From: Amgen Inc.
To: <Professional Society email>
Subject: WARNING: Serious Risks Associated with BLINCYTO™

BLINCYTO™ (blinatumomab) REMS

FDA-REQUIRED REMS SAFETY INFORMATION

Risk of:
- Cytokine Release Syndrome (CRS), which may be life-threatening or fatal
- Neurological Toxicities, which may be severe, life threatening or fatal
- Preparation and Administration Errors

December 2014

IMPORTANT SAFETY NOTICE

Dear <name>:

The FDA has required this safety notice as part of the BLINCYTO™ REMS (Risk Evaluation and Mitigation Strategy) to be distributed to the <insert Professional Society Name>. Amgen requests that you distribute the information to your members, informing them about the serious risks of BLINCYTO.

BOXED WARNING: Cytokine Release Syndrome
- Serious adverse events that may be associated with CRS included pyrexia, headache, nausea, asthenia, hypotension, increased alanine aminotransferase, increased aspartate aminotransferase, and increased total bilirubin.
- The highest elevation of cytokines was observed in the first 2 days following start of BLINCYTO infusion.

BOXED WARNING: Neurological Toxicities
- In patients receiving BLINCYTO in clinical trials, neurological toxicities have occurred in approximately 50% of patients.
- The median time to onset of any neurological toxicity was 7 days.
- Grade 3 or higher (severe, life-threatening or fatal) neurological toxicities following initiation of BLINCYTO administration occurred in approximately 15% of patients and included encephalopathy, convulsions, speech disorders, disturbances in consciousness, confusion and disorientation, and coordination and balance disorders. The majority of events resolved following interruption of BLINCYTO, but some resulted in treatment discontinuation.

Monitor patients closely for signs and symptoms of these events and interrupt or discontinue dosing of BLINCYTO.

Reference ID: 3667235
OTHER SERIOUS RISKS: Preparation and Administration Errors

- It is very important that the instruction for preparation (including admixing) and administration are strictly followed to minimize medication errors (including underdose and overdose).

Please see the non-promotional REMS Fact Sheet, reviewed by the FDA available at www.blincytoREMS.com and the full Prescribing Information for more detailed safety information. Additional copies of the Fact Sheet and other important information are available at: www.blincytoREMS.com.

BLINCYTO is a bispecific CD19-directed CD3 T-cell engager indicated for the treatment of Philadelphia chromosome-negative relapsed or refractory B-cell precursor acute lymphoblastic leukemia (ALL).

Sincerely,

Isma Benattia, MD, MBE
Vice President, Global Patient Safety

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