

1. ABSTRACT

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Contact:

PPD [REDACTED], MD
Amgen Inc.
One Amgen Center Drive
Thousand Oaks, CA 91320-1799

PPD [REDACTED]

Title:

Healthcare Providers' Awareness of the Risks and Safe Use Conditions Associated with BLINCYTO®: a REMS Assessment Survey

- **Keywords**

survey, risk awareness, blinatumomab, cytokine release syndrome (CRS), neurologic toxicity, preparation and administration errors

- **Rationale and Background**

BLINCYTO® (blinatumomab) is indicated for the treatment of relapsed or refractory B-cell precursor acute lymphoblastic leukemia (ALL) and B-cell precursor ALL in first or second complete remission with minimal residual disease (MRD) in the United States (US). A Risk Evaluation and Mitigation Strategy (REMS) with goals to reduce the risks of CRS, neurologic toxicities, and preparation and administration errors, were identified at the time of approval of the biological license application. The REMS communication plan consists of REMS letters for healthcare providers (HCPs), hospital and home healthcare pharmacists, and professional societies; a REMS Fact Sheet for HCPs; dissemination of REMS information at scientific meetings; and a REMS program website. The rationale for this survey of HCPs is to assess HCP awareness and knowledge of risks highlighted in the REMS communication plan.

- **Research Question and Objectives**

This study was conducted to determine the level of awareness on the risks and safe use conditions associated with BLINCYTO therapy and certain aspects of the BLINCYTO REMS Program among HCPs who have used BLINCYTO. Specifically, the objectives were to survey prescribers who have prescribed BLINCYTO, pharmacists who have prepared BLINCYTO, and nurses who have administered BLINCYTO to:

- 1) Evaluate HCPs' awareness and understanding of the risks of CRS, neurologic toxicity, and preparation and administration errors associated with BLINCYTO use.
- 2) Evaluate HCPs' awareness and understanding of the BLINCYTO indication.
- 3) Evaluate HCPs' awareness and use of the BLINCYTO Prescribing Information and the REMS materials.

- **Study Design**

Cross-sectional surveys were conducted in HCPs who have prescribed, dispensed, prepared, and/or administered BLINCYTO in the US in the past 12 months outside the clinical trial setting. This cross-sectional survey is being conducted 5 years after the approval of BLINCYTO in the US, and learnings from this survey may be incorporated into the 7-year assessment. Previous surveys were conducted at 18 months and 3 years after initial approval.

- **Setting**

This report represents the 5-year assessment. Surveys were administered through NAXION Research Consulting. A survey pretest was conducted, in which respondents participated in both a pretest and a retest session, separated by approximately 5 days. The objectives of the pretest/retest were to (1) pilot the REMS assessment survey with qualified respondents to ensure clarity and comprehensibility and (2) compare respondents' pretest and retest responses to conduct an analysis of the survey's reliability. Following final approval of the survey, the BLINCYTO REMS HCP knowledge survey was fielded from 25 September 2019 to 14 October 2019. Initial invitation was conducted via email and other communication channels. Healthcare providers also were invited by direct mail.

- **Subjects and Study Size, Including Dropouts**

Subjects included HCPs, defined as prescribers (medical doctor [MD], doctor of osteopathic medicine [DO], physician assistant [PA], nurse practitioner [NP]), nurses, and hospital and/or home healthcare pharmacists who have prescribed, dispensed, prepared and/or administered BLINCYTO therapy to patients outside of the clinical trial setting in the past 12 months. A total of 100 prescribers (65 MDs/DOs; 35 NPs/PAs), 102 nurses, and 102 hospital and/or home healthcare pharmacists participated in the survey.

- **Variables and Data Sources**

Respondents were recruited from a list supplied by Amgen, which included both institutions known to use BLINCYTO, and names of potential prescribers affiliated with those institutions. That list was matched to the Reckner Associates web-panel to facilitate recruiting of hematologist/oncologists, NP/PAs, registered nurses, and pharmacists. Additional off-list pharmacists and nurses were recruited from professional panels maintained by the recruiting agency. To qualify, HCPs were required to report having prescribed, dispensed, prepared, and/or administered BLINCYTO in the US within the past 12 months outside the clinical trial setting. To be considered to have knowledge of a given key risk domain, an individual participant must correctly answer $\geq 75\%$ of the items within that risk domain.

- **Results**

- Total prescribers (82%; including MD/DO [82%] and NP/PA [83%]) met the threshold for HCP awareness and/or understanding of the risk of CRS with use of BLINCYTO. Although nurses and pharmacists did not meet the 80% threshold, a high proportion of nurses and pharmacists (75% and 79%, respectively) were considered to have knowledge of the risk of CRS and the 95% CI contained 80% for both HCP types. The prescribers understood the symptoms of CRS and the importance of hospitalization in mitigating the risk of CRS.
- Pharmacists (84%) met the threshold for awareness and/or understanding of the risk of neurological toxicity associated with the use of BLINCYTO. Total prescribers (78%) and nurses (74%) failed to achieve the 80% knowledge rate threshold. When considering the subsets of total prescribers, MDs/DOs met the 80% threshold with 82% knowledge rate. The MDs/DOs understood the major signs and symptoms (encephalopathy, convulsions, speech disorders, confusion, and cranial nerve disorders) of neurological toxicities associated with use of BLINCYTO.
- The threshold for awareness and/or understanding of the risks of preparation and administration errors was met by NPs/PAs (80%). Total prescribers (74%), nurses (74%), and pharmacists (70%) had composite knowledge rates below the 80%

threshold. Greater than 90% of nurses and pharmacists reported that they should follow the preparation instructions provided in the Full Prescribing Information when preparing BLINCYTO.

- Most respondents understood the approved indication for BLINCYTO (84% of total prescribers, 81% of nurses, and 73% of pharmacists).
- Prescribing Information is the primary tool HCPs use to obtain safety information (72% total prescribers, 83% nurses, and 92% pharmacists). Awareness and use of the BLINCYTO REMS materials were relatively low.