns may shift based on survey uptake.
[4] Approval of the BKEMV REMS was on 28 May 2024. An assessment is to be submitted 12-months post approval. Due to the commercialization status of BKEMV, no data will be available for this reporting period.

8.2.1 Study Period

Data from the Patient KAB Survey, together with other REMS evaluation metrics, will be used to assess the REMS and determine whether changes need to be made to the REMS processes and/or educational materials to make them more effective in achieving the goals of the BKEMV REMS. The results of the Patient KAB Survey will be included in the 12-month assessment and will continue annually as required by the FDA.

8.2.2 Selection and Number of Sites

N/A

8.2.3 Respondent Eligibility

The Patient KAB Survey execution has an undetermined launch date at this time, based on the commercialization status of BKEMV. Once launched, the survey will target patients who have been dispensed at least 1 dose of BKEMV with BKEMV identified via the Specialty Pharmacy.

Termination of the respondent's participation in the survey will occur if they do not meet the eligibility criteria below.

8.2.3.1 Inclusion Criteria

Respondents must meet all the following inclusion criteria to be eligible for inclusion in the study:

- Patients who are 18 years of age or older who have been dispensed at least 1 dose of BKEMV
- Patients who have participated in QR.[2]
- Caregivers 18 years of age or older who care for patients of all ages who are unable to take the survey for themselves

8.2.3.2 Exclusion Criteria

Patients meeting any of the following criteria will not be included in the study:

- Respondents who do not agree to participate in the survey. *Patients and/or caregivers who respond 'no' to Question 1 that asks, "Do you agree to participate in this study about BKEMV?"*
- Respondents who are currently working for and/or whose immediate family members are currently working for or are consultants to Amgen, UBC, or the FDA.
- Respondents who reported having a conflict of interest.

Further details associated with respondents who do not meet the exclusion criteria established above will be addressed in the assessment report.

8.2.4 Matching - Comparison of the Survey Population to the BKEMV REMS Population Analysis

This analysis cannot be performed because patients are not enrolled in the BKEMV REMS.

8.2.5 Baseline Period

Given that the survey questions can change periodically over time, there is no specific baseline period for this type of study.

8.2.6 Study Follow-up

N/A

8.3 Variables

8.3.1 Exposure Assessment

N/A

2. Because of the time in which this qualitative evaluation takes place compared to when the quantitative survey is conducted and because the population targeted for the qualitative research are not patients being treated with BKEMV creates no inherent risk in influencing the outcome of whether patients who will be targeted during the quantitative survey are aware of the REMS objectives.

8.3.2 Outcome Assessment

The survey will assess each patient's and/or caregiver's knowledge, attitudes, and behaviors of the important information as presented in the key domain messages communicated through the BKEMV REMS.

The key message domain questions, which will be evaluated in this Patient KAB Survey, include the following:

Patients should understand that receiving treatment with BKEMV increases the chance of getting serious meningococcal infections, which may quickly become life-threatening and cause death if not recognized and treated early (Key Message Domain 1).

Patients should understand the need to be vaccinated against meningococcal infection and receive antibacterial drug prophylaxis if needed (Key Message Domain 2).

Patients should be able to recognize the signs and symptoms of meningococcal infection and the need for immediate medical evaluation (Key Message Domain 3).

The questions associated with key domain messages will be pre-tested (QR) prior to submission for FDA review as noted in Table 1. The key domain messages and the corresponding questions/statements can be found in Table 2, Table 3, and Table 4.

Table 2: Key Message Domain 1

Patients should understand that receiving treatment with BKEMV increases the chance of getting serious and potentially life-threatening meningococcal infections, which may quickly become life-threatening and cause death if not recognized and treated early.		
Question Number	**Question**	**Desired Response**
10	BKEMV is a medicine that may lower your immune system's ability to fight infection.	**True**
11	According to the BKEMV Patient Guide, indicate True, False, or I don't know for ***each statement*** about BKEMV.	
B	Meningococcal (meningitis) infections may quickly become life threatening or cause death if not recognized and treated early.	**True**
12	According to the BKEMV Patient Guide, indicate True, False, or I don't know for ***each statement*** about BKEMV.	
C	The patient's risk of meningococcal (meningitis) infection may continue for several months after his/her last dose of BKEMV.	**True**
13	Select the **best** option. BKEMV can ___the ability of the patient's immune system to fight infections.	**Lower**
16	BKEMV _____ the patient's chance of getting serious and life-threatening meningococcal (meningitis) infections.	**Increases**

To achieve the demonstrated understanding of 80%, 4 out of 5 questions are required to be answered correctly.

Table 3: Key Message Domain 2

Patients should understand the need to be vaccinated against meningococcal infection.		
Question Number	**Question**	**Desired Response**
11	According to BKEMV's Patient Guide, patients who are due to receive treatment with BKEMV should complete or update their vaccine for meningitis at least 2 weeks before their first dose.	**True**
12	According to the BKEMV Patient Guide, indicate True, False, or I don't know for ***each statement*** about BKEMV.	
B	If you have not completed your meningococcal vaccines and BKEMV must be started right away, you should receive the required vaccine(s) as soon as possible.	**True**
C	If you have not been vaccinated and treatment with BKEMV must be started right away, you should also receive antibiotics to take for as long as your healthcare provider tells you.	**True**
15	Even if you have had meningococcal (meningitis) vaccine(s) in the past, these might need to be updated before starting BKEMV.	**Yes**
20	BKEMV must be started right away but you have not completed or are not up to date with meningococcal (meningitis) vaccines, you must also take antibiotics as directed by your healthcare provider.	**True**

To achieve the demonstrated understanding of 80%, 4 out of 5 questions are required to be answered correctly.

Table 4: Key Message Domain 3

Patients should be able to recognize the signs and symptoms of meningococcal infection.		
Question Number	**Question**	**Desired Response**
12	According to the BKEMV Patient Guide, indicate True, False, or I don't know for ***each statement*** about BKEMV.	
D	If you think you may have a meningococcal infection, you should tell your healthcare provider at your next office visit.	**False**
14	Select the **best** option. What should you do if you experience any sign or symptom of a serious	**Immediately call your healthcare provider or seek**

	meningococcal (meningitis) infection while taking BKEMV?	**emergency medical care, preferably in a major emergency medical center.**
17	If you experience any of the signs or symptoms listed **below**, that could be a sign of a serious meningococcal (meningitis) infection, you should seek immediate medical attention. **Fever** **Fever and a rash** **Fever with high heart rate** **Headache with nausea or vomiting** **Headache and fever** **Headache with stiff neck or stiff back** **Confusion** **Eyes sensitive to light** **Muscle aches with flu-like symptoms**	**True**
18	You should carry the Patient Safety Card with you at all times during treatment and for 3 months after your last dose of BKEMV.	**Yes**
19	You should show the Patient Safety Card to any healthcare provider that treats you.	**True**
21	If you have any signs and symptoms of meningococcal infection (meningitis), seek medical care right away, even if you do not have your Patient Safety Card with you.	**True**

To achieve the demonstrated understanding of 80%, 5 out of 6 questions are required to be answered correctly.

The KAB survey will also collect demographic characteristics for those who complete all survey questions. These include:

- Type of respondent (patient versus caregiver)
- Patient age
- Education level
- Length of time being treated with BKEMV
- Past Completer versus Current Completer – if it is decided that prior survey completers are permitted to participate this analysis will be introduced. This decision will occur prior to Wave 2 and subsequent waves thereafter.
- Geographic location
- Survey completion status

Eligibility and reasons for ineligibility will be presented by counts and percentages.

8.3.3 Covariate Assessment

N/A

8.3.4 Validity and Reliability

N/A

8.4 Data Sources

The survey will be administered via a secure web-based internet connection, which will allow respondents who choose to participate to do so at a time and location that is convenient for them. The survey is written to reflect wording for both methods of survey administration: internet and telephone.

The structured survey comprises questions or statements written in several formats, which include specific key message domains:

- Questions or statements with a defined list of possible answers from which the respondent is required to choose one answer (i.e., multiple-choice).
- Questions or statements with a defined list of possible answers from which the respondent is required to choose one or more answers (e.g., select all that apply).
- Questions or statements with response options of “yes” or “true,” “no” or “false,” and “I don’t know” that require the respondent to indicate agreement or disagreement.

All answers for questions permitting multiple responses will be tallied to provide a broad picture of respondents' knowledge, attitudes, and behaviors.

The desired response for key message domain questions is generally “true” or “yes” indicating knowledge of the objectives of the BKEMV REMS. However, some questions are formatted to have the respondent disagree with the statement as written (“false” or “no”) to avoid having the same affirmative answer for all desired responses. Whenever possible within a key message domain, there will be an equal balance of questions with a “true” or “yes” and “false” or “no.”

Information from the Specialty Pharmacy database will be used to identify all patients for recruitment. The total number of patients included in the Specialty Pharmacy database are all patients who have been dispensed at least 1 dose of BKEMV. The total number patients who have been dispensed at least 1 dose of BKEMV as of 16 October 2024 is estimated to be at 250 at the time of the launch of the Wave 1 survey. Given that the total number of patients is anticipated to be limited for this Wave 1 survey, all patients who meet the eligibility criteria (Section 8.2.3) will be invited to participate in this survey. At this time, given the commercialization status of BKEMV, no patients are available for recruitment. The respondent characteristics captured in this dataset that will be used for randomization processing include geographic location. The patient characteristics that will be used for survey execution include first name, last name, and mailing address.

8.5 Study Size

Wave 1 will aim to reach, at a minimum, 153 completed surveys for patients and/or caregivers. Each survey will remain open for the entire scheduled fielding time but will close no earlier than 60 days prior to assessment report submission.

Personalized invitations will be sent to each selected participant using US Mail for communication Table 1.

Per Section 8.4, participants will be invited via the Specialty Pharmacy. To reduce burden on the Specialty Pharmacy and because the Pre-Notification Letter, while it provides notification to the potential participants about the upcoming survey, there is no specific data to date that indicates that this letter improves data collection, therefore, this letter will not be distributed prior to survey launch.

Upon launch of the survey, the selected patient population will be sent an Invitation Letter.

The Invitation Letter will include:

- Two methods (internet or telephone) for accessing the survey: a QR code for quick access, via a mobile device, to the secure website and a URL for the internet survey and a toll-free number to the SCC for the telephone interview.
- A unique code that the respondent must provide when accessing the survey via the internet or telephone.
- Notification that the survey should take approximately 20 minutes to complete depending on method chosen to complete it.
- Notification that participation in the survey or their choice to note participate in the survey will not affect their ability to receive treatment with BKEMV.
- Notification that payment meeting a fair market value amount will be provided to thank them for their participation will be made and or elect to receive the compensation.
- Notification that eligible patients and/or caregivers will receive compensation (if the respondent is able or chooses to receive compensation) for completing the survey. Additionally, potential patients and/or caregivers who are not eligible for compensation will be informed that, while they will not receive compensation for their participation, they may still participate in the survey but will not be compensated.

All targeted patients and/or caregivers who do not respond to the survey, regardless of the response rate, will be sent Reminder Letters that will assist in informing non-responders that others have completed the survey and letting them know that their help is needed to encourage them to respond to the survey (social validation). The intervals for sending Reminder Letters to non-responders will be condensed as necessary based on the actual rate of survey accrual relative to the proximity of the target survey close date and no sooner than 60 days prior to submission of the annual REMS assessment to the FDA. Reminder letters will be flagged with terms associated with social validation, for example, Reminder 1 - “Friendly Reminder,” Reminder 2 - “We need your help,” Reminder 3 – “Please respond,” and Reminder 4 - “Final Reminder” will be implemented. Additional reminder outreach may be conducted based on the time period in which the

survey is being conducted and survey uptake (Table 1). Based on the population size of patients identified via the Specialty Pharmacy, at this time, no random sampling will be performed. Furthermore, to minimize sampling error and bias, outbound calling may occur.

8.6 Data Management

A secure, web-based, proprietary Knowledge Survey System designed and built by UBC will be used for the Patient KAB Survey. The system meets Title 21 Code of Federal Regulations (CFR) Part 11, the Health Insurance Portability and Accountability Act (HIPAA) and the California Consumer Privacy Act guidelines for information systems. Respondent-identifying information will be stored separately from the survey responses.

Title 21 CFR Part 11 applies to records in electronic form that are created, modified, maintained, archived, retrieved, or transmitted under any records requirements set forth in Agency regulations; the application must provide protection, security, and dependability. Protection of the data requires that audit trails be under application control for all updates and deletions, and that date and time stamps are available. The UBC Pathways® Knowledge Survey System maintains an audit trail containing date and time stamps.

The security of the application requires physical and logical security. The UBC Pathways® Knowledge Survey System maintains user and group-level permissions, so that only relevant project team members will have appropriate access to the system.

Dependability of the application requires that the database be validated and documented evidence that the application does what it is purported to do and will continue to do so. UBC will thoroughly validate and document the testing of the UBC Pathways® Knowledge Survey System. The validation of this system begins with the development of a Project Strategy Document. The document details the strategy for testing. Product Backlog Items are created, and test scripts are written and executed.

All associated Title 21 CFR Part 11 requirements, including requirements for data entry, audit trails, date and time stamps, and security, are tested at baseline.

When survey respondents access the survey website to complete an online survey, they will be asked to enter the unique code from the invitation letter and pass the CAPTCHA (Completely Automated Public Turing test to tell Computers and Humans Apart) robot check shown on the screen. After the respondent has correctly entered the code and passed the CAPTCHA test, the system will advance to the survey welcome page from which the respondent can access the actual survey.

After the UBC end users, who can facilitate completion of a survey with a respondent via telephone, access the survey website for entry of survey information collected from respondents over the telephone, they will click “UBC Login” and enter their UBC network credentials. They will then access the survey assigned to the respondent by matching the code provided to the respondent code in the system.

All data entered will be single data entered by either the respondent or a designated UBC resource who has been trained to enter data for this program. Data will be checked in real time to ensure it is being entered according to acceptable parameters and requirements. This process will include a data extract, at a time point during survey execution where the data collected is a reasonable number (i.e., more than 25 completed surveys). This data extract will then follow the process in which it will be mapped to Statistical Analysis System

(SAS®) datasets and evaluated for any parameters that were not planned (i.e., skip pattern errors).

At the end of each survey cycle, the same process as outlined above will be followed which includes having all data extracted from the UBC Pathways® Knowledge Survey System and mapped to SAS datasets (SAS V9.4 or higher). The mapping of raw data will be validated, as will the programming of the analysis tables created from the SAS datasets.

8.6.1 Data Collection Tools (DCTs)/Electronic Data Record

As used in this protocol, the term data collection tool (DCT) (the survey) should be understood to refer to either a paper form or an electronic data record.

A completed DCT (the survey) is required for each included respondent. As defined (Section 8.7.1), a Completed Survey (Primary Population) is the population for a majority of the analyses includes only those respondents who completed all eligibility questions, met all inclusion criteria and none of the exclusion criteria, and answered all questions associated with at least 1 key message domain. The completed original DCTs (the surveys) are the sole property of Amgen and should not be made available in any form to third parties, except for authorized representatives of Amgen or appropriate regulatory authorities, without written permission from Amgen. UBC shall ensure that the DCTs (the surveys) are securely stored at UBC on a secure server to prevent access by unauthorized third parties.

UBC has ultimate responsibility for the collection and reporting of all data entered on the DCTs (the surveys) as required and ensuring that they are accurate, authentic/original, attributable, complete, consistent, legible, timely (contemporaneous), enduring, and available when required. The DCT (the survey) serves as the source document. Any corrections to entries made in the DCTs (the surveys) must be dated, initialed, and explained (if necessary) and should not obscure the original entry.

8.6.2 Record Retention

To enable evaluations and/or inspections/audits from regulatory authorities or Amgen, UBC agrees to keep all study-related records. The records should be retained by UBC according to local regulations or as specified in the Fully Executed Statement of Work, whichever is longer. UBC must ensure that the records continue to be stored securely for so long as they are retained.

If UBC becomes unable for any reason to continue to retain study records for the required period, Amgen should be prospectively notified. The study records must be transferred to a designee acceptable to Amgen.

Study records must be kept for a minimum of 15 years after completion or discontinuation of the study, unless UBC and Amgen have expressly agreed to a different period of retention via a separate written agreement. Record must be retained for longer than 15 years if required by applicable local regulations.

UBC must obtain Amgen's written permission before disposing of any records, even if retention requirements have been met.

8.6.3 Obtaining Data Files

N/A

8.6.4 Linking Data Files

N/A

8.6.5 Review and Verification of Data Quality

N/A

8.7 Data Analysis

8.7.1 Analysis Populations

Data from all respondents who access the survey will be collected. Only data from those survey respondents who were eligible to participate in the survey and answered every question ("completers") will be the primary analysis population. The population included in the analysis will be defined as follows:

- All Respondents – The "All Respondents" population consists of respondents who accessed the survey using a unique code. This population will be used as the denominator for percentages in survey administration statistics and in the survey eligibility results analysis. This population includes any individual who accesses the survey, regardless of whether or not they meet the study's eligibility criteria.
- Eligible Respondents – The "Eligible Respondents" are those who completed all eligibility questions designated as eligible for the survey, regardless of whether or not they completed the entire survey.
- Non-Completed Surveys – The population will be considered "Non-Completers" if the respondent completed all eligibility questions and answered at least 1 question associated with 1 key message domain but did not complete the entire survey.
- Completed Surveys (Primary Population) – The population for a majority of the analyses includes only those respondents with completed surveys. "Completed" is defined as an eligible respondent who completed all eligibility questions, met all inclusion criteria and none of the exclusion criteria, and answered all questions associated with at least 1 key domain message. Any remaining questions not answered by this population will be identified in each analysis as either "missing data" if the respondent discontinued the survey before answering the question(s) or skipped the question, or "N/A" if the question(s) was not presented to the respondent due to skip logic in the survey. The "completed surveys" population will be a subset of the "eligible respondents" population.
- BKEMV REMS Data Population – The BKEMV REMS Data Population consists of patients who have been dispensed at least 1 dose of BKEMV. Because patients are not enrolled in the BKEMV REMS, this analysis cannot be performed.

8.7.2 Planned Analyses

Statistical analyses will be descriptive in nature. Counts and percentages will be calculated for each question/item in the questionnaire. Ninety-five percent (95%) CIs for the survey end points will be calculated to provide an estimate of precision; however no formal hypothesis will be tested. All CIs around the percentages will be exact binomial 2-sided

95% CIs calculated according to the method of Clopper-Pearson. Analyses will be performed at the respondent level; therefore, within-respondent variation is not relevant.

8.7.3 Survey Administration Analyses

The survey administration data to be described in the Patient KAB assessment report includes:

- Number of Pre-Notification Letters distributed
- Number of Pre-Notification Letters returned as undeliverable
- Number of Invitation Letters distributed
- Number of Invitation Letters redistributed e-mail
- Number of Invitation Letters returned as undeliverable
- Number of Reminder Letters distributed
- Number of Reminder Letters returned as undeliverable
- Number of Reminder Letters redistributed
- Response rate after the Invitation Letter
- Response rate after each Reminder Letter
- Number of respondents screened for participation (All respondents)
- Number of respondents eligible for participation
- Number of respondents not eligible for participation
- Number of respondents eligible for participation who completed the survey
- Number of respondents who completed the survey via internet or telephone
- Time to complete survey (minutes)
- Description of survey participants includes:
    - Type of respondent (patient versus caregiver)
    - Patient age
    - Education Level
    - Length of time being treated with BKEMV
    - Past Completer versus Current Completer – if it is decided that prior survey completers are permitted to participate this analysis will be introduced. This decision will occur prior to Wave 2 and subsequent waves thereafter.
    - Geographic location
- Eligibility and reasons for ineligibility will be presented by counts and percentages.

8.7.3.1 Primary Analysis

The primary analysis will be executed upon data lock and data extraction of the Patient KAB Survey.

8.7.4 Planned Method of Analysis

8.7.5 General Considerations

Statistical analyses will mainly be descriptive; i.e., no formal hypothesis will be tested (the lower bound of the 95% CIs will not be compared but rather the point estimate will be compared against the pre-specified threshold). All analyses will be performed at the respondent level; therefore, within respondent variation is not relevant. Furthermore, descriptive analyses will be performed by patient and/or caregiver status. Counts and percentages will be calculated for each question/item in the questionnaire. In the case where the estimated percentage is equal to zero or 100 percent, the Clopper-Pearson method (Clopper and Pearson, 1934) will be utilized to estimate the CIs for zero and 100% using procedure freq in SAS (Nair, 2014). The following SAS code is provided below.

```
Proc freq data=<data>;
by <variable>;
tables <variable> / binomial (level = x) alpha = 0.05;
weight count /zero;
```

CIs for primary and secondary analyses will be calculated as inferential statistics to generalize the results to the entire targeted population. The p-values for comparison of how representative the respective survey respondents are to the respective stakeholder population will be obtained from the Chi-square test.

8.7.6 Primary Analysis

Primary analyses are performed for all key message domain questions and will be stratified by patient versus caregiver, if the number of caregivers exceeds 15. If the caregiver population is not exceeded, the analyses will be performed at the respondent level. Responses from all questions/items from each key domain message will be summarized by counts and percentages. The primary analysis for a key message domain question evaluates the rate for each correct response to each individual question/item defined by the key domain message. “Select all that apply” questions will be counted as a single correct response if the respondent selects 80% or more of the correct responses and does not select any incorrect response. The specific correct response to each question/item is identified in the body of the Key Domain Message Table 2, Table 3, and Table 4. Exact binomial two-sided 95% CIs will be calculated for the proportion of respondents who provide the correct responses. The completed surveys (Primary Population) will be used for this analysis.

Example Table Output 2: Primary Analysis of Responses to Questions Linked to Key Message Domain 1 - Completed Surveys

Question	**Overall (N=XX)[a] n (%) [95% CI][b]**
Question 1:	

Number not missing (if applicable)	XX
Yes[c]	XX (XX.0) [XX.X - XX.X]
No	XX
I don't know	XX

[a] Total number of eligible respondents completing the survey.
[b] Logit-transformed CIs will be used to take into account the finite population. Clopper-Pearson CIs were used for proportion estimates of zero and 100.
[c] Correct response.

8.7.7 Additional Analysis

This analysis of the key message domains will be performed consisting of a frequency distribution of the number of correct responses to each key message domain question (i.e., number and percentages will be shown by the number of correct responses). "Select all that apply" questions are handled as described in Section 8.7.6. Only those items that are presented to all respondents will be included in the secondary analysis. The completed surveys (Primary Population) will be used for this analysis.

A prespecified threshold of at least 80% has been set. This prespecified threshold aligns with the FDA general guidance that 80% or higher should be the general standard for each REMS key message domain.

Example Table Output 1: Additional Analysis of Key Message Domain 1 - Completed Surveys

Correct Responses	**Overall (N=XX)[a] n (%) [95% CI][b]**
0 correct responses	XX (XX.0)
1 correct response	XX (XX.0)
2 correct responses	XX (XX.0)
3 correct responses	XX (XX.0)
4 correct responses	XX (XX.0)
Demonstrated understanding of Key Message Domain1[c]	XX (XX.0) [XX.X - XX.X]

[a] Total number of eligible respondents completing the survey.
[b] Clopper-Pearson CIs will be used for proportion estimates of zero and 100.
[c] To demonstrate understanding of Key Domain Message 1, the respondent must have answered all 4 questions correctly.

Another analysis is the demonstrated understanding of each key domain message, defined as answering 80% or more questions/items in a key domain message correctly. "Select all that apply" questions are handled as described in Section 8.7.6. The proportion of respondents who demonstrated understanding of the key message domain will be presented with 95% CIs. Additionally, the number and percentages of respondents who demonstrated understanding of all key message domains will be provided with 95% CIs. In this analysis, the proportion of respondents who demonstrated an understanding of the key message domain will be presented with 95% CIs. The REMS will be considered meeting its goals if the point estimates of Key Message Domain 1, Key Message Domain 2, and Key Message Domain 3 receive a demonstrated understanding of 80% or above. Additionally, the number and percentages of respondents who demonstrated

understanding of all key risk messages will be provided with 95% CIs. As stated in the FDA draft Guidance for "Survey Methodologies to Assess REMS Goals That Relate to Knowledge: Guidance for Industry" although there is no standard knowledge performance threshold that is generally accepted for all REMS Programs, in most cases it should be 80% or higher for each Key Domian Message. The completed surveys (Primary Population) will be used for this analysis.

8.7.8 Trend Over Time Analysis

A descriptive comparison in correct response rates to key message questions and the demonstrated understanding of each key domain message across the survey waves will be conducted to address possible trends in the knowledge rates of the survey completers. For the trend analysis, only those questions will be considered for the demonstrated understanding rates that are asked in all survey waves. Therefore, the demonstrated understanding rates in the trend analysis may differ from the results of the previous waves. Additionally, the comparison will be completed to include no more than 2 previous waves and the current reporting period only. If any changes to the questions and/or the response options are made across the survey waves, those questions/responses will be identified as changed with an applicable footnote for identification.

This analysis will be performed following the completion of Wave 2.

8.7.9 Sub-Group Analysis

Subgroup analysis will be performed using the primary population (Completed Surveys) for each key domain message for both the primary and secondary analysis based on descriptive statistics. The sub-group analyses performed will be by type of respondent, respondent age, length of time being treated with BKEMV, awareness of the educational materials, responder versus non-responder, and geographic location.

The denominator for the calculation of percentages is the number of available responses. All sub-group analyses will be programmed; however, only those with a meaningful sample size, i.e., 25 or more respondents in at least 2 sub-groups, will be described in the Assessment Report. Sub-groups with low sample size may also be combined as appropriate.

All sub-groups will be derived from the survey data.

8.7.10 Analysis of Additional Survey Questions

All other questions, including those about demographics, inclusion/exclusion, behaviors, safety, requirements of the BKEMV REMS and awareness of the REMS educational materials, will be analyzed using descriptive statistics. The responses to each question will be summarized by frequency tables.

8.7.11 Categorization and Verbatim Responses

Free text and verbatim responses will be presented in data listings and, as appropriate, may be categorized for categorical data analysis.

8.7.11.1 Missing, Duplicate, or Incomplete Data and Lost to Follow-up

8.7.12 Missing Data

Regardless of survey method (internet/telephone) chosen to participate, there is a potential for missing data associated with demographic questions and non-related key message

domain questions (the main survey content). Any remaining questions not answered by this population will be identified in each analysis as either "missing data" if the respondent discontinued the survey before answering the question(s) or skipped the question, or not applicable ("N/A") if the question(s) was not presented to the respondent due to skip logic in the survey. The "completed surveys" population will be a subset of the "eligible respondents" population.

8.7.13 Duplicate Data

With any voluntary survey there is a possibility of duplicate surveys being received. If it is discovered that a respondent completed more than 1 survey (e.g., during fulfillment reconciliation), only the results from the first completed survey (based on time completed) will be included in the analyses.

8.7.13.1 Descriptive Analysis

8.7.13.1.1 Description of Study Enrollment

The target sample size was derived based on the total population available and calculated per the FDA draft guidance identifying the estimated population including a margin of error of ±5% and 95% CIs.

Table 5 shows the precision of the estimated level of understanding for the key message questions identified for respondents with exact binomial 2-sided 95% CIs for a sample size of 153 completed surveys.

Table 5: Precision of Estimated Rates of Understanding with a Sample Size of 153 (2-sided 95% CI)

Estimated Rate	Actual Number of Correct Responses	Lower Limit	Upper Limit	Precision	Margin of Error
0%	0/153 (0.00%)	0.0%	2.4%	0.0%; +2.4%	+/-0.0%
5%	8/153 (5.23%)	2.3%	10.0%	-2.9%; +4.8%	+/-3.5%
10%	15/153 (9.80%)	5.6%	15.7%	-4.2%; +5.9%	+/-4.7%
15%	23/153 (15.03%)	9.8%	21.7%	-5.3%; +6.7%	+/-5.7%
20%	31/153 (20.26%)	14.2%	27.5%	-6.1%; +7.2%	+/-6.4%
25%	38/153 (24.84%)	18.2%	32.5%	-6.6%; +7.6%	+/-6.8%
30%	46/153 (30.07%)	22.9%	38.0%	-7.1%; +7.9%	+/-7.3%
35%	54/153 (35.29%)	27.7%	43.4%	-7.5%; +8.1%	+/-7.6%
40%	61/153 (39.87%)	32.1%	48.1%	-7.8%; +8.2%	+/-7.8%
45%	69/153 (45.10%)	37.1%	53.3%	-8.0%; +8.2%	+/-7.9%
50%	76/153 (49.67%)	41.5%	57.9%	-8.2%; +8.2%	+/-7.9%
55%	84/153 (54.90%)	46.7%	62.9%	-8.2%; +8.0%	+/-7.9%
60%	92/153 (60.13%)	51.9%	67.9%	-8.2%; +7.8%	+/-7.8%
65%	99/153 (64.71%)	56.6%	72.3%	-8.1%; +7.5%	+/-7.6%
70%	107/153 (69.93%)	62.0%	77.1%	-7.9%; +7.1%	+/-7.3%
75%	115/153 (75.16%)	67.5%	81.8%	-7.6%; +6.6%	+/-6.8%
80%	122/153 (79.74%)	72.5%	85.8%	-7.2%; +6.1%	+/-6.4%
85%	130/153 (84.97%)	78.3%	90.2%	-6.7%; +5.3%	+/-5.7%
90%	138/153 (90.20%)	84.3%	94.4%	-5.9%; +4.2%	+/-4.7%
95%	145/153 (94.77%)	90.0%	97.7%	-4.8%; +2.9%	+/-3.5%
100%	153/153 (100.00%)	97.6%	100%	-2.4%; +0.0%	+/-0.0%

8.7.13.1.2 Description of Patient and/or Caregiver Characteristics

Patients who are 18 years of age who have been dispensed at least 1 dose of BKEMV will be invited to participate in this survey.

Caregivers of patients of all ages who have been dispensed at least 1 dose of BKEMV will be invited to participate in this survey.

8.7.13.2 Analysis of the Primary, Secondary, and Exploratory Endpoint(s)

Exact binomial 2-sided CIs are used to indicate that for an estimated comprehension level, the true population level of comprehension is at least as high as the lower limit of the 95% CI and may be as high as the upper limit of the 95% CI.

8.7.13.2.1 Stratified Analysis

N/A

8.7.13.2.2 Sensitivity Analysis for Residual Confounding and Bias

N/A

8.7.13.2.3 Other Sensitivity Analysis

N/A

8.7.14 Analysis of Safety Endpoint(s)/Outcome(s)

Safety data will not be collected or analyzed in this study.

8.8 Quality Control

The UBC Pathways® Knowledge Survey System programming will be reviewed by UBC's Quality Control (QC) and simulated users [User Acceptance Testing (UAT)] prior to implementation. At the completion of data collection, the Knowledge Survey System data will be mapped to SAS datasets (SAS v9.4 or higher) by a SAS programmer/designee. These original SAS datasets will be validated by double programming and QC. The validated original SAS datasets will then be used by a SAS programmer to create a set of summary tables and listings according to the analysis text and mock-up tables. If derived analysis datasets are required to produce these summary tables, the derived analysis datasets will be created and independently validated according Standard Operating Procedures (SOPs). All TL (Tables and Listings) output will be independently validated and documented according to the established SOPs. Summary tables will be reviewed by the appropriate team members and included in the assessment report that is sent to Amgen along with the final document to be submitted to the FDA. No respondent contact information is included in the tables or in the assessment report.

8.9 Limitations of the Research Methods

The Patient KAB Survey recruitment strategies are intended to recruit those meeting the inclusion criteria as stated earlier in this document. Patients and/or caregivers will be self-selected because they will voluntarily respond to the invitation to participate, so the potential exists that those who choose to respond to the survey may differ in their understanding of the REMS Program requirements from those who elect not to participate. This is a common limitation of all studies that rely on voluntary participation.

The second limitation is that the survey can assess respondents' understanding of the REMS requirements, but it cannot clearly determine which channel the respondents gained the information from. While the survey asks respondents where the information was gained, recall of information may not be reliable. Inherent in survey research is the reliance on the respondent's recall of whether the REMS educational materials were received and read. It is possible, however, that respondents may simply not recall receiving and/or reading any one or more of the REMS educational materials that were, in fact, received and/or read. It is also possible that the respondents have acceptable understanding of the important product information associated with the use of BKEMV despite not receiving or recalling that s/he received and/or read the REMS educational materials prior to completing the survey.

A third limitation is that of social desirability where respondents are more likely to answer "yes" when they are asked "did you read this?" or "did you do this?" because they assume this is the expected answer. Social desirability bias tends to result in higher scores, particularly for questions with a true/false response.

BKEMV is a rare disease drug, therefore, the population of patients may be limited.

8.9.1.1 Measurement Error(s)/Misclassification(s)

N/A

8.9.1.2 Information Bias

Controls will be in place to ensure the survey is conducted in a professional manner and to minimize biases, including the following:

- A standardized script will be used for telephone interviews, and all telephone interviewers will be carefully trained in interview techniques to minimize interviewer bias.
- The survey will be programmed to ensure:
  - Questions are asked in the appropriate sequence and all questions will be presented in a standard order to reduce exposure bias.
  - Respondents cannot skip ahead and will only allow for missing data when caused by skip patterns.
  - The list of response options within a multi-item question are randomized to minimize the potential for positional bias.

Regardless of modality, internet or telephone respondents will be instructed that they cannot go back to a question once they have progressed to the next question and cannot. Both the telephone and the internet questionnaire will be programmed with a standardized approach.

Respondents will be provided with a unique code during the recruitment process and will then be asked to provide the unique code to gain access to the internet-based system or when calling the SCC. The code will be inactivated after use to minimize exposure bias and fraud.

8.9.1.3 Selection Bias

Potential patients and/or caregivers will be self-selected since they will voluntarily respond to the invitation to participate. Reminder letters will be sent to non-responders to reduce non-response bias.

Additionally, the following measures are in place to assist in minimizing potential biases in the survey sample:

The population of potential patients and/or caregivers are those as defined in Section 8.2.3. No random sampling will be performed.

- To reduce exposure bias, the following will be excluded:
  - Respondents who do not agree to participate in the survey.
  - Respondents who are currently working for and/or whose immediate family members are currently working for or are consultants to Amgen, UBC, or the FDA.
  - Respondents who report having a conflict of interest.
- Respondents who have previously participated may be eligible to participate in future surveys. This eligibility criteria will be dependent upon the number of patients receiving treatment with BKEMV, prior to launch of subsequent survey waves.
- Two methods are available for survey completion: internet and telephone. Providing more than 1 method for survey data collection allows for wide survey access to a heterogeneous population and minimizes intervention bias.
- The list of respondent names will be checked for duplicates so that an individual's responses will not be included in the survey assessment more than once.

8.9.1.4 Confounding

N/A

8.9.2 External Validity of Study Design

N/A

8.9.3 Analysis Limitations

N/A

8.9.4 Limitations Due to Missing Data and/or Incomplete Data

N/A

8.10 Other Aspects

If any protocol deviations occur during survey processing that may have an impact on the survey data and analysis, they will be reported in the final assessment report.

9. Protection of Human Participants

9.1 Informed Consent

The survey will begin with an introduction to the survey providing the respondents with general information about the research sponsor and the survey expectations followed by letting them know how their information will be used, how their privacy will be protected,

how they can learn more about the survey, and instructions on taking the survey. Once this information is reviewed and the respondents proceed to the first survey question, they will be presented with one final statement which is: “Your agreement to participate in this survey confirms mutual understanding in connection with completion of the survey and compensation to be rendered in connection with those services”, concluding with their first question asking if they agree to participate in the survey about BKEMV. If respondents select “Yes” they will proceed through the screening module to confirm respondents’ eligibility and should they select “No”, the survey will immediately terminate, and their session will end. If deemed ineligible, respondents participating via the internet-based survey are immediately notified with a “thank you” message that survey participation has ended. For those respondents participating in the survey via the telephone with the SCC, the SCC Associate will communicate the “thank you” message that, based on the respondent’s answer, they are not eligible to participate.

9.2 Institutional Review Board/Independent Ethics Committee (IRB/IEC)

It is the responsibility of UBC to have prospective approval of the study protocol, protocol amendments, materials describing the consent process (e.g., statement regarding agreement to participate), and other relevant documents, (e.g., recruitment advertisements), if applicable, from the IRB. All correspondence with the IRB should be retained by UBC. Copies of IRB approvals should be forwarded to Amgen.

Please note that IRB approval is required for this study.

9.3 Participant Confidentiality

The investigator must ensure that the participant’s confidentiality is maintained for documents submitted to Amgen.

Participants will be assigned a unique identifier by the sponsor. All parties will comply with all applicable laws, including laws regarding the implementation of organizational and technical measures to ensure protection of participant personal data. Such measures will include omitting participant names or other directly identifiable data in any reports, publications, or other disclosures, except where required by applicable laws.

Participant personal data will be stored at UBC in encrypted electronic form and will be password protected to ensure that only authorized study staff have access. UBC will implement appropriate technical and organizational measures to ensure that the personal data can be recovered in the event of disaster. In the event of a potential personal data breach, UBC shall be responsible for determining whether a personal data breach has in fact occurred and, if so, providing breach notifications as required by law.

To protect the rights and freedoms of natural persons regarding the processing of personal data, when study data are compiled for transfer to Amgen and other authorized parties, any participants names will be removed and will be replaced by a single, specific, numerical code. All other identifiable data transferred to Amgen or other authorized parties will be identified by this single, participant-specific code. UBC will maintain a confidential list of participants who participated in the study, linking each participant’s numerical code to his or her actual identity. In the case of data transfer, Amgen will maintain high standards of confidentiality and protection of participants’ personal data consistent with the vendor contract and applicable privacy laws.

For serious adverse events reported to Amgen, participants are to be identified by their unique participant identification number, initials (for faxed reports, in accordance with local laws and regulations), and age (in accordance with local laws and regulations).

Documents that are not submitted to Amgen (e.g., signed informed consent forms) are to be kept in confidence by the investigator, except as described below.

In compliance with [governmental regulations/ICH GCP Guidelines], it is required that the investigator and institution permit authorized representatives of the company, of the regulatory agency(s), and the [IRB/IEC] direct access to review the participant's original medical records for verification of data. Direct access includes examining, analyzing, verifying, and reproducing any records and reports that are important to the evaluation of the study. The investigator is obligated to inform and obtain the consent of the participant to permit such individuals to have access to his/her study-related records, including personal information.

9.4 Participants Decision to Withdraw

Participants have the right to withdraw from the study at any time and for any reason.

Withdrawal of consent for a study means that the participant does not wish to or is unable to continue further study participation. Participant data up to withdrawal of consent will be included in the analysis of the study and, where permitted, publicly available data can be included after withdrawal of consent. As per local regulations, upon withdrawal of consent, the participant has the right to request removal of their data that was collected and not have it further processed. The investigator is to discuss with the participant appropriate steps for withdrawal of their consent from the study.

10. Collection, Recording, and Reporting of Safety Information and Product Complaints

10.1 Definition of Reportable Events

10.1.1 Adverse Events

An adverse event is any untoward medical occurrence in a participant administered a pharmaceutical product(s) irrespective of a causal relationship with this treatment.

An adverse event can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding, for example), symptom, or disease temporally associated with the use of a product(s), whether considered related to the product(s). The definition of an adverse event includes:

- Worsening of a pre-existing condition or underlying disease
- Events associated with the discontinuation of the use of a product(s), (e.g., appearance of new symptoms)

Adverse Device Effect

An adverse device effect is any adverse event related to the use of a combination product or medical device. Adverse device effects include adverse events resulting from insufficient or inadequate instructions for use, adverse events resulting from any malfunction of the device, or adverse events resulting from use error or from intentional misuse of the device.

10.1.2 Serious Adverse Events

A serious adverse event is any adverse event/adverse device effect as defined above that meets at least one of the following serious criteria:

- is fatal
- is life threatening (places the participant/patient at immediate risk of death)
- requires in-patient hospitalization or prolongation of existing hospitalization
- results in persistent or significant disability/incapacity
- is a congenital anomaly/birth defect
- is an “other medically important serious event” that does not meet any of the above criteria

A hospitalization meeting the regulatory definition for “serious” is any in-patient hospital admission that includes a minimum of an overnight stay in a healthcare facility.

“Other medically important serious events” refer to important medical events that may not be immediately life threatening or result in death or hospitalization but may jeopardize the participant/patient or may require intervention to prevent one of the other outcomes listed in the definition above. Examples of such events could include allergic bronchospasm, convulsions, and blood dyscrasias, drug-induced liver injury, events that necessitate an emergency room visit, outpatient surgery, or other events that require other urgent intervention.

10.1.3 Other Safety Findings

Other Safety Findings (regardless of association with an adverse event) include:

- Medication errors, overdose/underdose, whether accidental or intentional, misuse, addiction, or abuse involving an Amgen product,
- Use of an Amgen product while pregnant and/or breast feeding,
- Transmission of infectious agents,
- Reports of uses outside the terms for authorized use of the product including -off label use,
- Accidental or Occupational exposure,
- Any lack or loss of intended effect of the product(s).

10.1.4 Product Complaints

Product Complaints include any written, electronic, or oral communication that alleges deficiencies related to the identity, quality, durability, reliability, safety, effectiveness, or performance of a drug, combination product, or device after it is released for distribution to market or clinic. This includes any drug(s), device(s) or combination products provisioned and/or repackaged/modified by Amgen. Drug(s) or device(s) or combination product(s) includes investigational product.

10.2 Safety Collection, Recording and Submission to Amgen Requirements

This study is collecting information from patients and/or caregivers prospectively at one point in time through the completion of an online-based survey or telephone-based survey.

All reportable events (adverse events, product complaints, and other safety findings) considered to have occurred following exposure to BKEMV will be collected following patient and/or caregiver enrollment within the study through to the final study contact. The Vendor is responsible for ensuring that all reportable events they become aware of during the study period are recorded in the appropriate study documentation. It is the Vendor's responsibility to evaluate whether an adverse event is related to an Amgen product prior to reporting the adverse event to Amgen. If further safety-related data is needed to fulfill any regulatory reporting requirements for a reportable event, then additional information may need to be collected from the Vendor/participants. All reportable events must be submitted as individual safety reports to Amgen Safety via the applicable Amgen Safety Reporting Form (paper or electronic form) within the timelines stated in Table 6: Types of Safety Data to be Collected and Reported in Primary Data Collection Studies Collecting all Reportable Events.

Table 6: Types of Safety Data to be Collected and Reported in Primary Data Collection Studies Collecting all Reportable Events

Reportable Events/Event Type	* Reporting Timeframe
• Serious Adverse Events (related and non-related) • Other Safety Events (related and non-related) • Product Complaints (serious and non-serious) • Other Safety Findings (serious and non-serious) • Pregnancy and/or Lactation Exposure	• Within 1 business day from when Vendor first becomes aware of the event
• Non-serious Adverse Events (related and non-related)	• Within 15 calendar days from when Investigator/Vendor first becomes aware of the event

**** Please note, more stringent reporting timelines may apply per local requirements***

Reportable events that are suspected to be related to any Amgen medicinal product, combination product or device where there is no exposure to BKEMV should be spontaneously reported to Amgen within 1 business day of vendor's awareness. A list of all Amgen medicinal products can be found in the following link: https://wwwext.amgen.com/amgen-worldwide

To spontaneously report a reportable event to Amgen, refer to the following link to locate your Local Amgen contact information by country: https://wwwext.amgen.com/contact-us/product-inquiries

Additional details on what to collect and report to Amgen for the reportable event can be found in the following link: https://wwwext.amgen.com/products/global-patient-safety/adverse-event-reporting

Reportable events suspected to be related to any non-Amgen medicinal product should be reported to the local authority in line with the local country requirements.

See Appendix C for sample Safety Report Form(s) and Appendix D for sample Pregnancy and Lactation Notification Forms. The Investigator may be asked to provide additional information for any event submitted. Information provided about the event

must be consistent with information recorded in the study documentation where safety data may also be recorded.

10.2.1 Collection of Pregnancy and Lactation Information

Female Patients Who Become Pregnant

Vendor will collect pregnancy information on any female patient who becomes pregnant following exposure to BKEMV if reported by the patient and/or caregiver during completion of the online-based survey or telephone-based survey.

Information will be recorded on the Pregnancy Notification Form (see Appendix D). The worksheet must be submitted to Amgen Safety within 1 business day of when Vendor first becomes aware of the patient's pregnancy (Note: Vendor is not required to provide any information on the Pregnancy Notification Form that violates the country or regions local privacy laws).

After receipt of the Pregnancy Notification Form, Amgen Safety or designee will provide the reporter with a consent form and questionnaire to collect additional information. After obtaining the reporter's signed consent for release of pregnancy and infant health information, Amgen Safety or designee will collect pregnancy and infant health information and complete the pregnancy questionnaire for any female patient who becomes pregnant following exposure to BKEMV through [6 months after the last dose of BKEMV. This information will be forwarded to Amgen Safety per applicable processes. Generally, infant follow-up will be conducted up to 12 months after the birth of the child (if applicable).

Any termination of pregnancy will be reported to Amgen Safety per applicable processes, regardless of fetal status (presence or absence of anomalies) or indication for procedure.

While pregnancy itself is considered another safety finding, any pregnancy complication or report of a congenital anomaly or developmental delay, fetal death, or suspected adverse reactions in the neonate will be reported as an adverse event or serious adverse event. Note that an elective termination with no information on a fetal congenital malformation or maternal complication is generally not considered an adverse event, but still must be reported to Amgen as a pregnancy exposure case.

If the outcome of the pregnancy meets a criterion for immediate classification as a serious adverse event (e.g., female patient experiences a spontaneous abortion, stillbirth, or neonatal death or there is a fetal or neonatal congenital anomaly) the Vendor will report the event as a serious adverse event.

Male Patients with Partners who Become Pregnant or Were Pregnant at the Time of Enrollment

In the event the respondent notifies the vendor of a male patient who fathers a child following exposure to BKEMV the information will be recorded on the Pregnancy Notification Form. The form (see Appendix E) must be submitted to Amgen Safety within 1 business day of when the Vendor first becomes aware of the pregnancy. (Note: Vendor is not required to provide any information on the Pregnancy Notification Form that violates the country or region's local privacy laws).

After receipt of the Pregnancy Notification Form, Amgen Safety or designee will provide the respondent with a consent form and questionnaire to collect additional information. Amgen Safety or designee will attempt to obtain a signed consent for release of pregnancy

and infant health information directly from the pregnant female partner to obtain additional pregnancy information.

After obtaining the female partner's signed consent for release of pregnancy and infant health information, Amgen Safety or designee will collect pregnancy outcome and infant health information on the pregnant partner and her baby and complete the pregnancy questionnaires. This information will be forwarded to Amgen Safety per applicable processes.

Generally, infant follow-up will be conducted up to 12 months after the birth of the child (if applicable).

Any termination of the pregnancy will be reported to Amgen Safety per applicable processes regardless of fetal status (presence or absence of anomalies) or indication for procedure.

Collection of Lactation Information

Vendor will collect lactation information on any female patient who breastfeeds while taking BKEMV through 6 months after last dose if reported by the healthcare professional during completion of the online-based survey or telephone-based survey.

Information will be recorded on the Lactation Notification Form (see Appendix D) and submitted to Amgen Safety within 1 business day of when the Vendor's first becomes aware of the lactation exposure.

With the female patient's signed consent for release of mother and infant health information, Amgen Safety or designee will collect mother and infant health information and complete the lactation questionnaire on any female patient who breastfeeds while taking BKEMV through 6 months after last dose after discontinuing BKEMV.

10.2.2 Safety Reporting Requirement to Regulatory Bodies

Amgen will report safety data as required in accordance with local requirements to regulatory authorities, Investigators/institutions, IRBs/IECs, or other relevant ethical review board(s) in accordance with Pharmacovigilance guidelines and in compliance with local regulations. The Investigator is to notify the appropriate IRB/IEC or other relevant ethical review board of reportable events in accordance with local procedures and statutes.

11. Administrative and Legal Obligations

11.1 Protocol Amendments and Study Termination

Amgen may amend the protocol at any time. When Amgen amends the protocol and distributes the protocol amendment to the sites, written agreement from the Investigator must be obtained where applicable per local governing law and/or regulations. The IRB must be informed of all amendments and give approval for all protocol amendments that Amgen provides to the site. The Investigator **must** send a copy of the approval letter from the IRB to Amgen.

Amgen reserves the right to terminate the study at any time. Both Amgen and the Investigator reserve the right to terminate the Investigator's participation in the study according to the contractual agreement. The Investigator is to notify the IRB in writing of the study's completion or early termination and send a copy of the notification to Amgen.

12. Plans for Disseminating and Communicating Study Results

Once the survey results are finalized, if applicable, a discussion will be included to address the extent to which the REMS goals related to knowledge are met, how that determination is made, and if the demonstrated understanding is below the pre-specified threshold, outline steps to achieve the desired knowledge rates (e.g., enhancing REMS educational materials or outreach activities as outlined the BKEMV REMS Supporting Document).

During the reporting phase, all data analyses tables and listings will be generated in Excel and provided to Amgen for inclusion for submission to FDA.

The REMS Survey methodology protocol and instrument will be submitted to FDA in both a Portable Document Format and Word Format.

In the event of any prohibition or restriction imposed (e.g., clinical hold) by an applicable competent authority in any area of the world, or if the party responsible for collecting data from the participant is aware of any new information which might influence the evaluation of the benefits and risks of an Amgen product, Amgen should be informed immediately.

In addition, the investigator will inform Amgen immediately of any urgent safety measures taken by the party responsible for collecting data from the participant to protect the study participants against any immediate hazard, and of any serious breaches of this non-interventional study protocol that party becomes aware of.

12.1 Publication Policy

The results of this study will not be submitted for publication.

13. Compensation

All respondents, regardless of modality of survey completion, who complete the survey and who provide their contact information will receive a mailing to begin distribution at survey close and will be sent directly to the respondent based on the address provided during survey completion. This mailing will include:

- Thank you letter for completing the BKEMV REMS KAB Survey.
- Compensation meeting a fair market value amount will be provided for their time in completing the survey.
- Correct answers to important survey questions about the safe use of BKEMV.

14. References

1. Clopper CJ, Pearson ES. The use of confidence or fiducial limits illustrated in the case of the binomial. Biometrika. 1934; 26 (4):404–413.

2. Nair I., Patel B. (2014). Attain 100% Confidence Limits in Your Confidence Interval. Proceedings for PharmaSUG Conference 2014. Available at https://www.pharmasug.org/proceedings/2014/IB/PharmaSUG-2014-IB05.pdf.

3. Survey Methodologies to Assess REMS Goals That Relate to Knowledge: Guidance for Industry. Draft Guidance. https://www.fda.gov/media/119789/download. Issued January 24, 2019.

4. US Food & Drug Administration. REMS Assessment: Planning and Reporting. Draft guidance. January 2019. Accessed September 29, 2023. https://www.fda.gov/media/119790/download.

15. Appendices

Appendix A. List of Stand-alone Documents

None

Appendix B. ENCePP Checklist for Study Protocols

[Delete this Appendix if not a PASS study.]

<<A copy of the European Network of Centres for Pharmacoepidemiology and Pharmacovigilance (ENCePP) Checklist for study protocols is available at the following location: http://www.encepp.eu/standards_and_guidances/checkListProtocols.shtml *. It is to be completed and signed by the main author, as listed on the title page of the study protocol, and should be included in Appendix B. The checklist will facilitate the review of the protocol and evaluation of whether investigators have considered important methodological aspects.>>*

<<In question 9.5 of the Checklist Revision 1:

- *"Study start" means "Start of data collection"*
- *"Study progress" means "Progress Report(s)"*
- *"Study completion" means "End of data collection"*
- *"Reporting" means "final report of the study results">>*

LIST OF TABLES

LIST OF FIGURES

Not applicable.

ANNEX 1: LIST OF STAND-ALONE DOCUMENTS

None

ANNEX 2: PARTICIPANT QUALITATIVE RESEARCH PLAN AND SCREENER

Qualitative Research to Assess Comprehension and Clarity of Key Message Survey Questions Associated with the BKEMV Knowledge, Attitudes, and Behavior (KAB) Survey of Patients

Amgen Inc.

List of Abbreviations

AE	Adverse Event
Amgen	Amgen Inc.
ETASU	Elements to Assure Safe Use
FDA	Food and Drug Administration
HIPAA	Health Insurance Portability and Accountability Act
HIV	Human Immunodeficiency Virus
KAB	Knowledge, Attitudes, and Behavior
MIR	Medical Information Request
PC	Product Complaint
PNH	Paroxysmal Nocturnal Hemoglobinuria
QR	Qualitative Research
REMS	Risk Evaluation and Mitigation Strategy
SE PSP	Safety Event Project Specific Procedure
TDIs	Telephone In-Depth Interviews
UBC	United BioSource LLC
URL	Uniform Resource Locator
US	United States

OVERVIEW

BKEMV™ (eculizumab-aeeb) is indicated for the treatment of adults with paroxysmal nocturnal hemoglobinuria (PNH) to reduce hemolysis and for the treatment of adult and pediatric patients with aHUS to inhibit complement-mediated thrombotic microangiopathy. Eculizumab-aeeb binds to human C5 in the region of the protein that becomes C5b and blocks cleavage, thereby inhibiting the complement cascade and ultimately blocking terminal complement-mediated intravascular hemolysis.

Because of the increased risk of serious meningococcal infections (septicemia and/or meningitis), a Risk Evaluation and Mitigation Strategy (REMS) was determined necessary for BKEMV by the US Food and Drug Administration (FDA) to ensure that the benefits of the drug outweigh the risks. Amgen Inc, (hereinafter referred to as “Amgen”) received the FDA’s approval of BKEMV and the BKEMV REMS on 28 May 2024.

A component of the BKEMV REMS Assessment Plan is the conduct of a quantitative evaluation survey of patients/caregivers, to assess their awareness of the REMS materials, knowledge of the risks associated with BKEMV, and knowledge of the requirements of the BKEMV REMS. This noninterventional study (hereinafter referred to as the Patient KAB Survey) is part of the BKEMV REMS Assessment and is a commitment to the FDA.

To effectively evaluate the Patient KAB Survey, qualitative research, hereinafter referred to as QR, will be conducted on a subset of questions from the draft Wave 1 Patient KAB Survey with a representative sample of patients who have been diagnosed with a blood disorder, excluding human immunodeficiency virus (HIV) will be identified via direct outreach by a recruitment facility. The recruitment facility will utilize its nationwide proprietary database of patients who have expressed interest in participating in market research and opted-in to be contacted about potential research opportunities.

QR will be carried out in a double-blind manner, i.e., respondents will not know the identity of Amgen and the product under study and Amgen will not know the respondents who participated in the study. Note that in the event a patient reports information that meets the criteria as defined in the Safety Event Project Specific Procedure (SE PSP), the identity of the patient may be provided to Amgen.

Feedback elicited from the QR interviews will be used to support the identification of terms, questions, or topics that may require clarification or revision based on any areas of confusion or miscomprehension reported by interviewed participants.

Upon concluding this research, a findings presentation will be delivered by UBC, the KAB Survey Administrator, the company responsible for conducting this research, on behalf of Amgen. Findings and recommendations from QR will be reviewed and incorporated as appropriate to update the questions and response options prior to the implementation of the Wave 1 Patient KAB Survey.

RESEARCH DESIGN

This QR plan outlines the goals and objectives, research methodology, eligibility criteria, and interview design to be used in the qualitative evaluation of the patient knowledge, attitudes, and behaviors around the survey questions, and response options being testing for the Patient KAB Survey.

Objectives

The objectives of this research include the following:

- Review of survey questions and response options with respect to comprehension, relevance, and clarity.
- Identify terms, questions, or topics that require clarification or revision based on areas of confusion or miscomprehension by interviewed participants.
- Evaluate participants' overall understanding of the survey questions and response options; and
- Make recommendations for potential changes to the survey questions and/or response options based on QR findings.

Methodology

The goal of the qualitative research is to conduct twelve (12), 60-minute one-on-one Telephone In-Depth Interviews (TDIs) with a representative sample of patients diagnosed with a blood disorder, excluding HIV.

All interviews will be conducted by an experienced research moderator (hereinafter referred to as "moderator") to ensure consistency between participant interviews using a detailed discussion guide. All interviews will be audio recorded with the participants' consent and subsequently transcribed.

Eligibility Criteria

Inclusion Criteria:

Include 12 patients who:

- Are located in the US.
- Have been diagnosed with a blood disorder, excluding HIV.
- Do not work for or have immediate family who work for or are consultants of pharmaceutical company, UBC, or the FDA.
- Have access to a computer/tablet with access to the internet during the interview.
- Are willing and able to sign an Interview Release Form to participate in the research.

Exclusion Criteria:

Patients who do not meet all the inclusion criteria as listed above.

Recruitment

UBC will work with a recruitment vendor to identify participants who meet eligibility (Eligibility Criteria). Recruitment will consist of direct outreach to each potential participant, utilizing various outreach methods including mail, email and/or telephone calls. Up to 3 attempts will be made targeting non-responders. Eligible participants who complete the interview and would like to receive compensation can choose to receive compensation as fair market value for their time spent participating in the interview. All potential participants have the option of participating and not receiving compensation. Thank you materials can be found in, Appendix 4 of this document.

Participants will be screened (Appendix A) for eligibility as outlined in the Eligibility Criteria. When a respondent meets all eligibility criteria, the recruitment vendor will:

- Collect the participant's information and schedule an interview.
- Email/fax/mail and collect the Interview Release Form from the participant.
- Email/fax/mail participant confirmation letters which include the interview date and time, the teleconference dial-in information, and detailed instructions on how to join the interview.
- Notify participants at the completion of the interview and once the Interview Release Form that s/he will be compensated **$125** for their time spent participating in this 60-minute qualitative interview process.

The recruitment vendor will only share participant information with UBC that is necessary to determine eligibility, to coordinate the research interview with participants, and or to comply with reporting of information as outlined in the SE PSP. Depending on the information being queried, UBC may share information with Amgen to further the decision in support of this research.

If the participant does not want to be contacted about future research studies, their information will be removed from future contact attempts. If for any reason, the recruitment vendor is unsure about a participant's eligibility as it relates to this program, the recruitment vendor will contact UBC who will confirm with Amgen as needed.

INTERVIEW DESIGN

Prior to the Interview

Upon confirmation of each participant's eligibility and availability, the recruitment vendor will email or fax an interview confirmation letter to each participant.

Each participant will be informed that the interview will be conducted online where the moderator will share a screen with the participant and present the materials for review. As such, the participant will be advised that a computing device of reasonable size (i.e. desktop, laptop, or tablet; not a smartphone) will be needed with access to the internet at the time of the interview.

During the Interview

All participant interviews will follow a standard process and will be guided by a pre-scripted discussion guide. When the participant joins the interview, the moderator will go through introductions and disclosures with the participant. For example:

1. General introductions – The moderator will thank the participant for being part of the research and inform the participant that the interview will be audio taped only to help prepare a written report for research purposes. The moderator will reconfirm with the participant that audio taping may begin and will initiate recording upon the participant's agreement.

2. Confidentiality – The moderator will inform the participant that the information gathered is for research purposes only and s/he will not be identified by name in any reports. The moderator will assure the participants that their input and opinions will be reported in aggregate and are important to improve the program's research or educational materials.
3. Potential Adverse Event (AE), Other Safety Events (OSF), Potential Product Complaint (PC), Potential Medical Information Request (MIR), and/or Potential REMS-related Questions, Reporting – The moderator will inform the participant that should any Potential AE, OSF, PC, MIR, and/or REMS-related Questions be reported, the moderator is required to forward this information to the research sponsor and ask the participant if they are willing to waive their confidentiality for Potential AE, OSF, PC, MIR, and/or REMS-related Questions reporting purposes only.
4. Rapport building – The moderator will learn a little bit about the participant.
5. The moderator will remotely assist the participant in logging in to the secure website to review the materials via screen share.

After the above steps, the moderator will then review the associated question items with each participant. Additional details on interview content and conduct will be included in the Patient Moderator's Discussion Guide.

At the close of the interview, the participant will be thanked for his/her time and will log off the online platform. The participant will be informed that the recruitment vendor will mail compensation in the amount determined as fair market value, if eligible, for their time and efforts. For more information regarding compensation for participation efforts please refer to Recruitment.

INTERVIEW RELEASE PROCEDURES

All participants will provide a signed Interview Release Form prior to the interview. All participants will provide verbal consent to be audio recorded. Participants will be informed that the transcribed interviews may be shared with the sponsor and regulatory agencies; however, the moderator will explain that neither the participant's name nor other identifying information will be associated with the audio recording, or the responses provided during the interview. If a participant does not consent to the recording of their interview, the interview will be terminated, and another participant will be scheduled.

POTENTIAL ADVERSE EVENT, PRODUCT COMPLAINT, MEDICAL INFORMATION REQUEST, AND REMS-RELATED QUESTION REPORTING REQUIREMENTS

The SE PSP has been created to establish a process for the proper handling of potential AEs, OSF, PCs, MIRs, and/or REMS-Related Questions should personnel conducting this research become aware of such information.

While it is not the intent that any participant in QR will report information that meets the criteria of a potential AE, OSF, PC, MIR, and/or REMS-Related Question, it is possible that a participant may spontaneously report information that meets these criteria. If information pertaining to a potential AE, OSF, PC, MIR, and/or REMS Related Question is mentioned during a QR interview, a UBC QR team member will document the information and the participant's contact information, if consent to provide contact information is given. Information on all reports that may constitute a potential AE, OSF,

PC, MIR, and/or REMS Related Question will be forwarded to Amgen, according to the SE PSP and the Amgen requirements for management and reporting such information.

QUALITATIVE ANALYSIS & REPORTING

Data from all research interviews, including transcripts, and interviewer notes, will be thoroughly reviewed by UBC staff. A systematic content analysis approach will be used to assess the participant's understanding of the select KAB survey questions and response options evaluated. Emphasis will be placed on identifying areas of ambiguity or disagreement with, and/or gaps in understanding the survey questions and/or response options, and suggested changes for clarification and revision.

The QR findings will be reported in two formats. One format will consist of a PowerPoint presentation that will include but not be limited to:

- Participants select survey questions and response options
- QR findings that place emphasis on identifying specific points of confusion, disagreement or ambiguity
- UBC recommendations based on participant feedback
- Final decisions made by Amgen

The second format consists of a final report prepared by UBC in Microsoft Word. This final Summary Report will include an overview of the goals and objectives of the research, participant inclusion/exclusion criteria, methodology, a description of the participant demographics, a high-level summary of qualitative findings, and final decisions made by Amgen as applicable on any modifications required to the survey questions and/or response options. Additionally, this final Summary Report, along with the QR Plan and Screener, Recruitment Materials, Discussion Guide used to conduct QR, Interview Transcripts, and the Findings Presentation, will be available for inclusion as part of the submission to the regulatory authorities.

As this research is qualitative and exploratory in nature with a limited sample size, the number of participants who made a particular comment about specific language in the survey questions/response options will not be quantified in the final Summary Report (e.g., # of participants said that this question of the survey was easy to understand). Instead, the qualitative findings will highlight overall, common themes (e.g., most participants felt that…) to help qualitatively inform any revisions to the materials.

Appendix A: Participant Online Screener
TOPIC: Patient Qualitative Research (QR)
Participant SCREENER

LIST(S): GENERAL POPULATION OF PATIENTS WHO HAVE BEEN DIAGNOSED WITH A BLOOD DISORDER, EXCLUDING HIV.

PART 1 - INTRODUCTION FOR OUTBOUND CALLS:

[IF OUTBOUND CALL] Hello, my name is _____ and I am calling on behalf of [recruitment vendor]. May I speak with _____? **[INSERT CONTACT NAME]**

We are contacting you because we are conducting research interviews with patients to evaluate select survey questions and their response options to evaluate clarity.

[IF OUTBOUND CALL AND VOICEMAIL RECEIVED] Hello, my name is _____ and I am calling on behalf of UBC. I am calling to speak with _____. **[INSERT CONTACT NAME]**

We are contacting you because we are conducting research interviews with patients to evaluate select survey questions and their response options. If you are interested in participating, please return the call to **[INSERT PHONE NUMBER]**, ask to speak to **[INSERT SCREENER NAME]**.

[PROCEED TO PART 2 - SCREENING PREAMBLE AND SCREENING QUESTIONS]

PART 1 - INTRODUCTION FOR INBOUND CALLS:

[IF INBOUND CALL IN RESPONSE TO INITIAL OUTREACH] Thank you for your call. My name is _____. Can you please provide me with your first and last name?
[CONFIRM NAME IS ON LIST]
[IF NAME IS ON THE LIST] I would like to confirm that you are calling about a research interview for survey questions related to a specific medication. **(WAIT FOR RESPONSE AND CONTINUE.)**

We are contacting you because we are conducting research interviews with patients to evaluate select survey questions and their response options related to a specific medication.

[PROCEED TO PART 2 - SCREENING PREAMBLE AND SCREENING QUESTIONS]

PART 2 - SCREENING PREAMBLE AND SCREENING QUESTIONS:

[CONTINUE FOR EITHER OUTBOUND OR INBOUND CALL]

This research interview is confidential and is part of a Food and Drug Administration requirement to assess comprehension and clarity of select survey questions associated with a specific medication with patients. It is for informational purposes only and is not an attempt to sell you anything or promote a product.

If this is a convenient time, I would like to ask you a few questions to determine if you qualify for participation in this research study. **[IF NOT CONVENIENT ASK:** When would be a good time to schedule a few minutes to go through a few screening questions? **Call back on DATE: _____ TIME: _____]**

[ONLINE SCREENER]

[Introduction]

Thank you for your interest in this research to evaluate select survey questions and your response options related to a specific medication.

If you qualify and agree to participate in this research study, the answers you provide to the following screening questions will be shared with UBC, the company conducting this research, and Amgen Inc, the sponsor of this survey. We respect that the privacy of your personal information is important to you.

Your answers to these survey questions will be combined with answers given by others and reported in an anonymous form to the sponsor. All the information you provide will be kept confidential in accordance with all applicable laws. Your personal information will be used to send you compensation for your participation in this research interview. You will not be contacted for marketing purposes based on your personal information or your answers to the survey. Neither the sponsor nor its contractors will sell or rent your information. Your privacy will be protected; however, research survey records may be inspected by the regulatory authorities. Your choice to allow the sponsor to use your information is entirely voluntary but necessary to take part in this research.

If you qualify and agree to participate, the research interview should take approximately 60 minutes and we'll work to find an available time that fits your schedule. Following completion of the research interview, you will receive compensation, if eligible, based on fair market value for your time and efforts.

1) Based on the information given, would you like to proceed with the following questions to determine if you are eligible to participate?

   ❑ Yes
   ❑ No **[TERMINATE]**

2) Which of the following groups best describes your age?

   ❑ Under 18 **[TERMINATE]**
   ❑ 18 - 29
   ❑ 30 - 39

❑ 40 - 49
❑ 50 - 59
❑ 60 - 69
❑ 70 or older
❑ Prefer not to answer **[TERMINATE]**

[RECORD AND CONTINUE]

2) Have you been diagnosed with any of the following conditions? (Select all that apply)

❑ Crohn's Disease
❑ A Blood Disease **[MUST SELECT TO CONTINUE]**
❑ Arthritis
❑ Heart Failure
❑ HIV **[TERMINATE]**
❑ None of above **[TERMINATE]**

[RECORD AND CONTINUE]

3) How do you identify?

❑ Male
❑ Female
❑ Non-binary
❑ Prefer not to say
❑ Other

[RECORD AND CONTINUE]

3) Are you or a member of your immediate family currently employed by or consultants of a pharmaceutical company, UBC, or the FDA?

❑ Yes **[TERMINATE]**
❑ No **[CONTINUE]**
❑ I don't know **[TERMINATE]**

[RECORD AND CONTINUE]

4) What is the highest level of education you have completed?
❑ Less than high school/Some high school graduate/GED
❑ Trade school/Some College
❑ Associate degree/Bachelor's degree/Master's degree/Professional or Doctoral degree

[RECORD AND CONTINUE]

5) We are interested in speaking with individuals from many of the U.S. census categories. The following question is regarding race/ethnic background. For informational purposes only, can you please indicate which of the following US census categories best describes your race?
   - ❑ White
   - ❑ Black or African American
   - ❑ Other: _____
   - ❑ Prefer not to answer

   [RECORD AND CONTINUE]

6) During the telephone interview, you will be directed to a protected website to review materials. Will you have a computer or tablet with access to the internet during the telephone interview?

   - ❑ Yes
   - ❑ No **[TERMINATE]**

   [RECORD AND CONTINUE]

ELIGIBILITY SCRIPT:

Thank you for your time; you qualify for participation in this research.

The interview will last for approximately **60 minutes**, will be conducted by telephone and online, and will be audio taped for research purposes. This research is confidential and is for informational purposes only; it will not be used for commercial purposes. Your answers will be combined with answers given by other people participating in these interviews. Your answers and all information collected during the interviews will be shared with the study team involved in these research interviews and may also be shared with the regulatory authorities. Your answers will remain anonymous (they will not be attributed to you).

If during the interview you mention a product complaint or an adverse event related to a product that is marketed by the sponsor even if you have already reported it to the sponsor or regulatory authorities, you acknowledge that the moderator will ask you to confirm if you are willing to receive follow-up from the sponsor to discuss this further. A product complaint or adverse event report will be provided to the sponsor. The information within this report will only be used by the sponsor to satisfy its internal or regulatory requirements relating to the quality or safety of its product. You understand that your personal information will only be included in this report if you provide your consent.

You are eligible to receive compensation for your time and effort for completing the interview. Upon receipt of the Interview Release Form and completion of the interview, you may elect to receive compensation in the amount of **$125.**

7) Would you like to receive compensation?
   - ❑ Yes
   - ❑ No

[RECORD AND CONTINUE TO SCHEDULE]

[DISPLAY IF RESPONSE TO QUESTION 8 = NO]

Based on the response(s) to the question above, we want to remind you that you are not eligible for compensation for your time and effort in completing the Interview; but we do appreciate your participation!

[CONTINUE TO SCHEDULE]

SCHEDULING:

Now I would like to schedule your interview. These are the dates and times that are currently available. Please let me know what date and time works best with your schedule. **[INTERVIEWER: review calendar of availability to confirm interview date and time.]**

Thank you again for your time. I will send you a confirmation letter with information about the interview session, Interview Release Form, and instructions for returning these documents.

TERMINATION LANGUAGE TO BE USED THROUGHOUT
Thank you so much for your time. Based on one [or more] of your answers, you do not qualify for this research study.

STUDY SPECIFICATIONS SUMMARY

ATTEMPT TO RECRUIT 12 PATIENTS WHO:

- Diagnosed with a blood disorder excluding HIV
- Are located in the United States
- Include a mix ages, gender, and educational levels
- Do not work for or have immediate family who work for or consultants of a pharmaceutical company, UBC, or the FDA
- Have access to a computer/tablet with access to the internet during the interview
- Are willing and able to sign an Interview Release Form to participate in the research

ANNEX 3: PATIENT/CAREGIVER QUESTIONNAIRE

Survey Legend

- * Indicates field is required.
- **----------** indicates beginning and end of a unique page.
- **[PAGE TITLE]** indicates new page/ screen (only specify if needed).
- **[PROGRAMMER]** is used to indicate directions to the programmer and is set in bold, red, uppercase letters between square brackets.
- **(INTERVIEWER)** is used to indicate directions to the phone interviewer and is set in bold, blue text between parentheses. This text appears when content is to be administered by phone only (for example, spontaneous AE reporting).
- **[<MODALITY>]** indicates a section is to be displayed for a specific modality (i.e., Online, Phone).
- **[BEGIN <Section Description>]** and **[END <Section Description>]** represents the beginning and the end of a section (for example, Welcome Page).
- **[BEGIN INCLUSION/EXCLUSION QUESTIONS]** and **[END INCLUSION/EXCLUSION QUESTIONS]** are displayed next to responses that represent the beginning and the end of the inclusion/exclusion survey content.
- **[BEGIN KEY MESSAGE DOMAIN AND SAFE USE QUESTIONS]** and **[END KEY MESSAGE DOMAIN AND SAFE USE QUESTIONS]** are displayed next to responses that represent the beginning and the end of the main survey content.
- **[TERMINATE]** is displayed next to responses that should cause the survey to end. The following termination language will be programmed into the survey or read by the interviewer unless a different language is specified with the question.

Thank you very much for your time today. Based on your answer, you are not eligible to take this survey. We appreciate your interest in the survey.

- **[RANDOMIZE LIST]** is inserted before questions to indicate to the programmer that the responses should be randomized for both the online and telephone survey. Responses such as “I don’t know/I don’t remember,” “Prefer not to answer,” All of the above” or “None of the above” will always appear at the end of the randomized responses, where applicable.
- **[KEEP IN POSITION]** Indicates that the option / choice will remain in position. Note this is only needed if the list of randomized.
- **[MAKE URL ACTIVE]** Used to indicate that the URL provided should be made into an active link.
- **[EXCLUSIVE]** Used to indicate that the option / choice should unselect all other options / choices in the question.
- N indicates that the free text field will be included in the Free Text Review module.
- **[ANSWER TO Q#]** indicates dynamic text is present. This instruction should be placed on the question where the dynamic text should display. An instruction does not need to be added to the question from which the dynamic text is taken.
- **[TEXT LEN##]** indicates a single line text box with a max length of the number specified. Default is 200 unless otherwise noted.
- **[MULTI LEN##]** indicates a single line text box with a max length of the number specified. Default is 200 unless otherwise noted.

- **[NUM LEN##]** indicates a single line text box with a max length of the number specified numeric values only.
- **[DROP-DOWN LIST INPUT WITH US STATES/TERRITORY TABLE]** indicates to the programmer that the response should be a drop-down list containing the states in the table below.

Alabama	Guam	Mississippi	Ohio	Virginia
Alaska	Hawaii	Missouri	Oklahoma	Washington
American Samoa	Idaho	Montana	Oregon	West Virginia
Arizona	Illinois	Nebraska	Pennsylvania	Wisconsin
Arkansas	Indiana	Nevada	Puerto Rico	Wyoming
California	Iowa	New Hampshire	Rhode Island	
Colorado	Kansas	New Jersey	South Carolina	
Connecticut	Kentucky	New Mexico	South Dakota	
Delaware	Louisiana	New York	Tennessee	
District of Columbia	Maine	North Carolina	Texas	
Florida	Maryland	North Dakota	US Virgin Islands	
Georgia	Massachusetts	Northern Mariana Islands	Utah	
	Michigan		Vermont	
	Minnesota			

The following is used to categorize survey populations into standard geographic regions, but it is not displayed in the survey.

Geographic Distribution (based on address)[1]: Northeast, Midwest, South, and West regions

Northeast Region

New England Division - ME, NH, VT, MA, RI, CT
Middle Atlantic Division - NY, NJ, PA

Midwest Region

East North Central Division - OH, IN, IL, MI, WI

West North Central Division - MN, IA, MO, ND, SD, NE, KS

South Region

South Atlantic Division - DE, MD, DC, VA, WV, NC, SC, GA, FL

East South-Central Division - KY, TN, AL, MS

West South-Central Division - AR, LA, OK, TX

West Region

Mountain Division - MT, ID, WY, CO, NM, AZ, UT, NV

Pacific Division - WA, OR, CA, AK, HI

Other

Puerto Rico, Northern Mariana Islands, US Virgin Islands, American Samoa, and Guam

[1] US Census Bureau, last revised 01 April 2020

[BEGIN SURVEY HELP SECTION] If you have questions or problems with the survey, please contact the BKEMV Risk Evaluation and Mitigation Strategy (REMS) Knowledge, Attitudes, and Behavior (KAB) Survey Coordinating Center at [XXX] [END SURVEY HELP SECTION]

[BEGIN WELCOME PAGE]

Welcome! Thank you for deciding to participate in this very important survey. This survey should take approximately 20 minutes to complete.

If you are eligible to take the survey, please complete all survey questions as presented to you. If you are eligible to participate you will be offered payment in the amount of $35.00 for your time spent on completing the entire survey; however, you can choose not to be paid and still complete the survey. To receive this payment, you will be asked to provide your contact information [that is your full name and mailing address].

Consider the following important information before you start the survey:

- The application will time out after 30 minutes of inactivity. We ask that you please consider completing this survey in one sitting. If your session times out, and you wish to continue via telephone, please contact the BKEMV Survey Coordinating Center for assistance.
- Payment is provided only for surveys that meet a completed status.

If you are ready, click Continue to begin the survey. If you do not have enough time now, click Return Later and return to this site when it is convenient for you.

Note: Do not use the browser's Back button while entering data.

[END WELCOME PAGE]

[BEGIN SURVEY CONTENT]

[BEGIN TELEPHONE/ONLINE PREAMBLE]

This consent information is for patients at least 18 years of age who are being treated with BKEMV or caregivers of patients of all ages who are being treated with BKEMV.

Thank you for your interest in this BKEMV Risk Evaluation and Mitigation Strategy (otherwise known as REMS) research survey. **[BEGIN ONLINE]** Before you begin, **[END ONLINE] [BEGIN TELEPHONE]** Before we begin, **[END TELEPHONE]** there is important information to know.

The survey is being conducted by United BioSource LLC (hereinafter referred to as UBC), on behalf of Amgen Inc. (hereinafter referred to as Amgen), the manufacturer of BKEMV. Your participation helps to meet the requirements set forth by the Food and Drug Administration (hereinafter referred to as FDA) that include making sure that patients treated with BKEMV understand the risks and appropriate use of BKEMV as outlined in the BKEMV REMS. **[BEGIN TELEPHONE]** The survey will take approximately 20 minutes to complete. **[END TELEPHONE]** Approximately 153 men and women who are receiving treatment with BKEMV and caregivers of patients who are receiving treatment with BKEMV are being asked to participate in this survey. Your open and honest feedback is critically important to enable Amgen and the FDA to continuously improve efforts to ensure that patient safety is being prioritized, and that risk mitigation is being properly managed for BKEMV.

The ability for the patients who are being treated with BKEMV or caregivers of patients of all ages who are being treated with BKEMV to receive BKEMV will not be impacted by your decision to take part in the survey (or not), nor by your responses.

Your answers to the survey questions will be combined with answers given by other people taking the survey. All answers will be collected by UBC, compiled, and reported in anonymous form to Amgen and the FDA. Your name will not be used in any report. There is no cost to you to take the survey.

If you are eligible to take the survey, complete all the survey questions, and provide your full name and mailing address, and you are eligible and elect to receive payment, your name and address will be used to mail you $35.00 for your participation. You may decline payment and still participate in the survey. The mailing will be sent following the close of the survey and will also include a Thank You Letter and a copy of the correct answers to important survey questions about the safe use of BKEMV.

Providing a telephone number is optional. Your telephone number will be used only if there are any questions about your survey answers.

Should you choose to participate in the survey, you agree that any information you provide during the survey may be used or shared with Amgen, excluding your name, address, and telephone number.

How We Protect Your Privacy

UBC, on behalf of Amgen, respects the privacy of your personal information. To the extent permitted by applicable laws and regulations, the records identifying you will not be made publicly available. You will not be contacted for marketing purposes based on the personal information you provide during the survey or based on your answers to the survey questions. Neither Amgen nor its contractors will sell, transfer, or rent your information. Please note that research survey records may be inspected by the FDA and a company called Sterling Institutional Review Board (hereinafter referred to as IRB). Please note that research survey records may be inspected by the FDA. Your choice to allow Amgen to use your information is entirely voluntary but necessary to take part in this survey.

Please be assured that your contact information and your individual responses will be kept strictly confidential. As noted above, however, information you provide will be combined with information and survey responses provided by others and shared or reported in anonymous form. By participating in the survey, you acknowledge and agree that such combined anonymous data may be shared with and used by Amgen and disclosed to the FDA. By participating, you also acknowledge that the FDA and/or IRB may inspect the records related to this survey which may include your individual responses. The results of the survey, including your responses, may be presented at meetings or in articles written about the survey (publications). If the results of the survey, including your research information, are published, your identity will remain confidential.

How to Learn More about This Survey

If you have questions about the survey or problems with the survey, please contact the BKEMV Survey Coordinating Center at **[XXX]**. **[BEGIN TELEPHONE]** This is the phone number you received in your invitation; however, I am going to provide you with another phone number and an identification number to the IRB. If you would like to write these

numbers down, please let me know when you have a pen and paper ready. **[END TELEPHONE]**

If you have questions about your rights as a research participant or related concerns, you may contact Sterling IRB toll-free at **1-888-636-1062**. Your IRB identification number is **[XXX]**. Be sure to write down your questions and IRB identification number.
[BEGIN INTERNET] Your IRB identification number and the IRB telephone number will not be displayed again. **[END INTERNET]**
[BEGIN TELEPHONE]

Please feel free to ask me to repeat any questions or statements as we go through the survey. **[END TELEPHONE]**

You do not waive any legal rights by taking part in this survey.

Taking the Survey
If you are eligible to take the survey, please complete all the survey questions. If you are eligible to receive payment and elect to receive payment for participation in the survey (if allowable by state law), you will be asked to provide your contact information.

[BEGIN ONLINE] Once you have answered a question and moved on, you cannot go back and change your answers. Please note your survey cannot be reset if you have started answering any questions. If you exit this survey prior to completion, you will not be able to return using the online system, you will need to contact the BKEMV Survey Coordinating Center, and someone will assist you in finishing the survey via telephone. **[END ONLINE]**

[BEGIN TELEPHONE] Once I have read the question and you have provided an answer, I cannot go back and change the answers you have provided; therefore, please carefully respond to each question. Once you answer the first question and you end this call prior to completion, the only way to finish it is by returning a call to the BKEMV Survey Coordinating Center to finish via telephone picking up where you left off. **[END TELEPHONE]**

Thank you for your participation in this survey.

[BEGIN INCLUSION/EXCLUSION QUESTIONS]

1.* Do you agree to participate in this survey about BKEMV?

- ❍ Yes
- ❍ No **[TERMINATE]**

[DISPLAY ONLY AFTER WAVE 1]

1a.* Have you ever taken part in a REMS and KAB survey about BKEMV prior to today?

- ❍ Yes
- ❍ No
- ❍ I don't know

[BEGIN TELEPHONE] As a reminder, the text below is only needed if respondent asks for clarity around acronym. **[END TELEPHONE]**

*REMS = Risk Evaluation and Mitigation Strategy; KAB = Knowledge, Attitudes, and Behavior

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1b.* Have you ever taken part in a research interview (not including surveys) about BKEMV prior to today? You would have participated in this research interview in August 2024.

- ❍ Yes
- ❍ No
- ❍ I don't know

2.* Are you and/or any of your immediate family members currently working for or as a consultant to Amgen, UBC, or the FDA?

- ❍ Yes **[TERMINATE]**
- ❍ No
- ❍ I don't know **[TERMINATE]**

[BEGIN TELEPHONE] As a reminder, the text below is only needed if respondent asks for clarity around acronym. **[END TELEPHONE]** *UBC = United BioSource LLC; FDA = Food and Drug Administration

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3.* Do you have any conflicts of interest that may affect your answers to this survey?

- ❍ Yes **[TERMINATE]**
- ❍ No
- ❍ I don't know **[TERMINATE]**

[BEGIN TELEPHONE] (INTERVIEWER: IF RESPONDENT ASKS, "WHAT IS A CONFLICT OF INTEREST," LET THE RESPONDENT KNOW THAT YOU CANNOT ELABORATE ON THE REFERENCE TO CONFLICT OF INTEREST AS IT IS PARTICIPANT TO INTERPRETATION. ALL THAT CAN BE PROVIDED IS THE QUESTION AS STATED.) [END TELEPHONE]

4.* Which of the following best describes **you**?

- ❍ I am a patient receiving treatment with BKEMV. **[PATIENT]**
- ❍ I am the caregiver/legal guardian of a patient receiving treatment with BKEMV. A caregiver/legal guardian is someone who manages the patient's medication and speaks to the doctor on the patient's behalf. **[OTHER]**
- ❍ I am neither of the above. **[TERMINATE]**

5.* Which of the following groups best describes **your** age?

- ❍ Under 18 **[TERMINATE]**
- ❍ 18 – 29
- ❍ 30 – 39
- ❍ 40 – 49
- ❍ 50 – 59
- ❍ 60 – 69
- ❍ 70 or older
- ❍ Prefer not to answer **[TERMINATE]**

6.* **[OTHER]** Which of the following groups best describes the age of the person to whom you provide care?

- ❍ Under 18

- ❍ 18 – 29
- ❍ 30 – 39
- ❍ 40 – 49
- ❍ 50 – 59
- ❍ 60 – 69
- ❍ 70 or older

7.* If you choose to receive the $35.00 for completing the survey, your full name, and mailing address are required. You may participate in the survey even if you choose not to be compensated.

A ❍ I will participate in the survey.
B ❍ I will participate in the survey but choose not to be compensated.
C ❍ I do not wish to participate in the survey. **[TERMINATE]**

[DISPLAY FOR WAVE 2]

8.* Have you ever taken part in a REMS Knowledge, Attitudes, and Behavior (also referred to as KAB) survey about BKEMV before?

- ❍ Yes
- ❍ No
- ❍ I don't know

9.* Prior to treatment with BKEMV, were you treated with another medication that required a survey evaluating knowledge about serious and life-threatening meningococcal infections?

- ❍ Yes
- ❍ No
- ❍ I don't know

[BEGIN TELEPHONE] As a reminder, the text below is only needed if respondent asks for clarity around acronym. **[END TELEPHONE]** *REMS = Risk Evaluation and Mitigation Strategy

---

[BEGIN PREAMBLE 2]
The following questions are about important safety information relating to the use of BKEMV.

If you do not know the answer to a question, please select 'I don't know' rather than guess the answer.
[END PREAMBLE 2]
[BEGIN KEY MESSAGE DOMAIN AND SAFE USE QUESTIONS]

10.* BKEMV is a medicine that may lower your immune system's ability to fight infection.

- ❍ True
- ❍ False
- ❍ I don't know

---

11. According to the BKEMV Patient Guide, indicate True, False, or I don't know for ***each statement*** about BKEMV.

	[RANDOMIZE]	**True**	**False**	**I don't know**
A*	According to BKEMV's Patient Guide, patients who are due to receive treatment with BKEMV should complete or update their vaccine for meningitis at least 2 weeks before their first dose.	❍	❍	❍
B*	Meningococcal (meningitis) infections may quickly become life threatening or cause death if not recognized and treated early.	❍	❍	❍
C*	**[PATIENT]** If you must be treated with BKEMV right away and have not gotten the required meningococcal vaccine, you should receive the vaccine as soon as possible. **[OTHER]** If the person for whom you provide care must be treated with BKEMV right away and have not gotten the required meningococcal vaccine, s/he should receive the vaccine as soon as possible.	❍	❍	❍

12. According to the BKEMV Patient Guide, indicate True, False, or I don't know for ***each statement*** about BKEMV.

	[RANDOMIZE]	**True**	**False**	**I don't know**
A*	**[PATIENT]** If you must be treated with BKEMV right away and have not been vaccinated, you should <u>also</u> receive antibiotics for as long as your healthcare provider tells you. **[OTHER]** If the person for whom you provide care must be treated with BKEMV right away and have not been vaccinated, s/he should <u>also</u> receive antibiotics for as long as his/her healthcare provider tells him/her.	❍	❍	❍
B*	**[PATIENT]** If you think you may have a meningococcal (meningitis) infection, you should tell your healthcare provider at your next office visit. **[OTHER]** If you or the person for whom you provide care, thinks that s/he may have a meningococcal infection, you or s/he should tell his/her healthcare provider at his/her next office visit.	❍	❍	❍
C*	The patient's risk of meningococcal (meningitis) infection may continue for several months after his/her last dose of BKEMV.	❍	❍	❍

13.* Select the **best** option. BKEMV can ___the ability of the patient's immune system to fight infections.

[RANDOMIZE]

A ❍ lower

B ❍ raise

C ❍ have no impact on

D ❍ None of the above **[KEEP IN POSITION]**

E ❍ I don't know **[KEEP IN POSITION]**

14.* **[PATIENT]** Select the **best** option. What should you do if you experience any sign or symptom of a serious meningococcal (meningitis) infection while taking BKEMV?
[OTHER] Select the **best** option. What should you do if the person you provide care for experiences any sign or symptom of a serious meningococcal (meningitis) infection while taking BKEMV?

[RANDOMIZE]

A ❍ **[PATIENT]** Immediately call your healthcare provider or seek emergency medical care, preferably in a major emergency medical center.
[OTHER] Immediately call the healthcare provider of the person for whom you provide care or have him/her seek emergency medical care, preferably in a major emergency medical center.

B ❍ Tell the neighbor just in case help is needed

C ❍ Nothing

D ❍ None of the above **[KEEP IN POSITION]**

E ❍ I don't know **[KEEP IN POSITION]**

15.* **[PATIENT]** Even if you have had meningococcal (meningitis) vaccine(s) in the past, these might need to be updated before starting BKEMV.
[OTHER] Even if the person for whom you provide care has had meningococcal (meningitis) vaccine(s) in the past, these might need to be updated before starting BKEMV.

❍ Yes
❍ No
❍ I don't know

16.* BKEMV _____ the patient's chance of getting serious and life threatening meningococcal (meningitis) infections.

[RANDOMIZE]

A ❍ decreases

B ❍ increases

C ❍ removes

D ❍ I don't know **[KEEP IN POSITION]**

[BEGIN PREAMBLE 3] [PATIENT] The next statement is about symptoms that you could experience while taking BKEMV. Please remember, when responding to these questions, please answer based on what you KNOW and LEARNED about BKEMV from your healthcare provider or during review of the BKEMV materials that you received.
[OTHER] The next statement is about symptoms that the person for whom you provide care could experience while taking BKEMV. Please remember, when responding to these questions, please answer based on what you KNOW and LEARNED about BKEMV from his/her healthcare provider or during review of the BKEMV materials that you or s/he received.
[END PREAMBLE 3]

---

17. **[PATIENT]** If you experience any of the signs or symptoms listed **below**, that could be a sign of a serious meningococcal (meningitis) infection, you should seek immediate medical attention.
Fever
Fever and a rash
Fever with high heart rate
Headache with nausea or vomiting
Headache and fever
Headache with stiff neck or stiff back
Confusion
Eyes sensitive to light
Muscle aches with flu-like symptoms

[OTHER] If the patient for whom you provide care experiences any of the signs or symptoms listed **below**, that could be a sign of a serious meningococcal (meningitis) infection, he/she should seek immediate medical attention.
Fever
Fever and a rash
Fever with high heart rate
Headache with nausea or vomiting
Headache and fever
Headache with stiff neck or stiff back
Confusion
Eyes sensitive to light
Muscle aches with flu-like symptoms

❍ True

❍ False

❍ I don't know

---

18. **[PATIENT]** You should carry the Patient Safety Card with you at all times during treatment and for 3 months after your last dose of BKEMV.

[OTHER] The person form whom you provide care should carry the Patient Safety Card with him/her at all times during treatment and for 3 months after his/her last dose of BKEMV.

- ❍ Yes
- ❍ No
- ❍ I don't know

---

19. **[PATIENT]** You should show the Patient Safety Card to any healthcare provider that treats you.

[OTHER] You or the person for whom you provide care should show the Patient Safety Card to any healthcare provider that treats him/her.

- ❍ True
- ❍ False
- ❍ I don't know

20.* **[PATIENT]** If BKEMV must be started right away but you have not completed or are not up to date with meningococcal (meningitis) vaccines, you must also take antibiotics as directed by your healthcare provider.

[OTHER] If BKEMV must be started right away but the person for whom you provide care has not completed or are not up to date with meningococcal (meningitis) vaccines, s/he must also take antibiotics as directed by his/her healthcare provider.

- ❍ True
- ❍ False
- ❍ I don't know

---

21. **[PATIENT]** If you have any signs and symptoms of meningococcal infection (meningitis), seek medical care right away, even if you do not have your Patient Safety Card with you.

[OTHER] If the person for whom you provide care has any signs and symptoms of meningococcal infection (meningitis), seek medical care right away, even if s/he does not have your Patient Safety Card with him/her.

- ❍ True
- ❍ False
- ❍ I don't know

[BEGIN PREAMBLE 4]

The next questions are about informational materials for BKEMV and the BKEMV REMS.

[END PREAMBLE 4]

22.* Please select all that apply. From what sources have you received information about BKEMV?

A ☐ FDA
B ☐ Healthcare provider (such as a doctor or nurse)
C ☐ Pharmacist
D ☐ BKEMV Patient Guide
E ☐ BKEMV REMS website
F ☐ BKEMV website
G ☐ BKEMV Medication Guide
H ☐ BKEMV Patient Safety Card
I ☐ Other
A ☐ FDA
B ☐ Healthcare provider (such as a doctor or nurse)
C ☐ Pharmacist
D ☐ BKEMV Patient Guide
E ☐ BKEMV REMS website
F ☐ BKEMV website
G ☐ BKEMV Medication Guide
H ☐ BKEMV Patient Safety Card
I ☐ Other

23.* Prior to today, were you aware of the BKEMV Patient Guide?

❍ Yes
❍ No

[DISPLAY IF Q23 = Yes]

24.* Did you read the BKEMV Patient Guide?

❍ Yes
❍ No
❍ I don't remember

25.* Prior to today, were you aware of the BKEMV Patient Safety Card?

❍ Yes
❍ No

[DISPLAY IF Q25 = Yes]

26.* Did you read the BKEMV Patient Safety Card?

❍ Yes
❍ No
❍ I don't remember

27.* Do you have any questions about the BKEMV REMS educational materials or the BKEMV REMS requirements?

❍ Yes
❍ No

[BEGIN TELEPHONE] As a reminder, the text below is only needed if respondent asks for clarity around acronym. **[END TELEPHONE]**
*REMS = Risk Evaluation and Mitigation Strategy

[DISPLAY IF Q27 = YES]

28.* What are your questions?

[MULTI LEN200] 👁

[BEGIN DEMOGRAPHICS PREAMBLE 1]

There are just a few more questions to help us combine your answers with other answers we have received. These last few questions are for demographic purposes.
[END DEMOGRAPHICS PREAMBLE]

29.* **[PATIENT]** Have you taken at least one dose of BKEMV?

[OTHER] Has the patient you care for taken at least one dose of BKEMV?
❍ Yes
❍ No

[DISPLAY IF Q29 = YES]

30.* **[PATIENT]** How long have you been receiving treatment with BKEMV?
[OTHER] How long has the person for whom you provide care been receiving treatment with BKEMV?

A ❍ Less than 3 months
B ❍ 3-6 months
C ❍ 7-12 months
D ❍ More than 1 year
E ❍ More than 5 years

31.* What is the highest level of education you have completed?

❍ Less than high school/Some high school/graduate/GED
❍ Some college/Associate degree
❍ Bachelor's degree/Master's degree/Professional Doctoral degree
❍ Prefer not to answer

[BEGIN TELEPHONE] As a reminder, the text below is only needed if respondent asks for clarity around acronym. **[END TELEPHONE]**
*GED = General Education Diploma

32.* What is the <u>main</u> language you speak at home?

❍ English

- ❍ Spanish
- ❍ Other
- ❍ Prefer not to answer

33.* Are you Hispanic or Latino?

- ❍ Yes
- ❍ No
- ❍ Prefer not to answer

34.* Which of the following US census categories best describes your race?

- ❍ White
- ❍ Black or African American
- ❍ Two or more races
- ❍ Other
- ❍ Prefer not to answer

[BEGIN TELEPHONE] As a reminder, the text below is only needed if respondent asks for clarity around acronym. **[END TELEPHONE]**
*US = United States

35.* In which state or US territory do you live?

[DROP-DOWN LIST INPUT WITH STATES TABLE]

[BEGIN TELEPHONE] As a reminder, the text below is only needed if respondent asks for clarity around acronym. **[END TELEPHONE]**
*US = United States

[END SURVEY CONTENT]

[END ONLINE/TELEPHONE SURVEY CONTENT]
---------- ADVERSE EVENT/PRODUCT COMPLAINT----------

[TELEPHONE]

[BEGIN AE]

***(INTERVIEWER: Please record if respondent spontaneously reported an adverse event, product complaint, or any other information deemed reportable during the course of this interview. Upon completion, please complete the BKEMV Reportable Event Form and email it to the KAB Ops Team at kab_operational_team@ubc.com and copy the Call Center Manager.)**

- ❍ Yes
- ❍ No

[END AE]
[DISPLAY REMAINDER OF PAGE IF AE = Yes]
*Enter Safety Adverse Event Verbatim **[MULTI LEN 200]** 👁

(INTERVIEWER: Indicate to the respondent that someone may call back to ask questions about the information provided during the survey.)

[BEGIN ONLINE]

36.* Click here to download the correct answers to the important survey questions for the BKEMV Patient KAB Survey. **[DISPLAY** 'PatientCorrectAnswers.pdf' **IN NEW WINDOW UPON HYPERLINK SELECTION]**

Click Next to continue.
[END ONLINE]

[BEGIN ONLINE]

37.* Click here to locate all REMS educational materials, including the Medication Guide for BKEMV.

[DISPLAY '**https://www.BKEMVREMS.com**' **IN NEW WINDOW UPON HYPERLINK SELECTION]**

Click Next to continue.
[END ONLINE]

[BEGIN CLOSING 1 – DISPLAY IF Q7 = A]

We would like to send you $35.00 as fair market value compensation for your time spent participating in the survey and the correct answers to important survey questions at the time the survey closes, which is approximately March 29, 2026. We need your full name and mailing address to do so. If you do not provide this information, you will not receive compensation, or the educational materials listed above. [END CLOSING 1]

38.* Do you agree to give us your full name and mailing address so we can send you $35.00 and the BKEMV educational materials?

- ❍ Yes
- ❍ No

[DISPLAY IF Q34 = "Yes"] Please note that payment processing begins upon survey close which is targeted to be on or about March 29, 2026. Please allow 4-6 weeks for processing.

[BEGIN ONLINE] Click Next to continue. [END ONLINE]

[BEGIN CLOSING 1A - DISPLAY IF Q7]

We would like to send you a copy of the correct answers to important survey questions at the time the survey closes, which is approximately March 29, 2026, but we need your full name and mailing address to do so.

[END CLOSING 1A]

39.* Do you agree to give us your full name and mailing address so we can send you a copy of the correct answers to the survey questions?

- ❍ Yes
- ❍ No

[BEGIN ONLINE] Click Next to continue. [END ONLINE]

[BEGIN CLOSING 2]

We would also like to ask for your telephone number. Providing a telephone number is optional. Your telephone number will only be used if any follow-up is required. It will not be used for any telemarketing or shared outside the staff of this survey.

[END CLOSING 2]

40.* Do you want to provide your telephone number?

- ❍ Yes
- ❍ No

[BEGIN ONLINE] Click Next to continue. [END ONLINE]

[BEGIN CONTACT INFORMATION – DISPLAY IF Q38 = YES OR Q39 = YES OR Q40 = YES]

Because you have agreed to provide your contact information, please provide the following:

The field is displayed if: [InSurveyFlow] Equal to FALSE OR [Q38 = YES OR Q39 YES]
The required constraint only is applied if: [InSurveyFlow] Equal to True
FIRST NAME **[TEXT LEN50]**

The field is displayed if: [InSurveyFlow] Equal to FALSE OR [Q38 = YES OR Q39 YES]
The required constraint only is applied if: [InSurveyFlow] Equal to True
LAST NAME **[TEXT LEN50]**

The field is displayed if: [InSurveyFlow] Equal to FALSE OR [Q38 = YES OR Q39 YES]
The required constraint only is applied if: [InSurveyFlow] Equal to True
ADDRESS **[MULTI LEN200]**

The field is displayed if: [InSurveyFlow] Equal to FALSE OR [Q38 = YES OR Q39 YES]
The required constraint only is applied if: [InSurveyFlow] Equal to True
CITY **[TEXT LEN50]**

The field is displayed if: [InSurveyFlow] Equal to FALSE OR [Q38 = YES OR Q39 YES]
The required constraint only is applied if: [InSurveyFlow] Equal to True
STATE **[DROP-DOWN LIST INPUT WITH STATES TABLE]**

The field is displayed if: [InSurveyFlow] Equal to FALSE OR [Q38 = YES OR Q39 YES]
The required constraint only is applied if: [InSurveyFlow] Equal to True [EDIT CHECK: NUMERIC ONLY; MUST BE 5-DIGITS]
ZIP CODE **[TEXT LEN5]**

The field is displayed if: [InSurveyFlow] Equal to FALSE OR [Q40 = YES]
The required constraint only is applied if: [InSurveyFlow] Equal to True
[EDIT CHECK: NUMERIC ONLY; MUST BE 10-DIGITS]
TELEPHONE **[TEXT LEN10]**
[END CONTACT INFORMATION]

[BEGIN END OF SURVEY MESSAGE]

This is the end of the survey. If you have questions about the survey, please contact the BKEMV REMS KAB Survey Coordinating Center at 1-XXX-XXX-XXXXX. Thank you again for your help.

[END END OF SURVEY MESSAGE]
[END SURVEY CONTENT]

ANNEX 4: RECRUITMENT MATERIALS

Informational Letter to Patients

[CURR_DATE]

[PATIENT_FIRST_NAME] [PATIENT _LAST NAME], [TITLE]
[PATIENT _STREET_ADDR]
[PATIENT _CITY], [PATIENT _STATE] [PATIENT _ZIP]

Dear [PATIENT _FULL_NAME]:

We need your help!

Amgen Inc. is conducting a research survey as part of a Food and Drug Administration (FDA) requirement to find out if patients being treated with and caregivers of patients of all ages who are being treated with BKEMV understand important safety information related to the use of BKEMV. Approximately 153 men and women at least 18 years of age or a caregiver of patients of all ages who are receiving treatment with BKEMV are being asked to participate in this survey. The survey should take approximately 20 minutes to complete.

Eligible participants who complete the survey will be monetarily compensated in the amount of $35.00 for their time.

Please note, however, that if you work in any of these states, you may still complete the survey without receiving compensation.

UBC will be conducting the survey on behalf of Amgen Inc.

At this time, we are letting you know that because you have been identified as having been trained per the BKEMV REMS requirements.

The survey is expected to be conducted from September 02, 2025 – March 29, 2026.

Sincerely,
The BKEMV REMS KAB Survey Coordinating Center

Patient Invitation Letter

[CURR_DATE]

[PATIENT_FIRST_NAME] [PATIENT _LAST NAME], [TITLE]
[PATIENT _STREET_ADDR]
[PATIENT _CITY], [PATIENT _STATE] [PATIENT _ZIP]

Dear [PATIENT _FULL_NAME]:

You will need to provide this code prior to starting the survey: **[CODE_ID]**.

Amgen Inc. is conducting a REMS research survey as part of an FDA requirement to learn if patients being treated with, and caregivers of patients of all ages who are being treated with BKEMV understand important safety information related to the use of BKEMV. UBC is the research firm that is conducting the survey on behalf of Amgen Inc.

- Approximately 153 men and women at least 18 years of age or a caregiver of patients of all ages who are currently receiving treatment with BKEMV are being asked to participate in the survey.
- Respondents identified as eligible to participate in the survey are asked to answer all the survey questions, provide their contact information (full name and mailing address), and may be eligible for $35.00 as monetary compensation for their time.
- The survey should take approximately 20 minutes to complete depending on the method chosen to complete the survey.
- The survey is expected to continue through midnight on March 29, 2026.

Your participation in this survey is completely voluntary. Your answers to the questions or your decision to take part or not to take part in the survey will not affect your ability or the person for whom you provide care to receive treatment with BKEMV. For your convenience, the survey can be completed either online via a secure website or over the telephone with a survey team associate. You are under no obligation to take this survey.

For your convenience, the survey can be completed either online via a secure website or over the telephone with a BKEMV REMS KAB Survey Coordinating Center Associate. Please select the option that you would like to take to complete this very important survey about BKEMV and proceed as noted below.

1. Scan the code below using your smartphone or using a laptop, iPad, or other computing device to visit **www.BKEMVKnowledgeSurvey.com**

ENTER QR CODE

OR

2. Call **[xxx]**, 8 AM to 8 PM Eastern Time, Monday through Friday.

If you are completing this survey via internet or telephone, please have this letter with you at the time you take the survey.

We respect that the privacy of your personal information is important to you. If you choose to participate in the survey, you will be asked to provide name, address, and telephone number. Your name and address will be used to send you your monetary compensation; your telephone number will be used only if there are any questions about your survey

responses. In addition to the compensation, you will also receive a thank you letter and correct answers to important survey questions about the safe use of BKEMV.

Your answers to the survey will be combined with answers provided by others. Your name will not be used in any report. You will not be contacted for marketing purposes based on your personal information or your answers to the survey. Your information will not be sold, transferred, or rented.

If you have any questions about this survey, please contact the BKEMV REMS KAB Survey Coordinating Center at **[xxx]**.

Sincerely,
The BKEMV REMS KAB Survey Coordinating Center

Patient Reminder Letter

[CURR_DATE]

[PATIENT_FIRST_NAME] [PATIENT _LAST NAME], [TITLE]
[PATIENT _STREET_ADDR]
[PATIENT _CITY], [PATIENT _STATE] [PATIENT _ZIP]

Dear [PATIENT _FULL_NAME]:

Social Validation Messages will be included at the onset of each Reminder Letter Campaign.

You will need to provide this code prior to starting the survey: **[CODE_ID]**.

You recently received a letter asking if you would consider participating in a voluntary survey associated with the use of BKEMV.

On behalf of Amgen Inc., we are contacting you as a **reminder** to ask you to consider participating in this very important survey about BKEMV. **Currently, some of your colleagues have already responded. Each participant in this survey is important and helps to increase accuracy and understanding of effectiveness in communicating important risks associated with BKEMV. This survey will close soon, and your participation is valuable to us!**

For your convenience, the survey can be completed either online via a secure website or over the telephone with a BKEMV REMS KAB Survey Coordinating Center Associate. Please select the option that you would like to take to complete this very important survey about BKEMV and proceed as noted below.

For your convenience, the survey can be completed either online via a secure website or over the telephone with a BKEMV REMS KAB Survey Coordinating Center Associate. Please select the option that you would like to take to complete this very important survey about BKEMV and proceed as noted below.

1. Scan the code below using your smartphone or using a laptop, iPad, or other computing device to visit **www.BKEMVKnowledgeSurvey.com**

ENTER QR CODE

OR

2. Call **[XXX]**, 8 AM to 8 PM Eastern Time, Monday through Friday.

If you are completing this survey via internet or telephone, please have this letter with you at the time you take the survey.

If you have any questions about this survey, please contact the Patient KAB Survey Coordinating Center at **[XXX]**.

Sincerely,
The BKEMV REMS KAB Survey Coordinating Center

Patient Thank You Letter - Compensation

[CURR_DATE]

[PATIENT_FIRST_NAME] [PATIENT _LAST NAME], [TITLE]
[PATIENT _STREET_ADDR]
[PATIENT _CITY], [PATIENT _STATE] [PATIENT _ZIP]

Dear [PATIENT _FULL_NAME]:

On behalf of Amgen Inc., we would like to thank you for taking part in the Patient KAB Survey about BKEMV. To express our appreciation for your valuable time, enclosed is $35.00 as compensation for your time in completing this BKEMV survey.

To ensure that survey participants, like yourself, have accurate information about the risks associated with BKEMV, we have also enclosed the correct answers to important survey questions about the safe use of BKEMV.

We know that sharing important information about BKEMV is vital to ensuring that you understand all the safe use and risks associated with BKEMV. You can locate all of the REMS educational materials by copying the link below and retrieving the materials from the BKEMV REMS website: https://www.BKEMVREMS.com.

As it pertains to the $35.00 gift card, please read the terms and conditions included with this gift card. It is important to know that if the funds on this gift card are not used within 4 months of receipt, an administrative fee of $3.00 will be deducted monthly until funds are depleted. Also, please note that if you use this card for purchases online, you will be asked to include an address and you should use 933 Canyon Road, Morgantown, WV 26505. If you are trying to use this card as a debit card, you will need to set up a PIN by calling CT Payer (1-800-436-8902), however, you can use the card as a credit card without any PIN. If you have any issues with this card, please contact the BKEMV REMS KAB Survey Coordinator Center at **[XXX]**.

Sincerely,
The BKEMV REMS KAB Survey Coordinating Center

Enclosures:

- A copy of the correct answers to important survey questions about the safe use of BKEMV
- $35.00 gift card

Patient Thank You Letter – No Compensation

[CURR_DATE]

[PATIENT_FIRST_NAME] [PATIENT _LAST NAME], [TITLE]
[PATIENT _STREET_ADDR]
[PATIENT _CITY], [PATIENT _STATE] [PATIENT _ZIP]

Dear [PATIENT _FULL_NAME]:

On behalf of Amgen Inc., we would like to thank you for taking part in the Patient KAB Survey about BKEMV.

To ensure that survey participants, like yourself, have accurate information about the risks associated with BKEMV, we have enclosed the correct answers to important survey questions about the safe use of BKEMV.

We know that sharing important information about BKEMV is vital to ensuring that you understand all the safe use and risks associated with BKEMV. You can locate all the REMS educational materials by copying the link below and retrieving the materials from the BKEMV REMS website: https://www.BKEMVREMS.com.

Sincerely,
The BKEMV REMS KAB Survey Coordinating Center

Enclosures:

- A copy of the correct answers to important survey questions about the safe use of BKEMV

ANNEX 5: QUALITATIVE RESEARCH DOCUMENTS

QR Moderator Discussion Guide

QR Transcripts

QR Final Summary Report inclusive of Findings Presentation

See Section 8 for more information about these materials.

Appendix C. Sample Safety Reporting Form(s)

[Delete this Appendix if not applicable to the study.

All studies that report safety data are required to include a sample version of the Form(s) intended to capture all events that must be reported directly to Amgen Safety. This allows sites to familiarize themselves with the form reporting requirements.]

Appendix D. Additional Safety Reporting Information

General Instructions

The protocol will provide instruction on what types of events to report for the study.
***Indicates a mandatory field.**

What to report on this form:

- **All adverse events (AEs) are associated with the Amgen drug irrespective of causal relationship of the event to the study drug or seriousness, unless instructed differently by the protocol.**
- **The following safety findings are to be reported on this form as events regardless of association with an AE:**
  - **medication errors, overdose, whether accidental or intentional, misuse, or abuse, involving the Amgen product**
  - **transmission of infectious agents**
  - **reports of uses outside the terms for authorized use of the product including off label use**
  - **occupational exposure**
  - **any lack or loss of intended effect of the product(s)**
  - **product complaint (PC)**
  - **adverse device effect (ADE)**

The following should not be reported on this form and should be reported via the normal process set up for the study

- **pregnancy and lactation reports**

1. **Initial or Follow-up*** – Please tick the appropriate box
2. **Site Number* –** Enter your assigned site number for this study. **Subject Number* –** Enter the entire number assigned to the subject.
3. **Indicate event type* –** Tick the relevant box which applies to the event(s) you are reporting. Please note, more than one box can be ticked.
4. **Contact Details* –** Provide your name, phone, address, etc. (These contact details should be for the Vendor or Investigator)
5. **Reporter ID* –** Provide name or ID of reporter, phone, address, etc. (This could be the Investigator details if vendor details are added in section 4.
6. **HCP Contact Details (if other than reporter)* –** Provide name or ID of reporter, country, phone, address, etc.
7. **Patient* –** Enter the subjects demographic information.
8. **Medical History (include primary diagnosis)* –** Enter medical history that is relevant to the reported event, not the event description. This may include pre-existing conditions that contributed to the event, allergies and any relevant prior therapy, such as radiation. Include dates if available.
9. **Suspect Product Information (include dosing details)* –** Provide Product/Device information, Indication, start date, stop date, dose, route, frequency, Lot#, Serial#. It is important that all efforts are taken to provide the Lot number, were possible.
10. **AE, Other Safety Finding, PC/ADE Information*:**

    AE Diagnosis or Syndrome*:
    - If the diagnosis is known, it should be entered. Do not list all signs/symptoms if they are included in the diagnosis.
    - If a diagnosis is not known, the relevant signs/symptoms should be entered.
    - If the event is fatal, the cause of death should be entered and autopsy results should be submitted, when available.

Onset Date* – Enter date the AE first started rather than the date of diagnosis or hospitalization. For serious events, the start date is the date the event started, not the date on which the event met serious criteria. **This is a mandatory field.**

Resolved Date* – Enter date the AE ended. For serious events, this is not the date when the event no longer met serious criteria. If the event has not ended at the time of the initial report, a follow-up report should be completed when the end date is known. If the event is fatal, enter the date of death as the end date.

Hospitalization* – If the subject was hospitalized, enter admission and discharge dates. Hospitalization is any in-patient hospital admission for medical reasons, including an overnight stay in a healthcare facility, regardless of duration. A pre-existing condition that did not worsen while on study which involved a hospitalization for an elective treatment, is not considered an AE. Protocol specified hospitalizations are exempt.

Serious Criteria Code* – This is a mandatory field for serious events. Select the appropriate code for the event(s) being reported

Action Taken* – State what action has been taken with suspect drug/device.

Outcome* – Enter the code for the outcome of the event at the time the form is completed if outcome is known.

Severity* – State the severity of the safety event being reported.

Relationship to Product/Device*:

Relationship to Amgen drug under study* – The Investigator must determine and enter the relationship of the event to the Amgen drug under study at the time the event is initially reported.

Relationship to Amgen device* – The Investigator must determine and enter the relationship of the event to the Amgen device (e.g., prefilled syringe, auto-injector) at the time the event is initially reported. **If the study involves an Amgen device, this is a mandatory field. This question does not apply to non-Amgen devices used in the study (e.g., heating pads, infusion pumps)**

11. **Concomitant Medications* –** Indicate if there are any medications.

Medication Name, Start Date, Stop Date, Dose, Route, and Frequency – Enter information for any other medications the subject is taking. Include any study drugs not included in section 5 (Product Administration) such as chemotherapy, which may be considered co-suspect.

Co-suspect – Indicate if the medication is co-suspect in the event.

Continuing – Indicate if the subject is still taking the medication.

Event Treatment – Indicate if the medication was used to treat the event.

12. **Relevant Laboratory Tests* –** Indicate if there are any relevant laboratory values.

For each test type, enter the test name, units, date the test was run and the results.

13. **Other Relevant Tests* –** Indicate if there are any tests, including any diagnostics or procedures.

For each test type, enter the date, name, results, and units (if applicable).

14. **Description* –** Describe Event.

Enter summary of the event. Provide narrative details of the events listed in section 3. Include any therapy administered, such as radiotherapy; (excluding medications, which will be captured in section 6). If necessary, provide additional pages to Amgen.

Complete the signature section at the bottom of each page and fax the form to Amgen.

Project ID: 20240214	**A**	**Observational Research Safety Reporting Form**	**Date of Reporter Awareness:**
			Date Reported to Amgen:
	Fax reports to: Amgen Local Office	*<<populate LAO fax here or delete language>>*	

1. Initial: ☐ **Follow-up:** ☐

2. Site Number: **Subject Number:**

3. Indicate event type: ***(Please tick all that apply)*** ☐ **AE/Other Safety Finding** ☐ **Product Complaint (PC)** ☐ **Adverse Device Effect (ADE)**

4. Contact Details (Vendor/Investigator)

Name	*Phone*	*Fax*
Address		
City	*State/Province*	
Postal Code	*Country*	

5. Reporter ID

Name or ID	*Phone*	*Fax*
Address		
City	*State/Province*	
Postal Code	*Country*	

6. HCP Contact Details (if other than reporter)

Name		
Country		
Address		
City	*State/Province*	*Postal Code*
Phone	*Fax*	

7. Patient

Initials (optional)	*Sex*	*Age (at time of event)*	*Was consent obtained to follow-up with HCP?*
	☐ F ☐ M		☐ Yes ☐ No

Weight	*Height*	*Race*	*Is patient also reporter?*
☐ lbs ☐ kg	☐ in ☐ cm		☐ Yes ☐ No

8. Medical History (include primary diagnosis)

9. Suspect Product Information (include dosing details)

Product/Device: _____

Indication: _____

	Start Date (day month year)	Stop Date (day month year)	Dose	Route	Frequency

Pregnant? ☐ Yes ☐ No Lactating? ☐ Yes ☐ No

Allergy: _____

Prefilled Syringe? ☐ Yes ☐ No

Other Device _____

Lot # _____ ☐ Unknown

Serial # _____ ☐ Unavailable / Unknown

Vial Size

10. AE, Other Safety Finding, or PC/ADE information

Finding (List main event first; one event per line)	**Onset Date** (day month year)	**Resolved Date** *(If patient died, list date of death)* ***Cause of Death:*** *(provide autopsy report)* (day month year)	**Hospitalization** Hospitalized? ☐ Yes ☐ No Prolonged Hospitalization? ☐ Yes ☐ No Admitting dx _____ **Date Admitted** (day month year)	**Date Discharged** (day month year)	**Serious Criteria** **01** Fatal **02** Immediately life-threatening **03** Required/Prolonged hospitalization **04** Persistent or significant disability /incapacity **05** Congenital anomaly/birth defect **06** Other significant medical hazard **07** Non serious	**Action Taken** 1=none 2=dose reduced 3=dose increased 4=drug withdrawn 5=drug rechallenge (state outcome)	**Outcome** **01** Recovered/ Resolved **02** Recovering/ Resolving **03** Not recovered/not resolved **04** Recovered/ resolved with sequelae **05** Fatal **06** Unknown	**HCP ONLY** **Severity** 1=mild 2=moderate 3=severe	**Relationship to Product/Device** Is there a reasonable possibility that this event may have been caused by the Product/Device? Product	Device
									Y N	Y N
									Y N	Y N
									Y N	Y N

									Y N	Y N
									Y N	Y N
									Y N	Y N

11. Concomitant Medications (eg, chemotherapy)

Medication Names	Start Date Day Month Year	Stop Date Day Month Year	Co-suspect No	Co-suspect Yes	Continuing No	Continuing Yes	Dose	Route	Frequency	Treatment Meds

12. Relevant Laboratory Values (include dates, allergies, and any relevant prior therapy)

Date Day Month Year	Test / Unit										

13. Other Relevant Test (diagnostics and procedures)

Date Day Month Year	Additional Tests	Results	Units

14. Description: Provide chronological summary and details of AE symptoms, PC or ADE that are listed in section 10 (signs, diagnosis, treatment, concomitant medications including those used to treat event).

Appendix E. Pregnancy and Lactation Notification Forms

AMGEN® Pregnancy Notification Form

Report to Amgen at: USTO fax: +1-888-814-8653, Non-US fax: +44 (0)207-136-1046 or email (worldwide): svc-ags-in-us@amgen.com

1. Case Administrative Information

Protocol/Study Number: _20240214_____

Study Design: ☐ Interventional ☒ Observational (If Observational: ☐ Prospective ☐ Retrospective)

2. Contact Information

Investigator Name _____ **Site #** _____

Phone (____)_____ **Fax** (____)_____ **Email** _____

Institution _____

Address _____

3. Subject Information

Subject ID # _____ **Subject Gender:** ☐ Female ☐ Male **Subject age (at onset):** ____(in years)

4. Amgen Product Exposure

Amgen Product	Dose at time of conception	Frequency	Route	Start Date
				mm____/dd____/yyyy____

Was the Amgen product (or study drug) discontinued? ☐ Yes ☐ No

If yes, provide product (or study drug) stop date: mm _____/dd_____/yyyy_____

Did the subject withdraw from the study? ☐ Yes ☐ No

5. Pregnancy Information

Pregnant female's last menstrual period (LMP) mm_____/ dd_____/ yyyy_____ ☐Unknown ☐N/A

Estimated date of delivery mm_____/ dd_____/ yyyy_____

If N/A, date of termination (actual or planned) mm_____/ dd__/ yyyy_____

Has the pregnant female already delivered? ☐Yes ☐No ☐Unknown ☐N/A

If yes, provide date of delivery: mm _____/ dd_____/ yyyy_____

Was the infant healthy? ☐Yes ☐No ☐Unknown ☐N/A

If any Adverse Event was experienced by the infant, provide brief details:_____

_____

_____

Form Completed by:

Print Name: _____ **Title:** _____

Signature: _____ **Date:** _____

FORM-115199 Version 1.0 Effective Date: 24-Sept-2018

Internal Use Only General and Administrative

AMGEN® Lactation Notification Form

Report to Amgen at: USTO fax: +1-888-814-8653, Non-US fax: +44 (0)207-136-1046 or email (worldwide): svc-ags-in-us@amgen.com

1. Case Administrative Information

Protocol/Study Number: _20240214_____

Study Design: ☐ Interventional ☒ Observational (If Observational: ☐ Prospective ☐ Retrospective)

2. Contact Information

Investigator Name _____ **Site #** _____

Phone (_____)_____ **Fax** (_____)_____ **Email** _____

Institution _____

Address _____

3. Subject Information

Subject ID # _____ **Subject age (at onset):** ____(in years)

4. Amgen Product Exposure

Amgen Product	Dose at time of breast feeding	Frequency	Route	Start Date
				mm____/dd____/yyyy____

Was the Amgen product (or study drug) discontinued? ☐ Yes ☐ No

If yes, provide product (or study drug) stop date: mm _____/dd_____/yyyy_____

Did the subject withdraw from the study? ☐ Yes ☐ No

5. Breast Feeding Information

Did the mother breastfeed or provide the infant with pumped breast milk while actively taking an Amgen product? ☐Yes ☐ No

If No, provide stop date: mm_____/dd_____/yyyy_____

Infant date of birth: mm_____/dd_____/yyyy_____

Infant gender: ☐ Female ☐ Male

Is the infant healthy? ☐Yes ☐ No ☐ Unknown ☐N/A

If any Adverse Event was experienced by the mother or the infant, provide brief details:_____

_____

_____

Form Completed by:

Print Name: _____ **Title:** _____

Signature: _____ **Date:** _____

FORM-115201 Version 1.0 Effective Date: 24-Sept-2018

Internal Use Only General and Administrative

Appendix F. Correct Answer Document

The correct answers to the key message questions can be found below.

Correct Responses to Select PATIENT Survey Questions about Important Safety Messages for BKEMV™ (eculizumab)

Question	Desired Response
BKEMV is a medicine that affects your immune system.	**True**
According to the BKEMV Patient Guide, indicate True, False, or I don't know for ***each statement*** about BKEMV.	
Meningococcal infections may quickly become life threatening or cause death if not recognized and treated early.	**True**
The patient's risk of meningococcal infection may continue for several months after his/her last dose of BKEMV.	**True**
Select the **best** option. BKEMV can ___the ability of the patient's immune system to fight infections.	**Lower**
BKEMV _____ the patient's chance of getting serious and life-threatening meningococcal infections.	**Increases**
Patients who are receiving treatment with BKEMV should complete or update their meningococcal vaccine(s) at least 2 weeks before their first dose**.**	**True**
According to the BKEMV Patient Guide, indicate True, False, or I don't know for ***each statement*** about BKEMV.	
If you have not completed your meningococcal vaccines and BKEMV must be started right away, you should receive the required vaccine(s) as soon as possible.	**True**
If you have not been vaccinated and treatment with BKEMV must be started right away, you should also receive antibiotics to take for as long as your healthcare provider tells you.	**True**
If you have had meningococcal vaccine in the past, you might need additional vaccinations before starting BKEMV.	**Yes**
If you have not completed or are not up to date with meningococcal vaccines at least 2 weeks before your first dose of BKEMV and BKEMV therapy must be started right away, take antibiotics as directed by your healthcare provider.	**Yes**
According to the BKEMV Patient Guide, indicate True, False, or I don't know for ***each statement*** about BKEMV.	
If you think you may have a meningococcal infection, you should tell your healthcare provider at your next office visit.	**False**
Select the **best** option. What should you do if you experience any sign or symptom of a serious infection while taking BKEMV?	**Immediately call your healthcare provider or seek emergency medical care, preferably in a**

Question	Desired Response
	major emergency medical center.
If you experience any of the signs or symptoms listed **below**, that could be a sign of a serious meningococcal infection, you should seek immediate medical attention. **Fever** **Fever and a rash** **Fever with high heart rate** **Headache with nausea or vomiting** **Headache and fever** **Headache with stiff neck or stiff back** **Confusion** **Eyes sensitive to light** **Muscle aches with flu-like symptoms**	**True**
You should carry the Patient Safety Card with you at all times during treatment and for 3 months after your last dose of BKEMV.	**Yes**
You should show the Patient Safety Card to any healthcare provider that treats you.	**Yes**
You should get treatment right away for any signs and symptoms of a meningococcal infection even if you do not have your Patient Safety Card on you.	**Yes**

If you have any questions about BKEMV, please contact your healthcare provider.

Approval Signatures

Document Name: Protocol Conditionally Approved eculizumab biosimilar 20240214

Document Description: 20240214 BKEMV Updated post ORRG Meeting for conditional approval

Document Number: CLIN-000359594

Approval Date: 23 Nov 2024

Type of Study Protocol: Conditionally Approved

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Document Approvals	
Reason for Signing: Functional Area	Name: PPD Date of Signature: 23-Nov-2024 05:28:08 GMT+0000