APPENDIX

DIVERGENT POSITION DATED 15 NOVEMBER 2018

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BLINCYTO EMEA/H/C/II/11

The undersigned members of the CHMP did not agree with the CHMP's positive opinion recommending the approval of the variation to the terms of the marketing authorisation for BLINCYTO.

Reasons for divergent opinion were the following:

- The appropriateness of MRD response as a validated surrogate endpoint of direct clinical benefit is not established. Moreover, Although no optimum cut-off has been established, 10^{-3} is not considered stringent enough.

- Per guideline, RFS, OS and TTHR should be calculated from the time of the bone marrow aspiration when CR or CRh* was detected for the first time, until the date of documented event;

- Uncertainties in long term outcome of patients after HSCT, with median RFS and OS were shorter in transplanted subjects than in non-transplanted subjects after Blincyto;

As a conclusion, the benefit-risk balance of Blincyto in the treatment of adults with minimal residual disease (MRD) positive B-cell precursor acute lymphoblastic leukaemia (ALL) has not been established.

CHMP Member expressing a divergent position:

Alexandre Moreau
Daniela Melchiorri