Title: Healthcare Providers' Awareness of the Risks and Safety Associated With BLINCYTO® use: A 2021 REMS Assessment Survey

Amgen Protocol Number 20210065

Study Sponsor:	Amgen One Amgen Center Drive Thousand Oaks, CA 91320
Department:	Global Safety
Therapeutic Area:	Oncology
Key Sponsor Contact:	PPD PPD
Date:	22 March 2021
Version:	Version 1.0

Confidentiality Notice

This document contains confidential information of Amgen Inc.

This document must not be disclosed to anyone other than the site study staff and members of the Institutional Review Board/Independent Ethics Committee/Institutional Scientific Review Board or equivalent, as applicable.

The information in this document cannot be used for any purpose other than the evaluation or conduct of the research without the prior written consent of Amgen Inc.

Table of Contents

List of Tables

List of Appendices

1. BACKGROUND AND RATIONALE

BLINCYTO® (blinatumomab) is a bispecific T-cell engager indicated for the treatment of relapsed or refractory (R/R) CD19-positive B-cell precursor acute lymphoblastic leukemia (ALL). A Risk Evaluation and Mitigation Strategy (REMS) with goals to mitigate the risks of cytokine release syndrome (CRS), neurologic toxicities, and preparation and administration errors, was identified at the time of approval of the biological license application (BLA). The REMS communication plan consists of REMS Letters for Healthcare Providers (HCPs, including physicians and nurses), REMS Letter for Hospital and Home Healthcare Pharmacists, and REMS Letter for Professional Societies; a REMS Fact Sheet for Healthcare Providers; dissemination of REMS information at scientific meetings; and a REMS program website. Previous REMS assessment surveys have studied three populations: prescribers such as medical doctors, physician assistants, and nurse practitioners; nurses; and pharmacists. Results from the 5-year REMS assessment (submitted December 2019) indicated that surveyed physicians, pharmacists and nurses demonstrated adequate knowledge of the risks of cytokine release syndrome and neurological toxicity associated with BLINCYTO. Surveyed pharmacists and nurses, however, had lower understanding of the risk of preparation and administration errors associated with the use of BLINCYTO. The present REMS assessment conducted 7 years after the launch of BLINCYTO in the US will assess awareness and knowledge of preparation and administration errors associated with BLINCYTO use among pharmacists and nurses.

2. OBJECTIVES

The broad objective of this study is to determine the level of awareness of the risks and safety associated with BLINCYTO therapy and certain aspects of the BLINCYTO REMS Program among pharmacists and nurses who have used BLINCYTO for patients in the treatment of relapsed or refractory B-cell precursor acute lymphoblastic leukemia (ALL). The specific objective is to:

- Evaluate the awareness and understanding of the preparation and administration errors associated with BLINCYTO use among pharmacists who have prepared BLINCYTO, and nurses who have administered BLINCYTO.

3. STUDY POPULATION/SAMPLE SIZE/STATISTICAL ANALYSES PLANS

Study Design

An online cross-sectional survey will be conducted among pharmacists and nurses who have dispensed, prepared and/or administered BLINCYTO in the US in the past

12 months outside the clinical trial setting. Previous similar surveys were conducted at 18 months, 3 years and 5 years after the launch of BLINCYTO. This cross-sectional survey is being conducted 7-years after the launch of BLINCYTO in the US.

Study Population

Inclusion criteria include HCPs, defined as nurses (RNs, BSNs), and hospital and/or home healthcare pharmacists who have dispensed, prepared and/or administered BLINCYTO therapy to patients outside of the clinical trial setting in the past 12 months. HCPs or their immediate family members (eg, spouse, children, and/or parent) who are or were employed by Amgen, Naxion, or the FDA will be excluded from participation. HCPs who have been part of previous assessments (at 18 months, 3 years, and 5 years after the launch of BLINCYTO) will also be eligible to participate.

A list of HCPs targeted by the REMS Program will be matched to the survey vendor's Panels and/or other target sources to determine a list of respondents. All HCPs that are identified via these sources will be invited to participate in this survey.

Survey Pre-testing

The main data collection method for this assessment will be online surveys. Before actual data collection, Naxion will conduct telephone-assisted online pilot surveys with appropriate HCPs (eg, approximately 5 each of oncology nurses and hospital-based pharmacists) on the proposed survey questions. Pre--tests will be used to assess the survey research instrument for each of the following:

- *Directionality: Confirm that all questions are clearly understood by pre-test respondents.*
- *Survey duration: An estimation of the average duration of the survey will assist in planning the duration of the actual study.*
- *Completeness: Confirm that the response options provided are exhaustive and that no reasonable response options are omitted from closed-ended list questions.*
- *Question order effects: Determine whether there are question order effects (influence of previous question text or response on a following question) that can be controlled for by re-ordering questions.*

The findings from the pre-test will be used to improve the survey instrument and generate a final document for the survey.

Survey Methodology

Healthcare providers will be initially invited to participate in the survey by email (recruitment material, Appendix B). Majority of the surveys will be administered online and supplemented with telephone surveys. For those HCPs that opt for responding by telephone, the survey will be administered using computer-assisted telephone interviewing (CATI). In addition, direct mail invitations to participate in the online survey and/or hard copy surveys will be used to reach our target of completed surveys.

Screening questions will be placed at the beginning of the survey in order to determine whether HCPs are eligible to take part in a study. HCPs deemed ineligible by these questions are then terminated from the survey.

All possible answers for each survey question (not including screening questions) will be randomized. Participants will not be allowed to return to questions or be allowed to skip ahead during the survey administration. The correct answer choices will be provided on a screen at the end of the online survey. If the survey is completed by telephone, the correct answer choices will be provided by mail.

Survey Questions

The survey instrument includes questions about:

- screening and demographics
- the risk of preparation and administration errors associated with BLINCYTO use
- preparation instructions, access to checklists and Product Information/Package Insert (PI) in the workplace setting of pharmacists and nurses
- awareness and utilization of REMS materials.
- specific questions about preparation and administration errors including frequency of errors, medication errors (for example underdosing and overdosing), adherence to instructions and guidelines for change of infusion bags, and reconstitution of BLINCYTO.

The survey questions are included as Appendix A.

Endpoints

The main endpoint of interest in this assessment is the awareness of the risk of preparation and administration errors associated with use of BLINCYTO

Sample Size

The sample size for this assessment will be 200, including 100 pharmacists and 100 nurses. The precision for the estimates of the awareness of different endpoints specified above for samples sizes of 100 each for pharmacists and nurses, and a pooled

sample of 200 healthcare workers are shown in Table 1 below assuming 5% level of significance.

Table 1. Precisions for Sample Sizes of 100 and 200 at Varying Proportions With the Outcome and at 95% Confidence

Sample size	Proportion with outcome				
	10%	20%	30%	40%	50%
100	0.059	0.078	0.090	0.096	0.098
200	0.042	0.055	0.064	0.068	0.069

Descriptive Analyses

Separate analyses will be performed for nurses and pharmacists, as well as a pooled analysis of the two groups to assess the participants' understanding of the preparation and administration errors associated with the use of BLINCYTO. Categorical variables will be summarized using frequencies and proportions while quantitative data will be summarized using means and standard deviation for normally distributed data and medians and interquartile range for skewed data. For each survey question, the proportion and 95% CI of each response option including the 'not sure' and 'I routinely look it up' response categories will be reported. For each knowledge question, the proportion of HCPs selecting the correct response and corresponding 95% CI will be calculated. Analyses for each of the objectives are described in detail below.

Results will be presented for each HCP type separately, as well as pooled. For the main endpoint of the study, the understanding of preparation and administration errors, an individual participant must correctly answer at least 75% of the items to be considered to have knowledge. Specifically, knowledge will be assessed as follows:

- Nurses: Must correctly identify at least 75% of Questions 7, 10, and 11 (ie, 6 out of 8 items) to be considered to have knowledge (see Appendix A)
- Pharmacists: Must correctly identify at least 75% of Questions 8, 10, and 11 (ie, 6 out of 8 items) to be considered to have knowledge (see Appendix A)

A threshold knowledge score and corresponding 95% CI will be estimated as the proportion of HCPs (by type and overall) having knowledge of preparation and administration errors. Furthermore, the proportion of respondents deemed to have knowledge (ie, the proportion of respondents who have correctly identified at least 75% of the items) will be evaluated against a pre-specified threshold of 80% of a given HCP type. The percentage of respondents above and below the threshold knowledge score

will also be calculated. Responses for questions related to preparation instructions and access to checklists and Product Information/Package Insert (PI) in the workplace setting and knowledge of indication for BLINCYTO will be described with proportions and 95% CIs for each response option. Similarly, proportions and 95% CIs will be reported for the awareness and use of the REMS materials (responses for Questions 15 to 32 in Appendix A).

4. COLLECTION, RECORDING, AND REPORTING OF SAFETY INFORMATION AND PRODUCT COMPLAINTS

In the situation that an adverse event, product complaint and/or other safety finding is identified/reported, these will be reported to Amgen Safety consistent with standard practices.

4.1 Definition of Reportable Events

4.1.1 Adverse Events

An adverse event is any untoward medical occurrence in a subject/patient 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 or not 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), (eg, appearance of new symptoms)

It is Naxion's responsibility to evaluate whether an adverse event is related to an Amgen product prior to reporting the adverse event to Amgen.

4.1.2 Serious Adverse Events A serious adverse event is any adverse event as defined above that meets at least one of the following serious criteria:

- is fatal
- is life threatening (places the 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 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.

4.1.3 Other Safety Findings

Other Safety Findings (regardless of association with an adverse) 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).

4.1.4 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. Amgen will collect product complaints for BLINCYTO.

4.2 Safety Collection, Recording and Submission to Amgen Requirements

This study is collecting information from HCPs at a point in time (survey). All reportable events (adverse events, product complaints, and other safety findings) reported by the HCP or interviewer that occur in patients treated with BLINCYTO will be collected from HCP enrollment to final study contact during the pretest and main survey. The Vendor (Naxion) is responsible for ensuring that all reportable events (adverse events, product

complaints and other safety findings) they become aware of during the study period (including the pretest and main survey) are recorded in the appropriate study documentation. Additionally, these reportable events must be reported by the HCP or interviewer that occur in patients treated with BLINCYTO after study enrollment through the final study contact and are recorded in the HCP's study documentation. 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 subject's/patient's records and provided by the nurse or pharmacist..

All reportable events must be submitted as individual case safety reports to Amgen via the applicable Amgen Safety Reporting Form (paper or electronic form) within 1 business day of awareness (Table 1). Non-serious Adverse Events (AEs) must be reported in an expeditious manner, not to exceed 15 calendars days of Vendor (Naxion) awareness.

Reportable events that are suspected to be related to any medicinal product where there is no exposure to Blincyto must be reported to the local authority in line with the local country requirements.

See Appendix C. for the Amgen Safety Reporting Form, Appendix D. for Additional Safety Reporting Information regarding the adverse event grading scale used in this study, and Appendix E. for sample Pregnancy and Lactation Notification Forms.

The HCP may be asked to provide additional information for any event submitted, which may include a discharge summary or extracts from the medical record. Information provided about the event must be consistent with medical records and information recorded in the study documentation where safety data may also be recorded.

Table 1 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) • Product Complaints (serious and non-serious) • Other Safety Findings (serious and non-serious) • Pregnancy and/or Lactation Exposure	• Within 1 business day from when <<Investigator/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***

Collection of Pregnancy and Lactation Information

Female Subjects Who Become Pregnant

The Vendor (Naxion) will collect pregnancy information on any female subject/patient who becomes pregnant following exposure to BLINCYTO through 48 hours.

Information will be recorded on the Pregnancy Notification Form (see Appendix E). The form must be submitted to Amgen Safety within 1 business day of learning of when the Vendor first becomes aware the subject'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 will provide Investigator with a consent form and questionnaire to collect additional information. After obtaining the female subject's signed consent for release of pregnancy and infant health information, the Vendor will collect pregnancy and infant health information and complete the pregnancy questionnaire for any female subject who becomes pregnant following exposure to BLINCYTO through 48 hours of the BLINCYTO. This information will be forwarded to Amgen Safety. 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, regardless of fetal status (presence or absence of anomalies) or indication for procedure. While pregnancy itself is not considered to be an adverse event or serious adverse event, 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 (eg, female subject 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 Subjects with Partners who Become Pregnant [or Were Pregnant at the Time of Enrollment]

In the event a male subject fathers a child following exposure to BLINCYTO, and for an additional 48 hours after discontinuing BLINCYTO, 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: The 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 will provide Investigator with a consent form and questionnaire to collect additional information. The Vendor 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, the Vendor 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.

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 Global Patient Safety 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 subject who breastfeeds while taking BLINCYTO through 48 hours.

Information will be recorded on the Lactation Notification Form (see Appendix E) and submitted to Amgen Safety within 1 business day of when the Vendor first becomes aware of the lactation exposure. With the female subjects signed consent for release of mother and infant health information, the Vendor will collect mother and infant health information and complete the lactation questionnaire on any female subject who breastfeeds while taking BLINCYTO through 48 hours after discontinuing BLINCYTO.

4.2.1 Safety Reporting Requirement to Regulatory Bodies

Amgen will report safety data as required 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.

5. SUBJECT CONFIDENTIALITY

This study will comply with all applicable laws regarding subject privacy. No direct subject contact or collection of additional subject data will occur. Study results will be in tabular form and aggregate analyses that omits subject identification. Any reports will not include subject identifiers.

6. PUBLICATION INTENT

There is no intent to publish the results of these analyses.

7. COMPENSATION

Healthcare professionals will receive payment for their participation in the surveys.

This compensation will be based on a Fair Market Value (FMV) assessment (eg, time and effort).

Table 2: Survey Respondent Compensation

Healthcare provider	Compensation for online survey ($)
Pharmacist	$65
Registered nurse	$65

Appendix A. Questionnaire

Screening questions:

1. Have you personally prepared, dispensed, and/or administered BLINCYTO therapy to patients **outside of the clinical trial setting** in the last 12 months?

   (Select all that apply)

a. I have personally prepared BLINCYTO therapy outside the clinical trial setting	○	
b. I have personally dispensed BLINCYTO therapy outside the clinical trial setting	○	
c. I have personally administered BLINCYTO therapy outside the clinical trial setting	○	
d. None of the above	○	**TERMINATE**

PROGRAMMING:

1) **Ask all respondents**

1a. Approximately how many BLINCYTO infusions have you prepared, dispensed, or administered outside of the clinical trial setting in the last 12 months?

Number of infusions
_____

PROGRAMMING:

1) **Ask all respondents**

1b. How many patients have you prescribed, dispensed, prepared, and/or administered BLINCYTO therapy to **outside of the clinical trial setting** in the past 12 months?

___[#]___ patients who have received BLINCYTO

PROGRAMMING:

1) **Ask all respondents**
2) **Terminate if 0**

2. In what country is your workplace located? If you workplace in more than one country, please select the primary country in which you work.

   (Select one answer)

   [Drop down list of standard responses]

PROGRAMMING:

1) **Ask all respondents**
2) **If** workplace **is located in the U.S. and territories, proceed to Question 3; others TERMINATE**

3. In what state is your workplace located? If you work in more than one state, please select the state where you consider your primary workplace to be located.

   (Select one answer)

   [Drop down list of states]

PROGRAMMING:

1) **Ask all respondents**
2) **VT and ME responders: give option to continue but decline compensation**

4. Are you or any member of your immediate family (household) currently, or have been previously, employed in any capacity (eg, clinical investigator, consultant, researcher, etc.) by Amgen, Naxion, or the FDA?

   (Select one answer)

a. Yes	**TERMINATE**
b. No	

PROGRAMMING:

1) **Ask all respondents**

5. What type of healthcare provider are you?

(Select one answer)

a. Doctor (MD, DO)	○	**TERMINATE**
b. Physician Assistant/Nurse Practitioner	○	**TERMINATE**
c. Registered Nurse	○	
d. Hospital-Based Clinical Pharmacist	○	
e. Home Healthcare Pharmacist	○	
f. Director of Pharmacy	○	
g. Other (please specify:_____)	○	**TERMINATE**

PROGRAMMING:

1) **Ask all respondents**
2) **Question to be asked of all responders. Subsequent survey questions are to be asked based on the type of healthcare provider the responder identifies as. Responders selecting response option "c" to be asked specific questions for "nurses" and "all responders". Responders selecting response option "d", "e", or "f" to be asked specific questions for "pharmacists" and "all responders".**

You have qualified for our study, and we'd like to invite you to participate in our survey.

The survey will require about 15 minutes to complete. We ask for your undivided attention as you **complete the survey in one sitting**.

If you do not have 15 minutes right now, please click "stop," and return any time during the next 24 hours when you have an <u>uninterrupted</u> 15 minutes.

Again, please note that your responses will remain confidential, and will be reported only in the aggregate.

From time to time, surveys are conducted to evaluate the effectiveness of pharmaceutical company communications. The goal of this particular survey is to gauge healthcare providers' knowledge and current understanding of the labeling for BLINCYTO® (blinatumomab). Please note that this particular survey pertains to all indications in the labeling for BLINCYTO® (blinatumomab).

We want to emphasize that this is not a "test" of HCPs; rather, it is an attempt to assess pharmaceutical company educational activities.

Please read each question carefully and select the answer that you feel is most accurate, based only on your current knowledge and understanding of the educational materials you have reviewed. We want to inform you that you should not look-up online or other outside information while taking the survey. You should answer the questions based on your memory of the labeling and pharmaceutical company communications for BLINCYTO® (blinatumomab).

Note that your participation in this survey will NOT affect your ability to prescribe BLINCYTO® (blinatumomab).

For some of the survey questions, images are provided to give you a visual example of the document that we are referring to in the question. The writing in the image is intentionally blurred because we would like you to answer questions about the documents from memory.

PROGRAMMING:

1) **Ensure that question instructions are clearly visible to responders by using appropriate font size and bold font**

Survey questions:

Key Risk Message Questions

7. According to the BLINCYTO **Prescribing Information/Package Insert**, please answer if the following statements are true or false. If you are not sure, please select "not sure."

	BLINCYTO Preparation and Administration	**True**	**False**	**Not sure**
L1	Preparation and administration errors have occurred with BLINCYTO treatment. *NOTE: We are not asking whether you have personally seen these issues at your facility.*	○	○	○
L2	The recommended dose for BLINCYTO is based on patient body surface area (BSA) for patients who weigh less than 45 kg and is fixed (ie, not based on BSA) for patients who weigh greater than or equal to 45 kg.	○	○	○
L3	Medication errors such as underdosing and overdosing can occur if BLINCYTO is prepared or administered incorrectly. *NOTE: We are not asking whether you have personally seen these issues at your facility.*	○	○	○
L4	When preparing BLINCYTO, you should follow the preparation instructions provided in the Full Prescribing Information.	○	○	○
L5	The BLINCYTO infusion line or intravenous catheter should not be flushed when changing infusion bags because it can result in excess dosage.	○	○	○
L6	The use of BLINCYTO prepared with benzyl alcohol preservative is recommended for use in adult and pediatric patients across all weight ranges.	○	○	○

PROGRAMMING:

1) **Ask NURSE respondents**
2) **Example Prescribing Information visual aid to be displayed on screen**
3) **Display rows L4 and L6 ONLY if Q1 answer includes "a"**
4) **Randomize order of rows**

8. Based on the BLINCYTO **Prescribing Information/Package Insert,** please answer if the following statements are true or false. If you are not sure, please select "not sure."

	BLINCYTO Preparation and Administration	**True**	**False**	**Not sure**
L1	Preparation and administration errors have occurred with BLINCYTO treatment. *NOTE: We are not asking whether you have personally seen these issues at your facility.*	○	○	○
L2	The recommended dose for BLINCYTO is based on patient body surface area (BSA) for patients who weigh less than 45 kg, and is fixed (ie, not based on BSA) for patients who weigh greater than or equal to 45 kg.	○	○	○
L3	Medication errors such as underdosing and overdosing can occur if BLINCYTO is prepared or administered incorrectly. *NOTE: We are not asking whether you have personally seen these issues at your facility.*	○	○	○
L4	When preparing BLINCYTO, you should follow the preparation instructions provided in the Full Prescribing Information.	○	○	○
L5	Reconstitute BLINCYTO with IV Solution Stabilizer for Injection.	○	○	○

PROGRAMMING:

1) **Ask PHARMACIST respondents**
2) **Example Prescribing Information visual aid to be displayed on screen**
3) **Randomize order of rows**

10. The Full Prescribing Information/Package Insert contains the most complete instructions on BLINCYTO preparation (including admixing) and administration to minimize medication errors (including underdose and overdose).

(Select one answer)

a. True
b. False
c. I am not sure

PROGRAMMING:

1) **Ask all respondents**

11. Aseptic technique must be strictly observed when preparing or administering the BLINCYTO solution for infusion.

(Select one answer)

a. True
b. False
c. I am not sure

PROGRAMMING:

1) Ask all respondents

12a. Which of the following are true of your workplacesetting:

(Select all that apply)

a. Step-by-step instructions for preparing BLINCYTO are kept open for reference when BLINCYTO is prepared	□
b. Preparation instructions were developed by our facility based on prescribing information/package insert	□
c. Prescribing information/package insert is kept open for reference when BLINCYTO is prepared	□
d. Preparation of BLINCYTO is checked by two pharmacists	□
e. Proper dosing calculations for BLINCYTO are programmed into my facility's EMR	□

PROGRAMMING:

1) Ask all PHARMACIST respondents
2) Randomize order of rows

13a. Which of the following are true of your workplace setting:

(Select all that apply)

a. Tubing is primed by pharmacy staff before BLINCYTO is delivered for administration	□
b. Dose on bag is checked by two nurses before BLINCYTO is administered	□
c. Check-list for proper BLINCYTO administration is delivered, on paper, along with drug	□
d. Check-list for proper BLINCYTO administration is kept on floor with similar information about other oncolytic agents	□
e. Check-list for proper BLINCTYO administration is part of EMR	□

PROGRAMMING:

1) **Ask all NURSE respondents**
2) **Randomize order of rows**

HCPs awareness and utilization of BLINCYTO REMS materials

15. Prior to today, were you aware of the BLINCYTO REMS Website (www.blincytorems.com)?

(Select one answer)

a. Yes
b. No

PROGRAMMING:

1) **Ask all respondents**
2) **If "Yes," proceed to Question 16; if "No," skip to Question 18**

16. Prior to today, have you accessed the BLINCYTO REMS website?

(Select one answer)

a. Yes
b. No

PROGRAMMING:

1) **Ask if Q15 is "Yes"**
2) **If "No," proceed to Question 17a; if "Yes," skip to Question 17b**

17a. Why have you not accessed the BLINCYTO REMS website?

(Select all that apply)

a. I have all the product information I need (eg, Full Prescribing Information/Package Insert) without referring to the website
b. I prefer to obtain information from other sources (eg, Lexicomp, colleagues, sales representatives, societies)
c. I do not have time in my workplace to access websites

PROGRAMMING:

1) **Ask if Q16 is "No"**

17b. How familiar are you with the content of the BLINCYTO REMS website?

(Select one answer)

a. Very familiar
b. Somewhat familiar
c. Not very familiar

PROGRAMMING:

1) **Ask if Q16 is "Yes"**

18. From what sources have you learned about the risk of preparation and administration errors associated with the use of BLINCYTO? Select all that apply.

(Select one answer in each row)

Source	Yes	No
Full Prescribing Information/Package Insert	□	□
BLINCYTO REMS Fact Sheet	□	□
BLINCYTO REMS Website	□	□
BLINCYTO promotional materials	□	□
BLINCYTO product website	□	□
Sales representatives from the manufacturer	□	□
Medical science liaisons from the manufacturer	□	□
Other healthcare professionals/colleagues	□	□
BLINCYTO REMS communications (email, letters)	□	□
Press Releases	□	□
Professional Societies (eg, Oncology Nursing Society [ONS], American Society of Clinical Oncology [ASCO])	□	□
Drug and prescribing information databases (eg, Physician's Desk Reference, Epocrates, Micromedex, Lexi-comp, others)	□	□
Other (please specify:_____)		

PROGRAMMING:

1) **Ask all respondents**
2) **Randomize rows**
3) **Free text field for the "Other" response option is a force response**

19. Prior to today, were you aware of the **BLINCYTO REMS Letter or email for Healthcare Providers?**

(Select one answer)

a. Yes
b. No
c. I am not sure

PROGRAMMING:

1) **Ask all respondents**
2) **Example BLINCYTO REMS Letter or Email for Healthcare Providers visual aid to be displayed on screen**
3) **If "Yes," proceed to Question 20; if "No" or "I am not sure," skip to Question 22**

20. Did you receive and/or do you have access to the **BLINCYTO REMS Letter or email for Healthcare Providers?**

(Select one answer)

a. Yes
b. No
c. I am not sure

PROGRAMMING:

1) **Ask if Q19 is "Yes"**
2) **Example BLINCYTO REMS Letter or Email for Healthcare Providers visual aid to be displayed on screen**
3) **If "Yes," proceed to Question 21; if "No" or "I am not sure," skip to Question 22**

21. Which of the following best describes how much of the **BLINCYTO REMS Letter or email for Healthcare Providers** you had an opportunity to read?

(Select one answer)

a. All of it
b. Most of it
c. Some of it
d. None of it

PROGRAMMING:

1) **Ask if Q20 is "Yes"**

2) Example BLINCYTO REMS Letter or Email for Healthcare Providers visual aid to be displayed on screen

22. Prior to today, were you aware of the BLINCYTO REMS materials through information disseminated by **Professional Societies**?

(Select one answer)

a. Yes
b. No
c. I am not sure

PROGRAMMING:

1) **Ask all**
2) **Example BLINCYTO REMS materials disseminated by Professional Societies visual aid to be provided on screen**
3) **If "Yes," proceed to Question 23; if "No" or "I am not sure," skip to Question 25**

23. Did you receive and/or do you have access to the **BLINCYTO REMS Letter or email for Professional Societies**?

(Select one answer)

a. Yes
b. No
c. I am not sure

PROGRAMMING:

1) **Ask if Question 22 is "Yes"**
2) **Example BLINCYTO REMS materials disseminated by Professional Societies visual aid to be provided on screen**
3) **If "Yes," proceed to Question 24; if "No" or "I am not sure," skip to Question 25 if PHARMACIST respondent OR skip to Question 28 if RN respondent**

24. Which of the following best describes how much of the **BLINCYTO REMS Letter or email for Professional Societies** you had an opportunity to read?

(Select one answer)

a. All of it
b. Most of it
c. Some of it
d. None of it

PROGRAMMING:
1) **Ask if Question 23 is "Yes"**
2) **Example BLINCYTO REMS materials disseminated by Professional Societies visual aid to be provided on screen**

25. Prior to today, were you aware of the **BLINCYTO REMS Letter or email for Hospital and Home Healthcare Pharmacists**?

(Select one answer)

a. Yes
b. No
c. I am not sure

PROGRAMMING:
1) **Ask all PHARMACIST respondents**
2) **Example BLINCYTO REMS Letter or email for Hospital and Home Healthcare Pharmacists visual aid to be provided on screen**
3) **If "Yes," proceed to Question 26; if "No" or "I am not sure," skip to Question 28**

26. Did you receive and/or do you have access to the **BLINCYTO REMS Letter or email for Hospital and Home Healthcare Pharmacists**?

(Select one answer)

a. Yes
b. No
c. I am not sure

PROGRAMMING:
1) **Ask if Q25 is "Yes"**
2) **Example BLINCYTO REMS Letter or email for Hospital and Home Healthcare Pharmacists visual aid to be provided on screen**
3) **If "Yes," proceed to Question 27; if "No" or "I am not sure," skip to Question 28**

27. Which of the following best describes how much of the **BLINCYTO REMS Letter or email for Hospital and Home Healthcare Pharmacists** you had an opportunity to read?

(Select one answer)

a. All of it
b. Most of it
c. Some of it
d. None of it

PROGRAMMING:

1) **Ask if Q26 is "Yes"**
2) **Example BLINCYTO REMS Letter or email for Hospital and Home Healthcare Pharmacists visual aid to be provided on screen**

28. Prior to today, were you aware of the **BLINCYTO REMS Fact Sheet**?

(Select one answer)

a. Yes
b. No
c. I am not sure

PROGRAMMING:

1) **Ask all respondents**
2) **Example BLINCYTO REMS Fact Sheet visual aid to be provided on screen**
3) **If "Yes," proceed to Question 29; if "No" or "I am not sure," skip to Question 31**

29. Did you receive and/or do you have access to the **BLINCYTO REMS Fact Sheet**?

(Select one answer)

a. Yes
b. No
c. I am not sure

PROGRAMMING:

1) **Ask if Question 28 is "Yes"**
2) **Example BLINCYTO REMS Fact Sheet visual aid to be provided on screen**
3) **If "Yes," proceed to Question 30; if "No" or "I am not sure," skip to Question 31**

30. Which of the following best describes how much of the **BLINCYTO REMS Fact Sheet** you had an opportunity to read?

(Select one answer)

a. All of it
b. Most of it
c. Some of it
d. None of it

PROGRAMMING:

1) **Ask if Question 29 is "Yes"**
2) **Example BLINCYTO REMS Fact Sheet visual aid to be provided on screen**

31. Did you receive and/or do you have access to the Full Prescribing Information for BLINCYTO?

(Select one answer)

a. Yes
b. No
c. I am not sure

PROGRAMMING:

3) **Ask all respondents**
4) **Example Full Prescribing Information for BLINCYTO visual aid to be provided on screen**
5) **If "Yes," proceed to Question 32; if "No" or "I am not sure," skip to Question 33**

32. Have you read the Full Prescribing Information for BLINCYTO?

(Select one answer)

a. Yes
b. No

PROGRAMMING:

1) **Ask if Question 31 is "Yes"**
2) **Example Full Prescribing Information for BLINCYTO visual aid to be provided on screen**

Demographic Questions

35. How long have you worked as a healthcare provider (starting with the completion of your postgraduate training, if applicable)?

(Select one answer)

a. Less than 1 year
b. 1 to 5 years
c. 6 to 10 years
d. More than 10 years

PROGRAMMING:

1) **Ask all respondents**

Appendix B. Recruitment Material (Sample Letter)

FIRST_NAME LAST_NAME
ADDRESS 1
ADDRESS 2
CITY, STATE ZIP

Dear FIRST_NAME LAST_NAME,

The US Food and Drug Administration requires periodic surveys on awareness of the risks of Blincyto®.

NAXION is conducting a nationwide survey concerning Blincyto® usage among physicians and healthcare professionals, and we would greatly appreciate your participation. We strongly encourage you to participate, so that all representative types of hospitals will be included in this research.

You will be asked a few brief questions and if you qualify, you will be eligible to participate. The survey should take approximately 15 minutes to complete. In return for your time and participation, we are offering a **$60.00 honorarium**.
For your convenience, this survey is being conducted via the internet and must be completed in one sitting. Please be assured that -- as in *all* of our research – your responses will be held in the strictest confidence. All data from the project will be tabulated and reported in the aggregate only. To participate, please direct your web browser to:

https://www.naxionsurvey.com/launch/QX29113.aspx

User ID: USERID
Password: PASSWORD

We will close the survey website when we reach the required number of interviews, so everyone benefits if you act sooner rather than later. If you have any questions or concerns, please call PPD at PPD or email at PPD. If you would prefer to take this survey via telephone, please call PPD.

We very much appreciate your help. Thanks for considering to participate in this important survey.

Sincerely,
PPD

NAXION
PPD Ph.D.
Chief Executive Officer

Appendix C. Amgen Safety Reporting Form

Project ID: 20210065	**A**	**Observational Research Safety Reporting Form**	**Date of Reporter Awareness:** **Date Reported to Amgen:**
	Amgen Safety Fax: 1-888-814-8653 or	email: svc-ags-in-us@amgen.com	

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)			**5. Reporter ID**		
Name	*Phone*	*Fax*	*Name or ID*	*Phone*	*Fax*
Address			*Address*		
City	*State/Province*		*City*	*State/Province*	
Postal Code	*Country*		*Postal Code*	*Country*	

6. HCP Contact Details (if other than reporter)			**7. Patient**			
Name			*Initials (optional)*	*Sex* ☐ F ☐ M	*Age (at time of event)*	*Was consent obtained to follow-up with HCP?* ☐ Yes ☐ No
Country						
Address						
City	*State/Province*	*Postal Code*	*Weight* ☐ lbs ☐ kg	*Height* ☐ in ☐ cm	*Race*	*Is patient also reporter?* ☐ Yes ☐ No
Phone	*Fax*					

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 **HCP ONLY**

Finding (List main event first; one event per line)	**Onset Date**	**Resolved Date** *(If patient died, list date of death)* ***Cause of Death:***	**Hospitalization** Hospitalized? ☐ Yes ☐ No Prolonged Hospitalization? ☐ Yes ☐ No	**Serious Criteria** **01** Fatal **02** Immediately life-threatening **03** Required/Prolonged hospitalization **04** Persistent or significant	**Action Taken** 1=none 2=dose reduced 3=dose increased	**Outcome** **01** Recovered/ Resolved **02** Recovering/ Resolving	**Severity** 1=mild 2=moderate 3=severe	**Relationship to Product/Device** Is there a reasonable possibility that

		(provide autopsy report)	**Admitting dx** _____ **Date Admitted** **Date Discharged**		disability /incapacity **05** Congenital anomaly/birth defect **06** Other significant medical hazard **07** Non serious	4=drug withdrawn 5=drug rechallenge (state outcome)	**03** Not recovered/not resolved **04** Recovered/ resolved with sequelae **05** Fatal **06** Unknown		this event may have been caused by the Product/Device ?	
	day month year	day month year	day month year	day month year					Product	Device
									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 D. Additional Safety Reporting Information

Adverse Event Severity Scoring System

Grade	Amgen Standard Adverse Event Severity Scoring System
1	MILD: Aware of sign or symptom, but easily tolerated
2	MODERATE: Discomfort enough to cause interference with usual activity
3	SEVERE: Incapacitating with inability to work or do usual activity

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: Amgen Protocol Number 20210065

☐ **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
BLINCYTO (blinatumomab)				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:** _____

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: **Amgen Protocol Number: 20210065**

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
BLINCYTO (blinatumomab)				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:** _____

Approval Signatures

Document Name: Protocol-Published Original Blinatumomab 20210065

Document Description:

Document Number: CLIN-000270195

Approval Date: 09 Jun 2021

Type of Study Protocol: Original

Protocol Amendment No.:

Document Approvals	
Reason for Signing: Functional Area	Name: Gerhard Zugmaier Date of Signature: 09-Jun-2021 13:03:43 GMT+0000