APPENDIX

DIVERGENT POSITION DATED 13 November 2025

Official address Domenico Scarlattilaan 6 ● 1083 HS Amsterdam ● The Netherlands
Address for visits and deliveries Refer to www.ema.europa.eu/how-to-find-us
Send us a question Go to www.ema.europa.eu/contact **Telephone** +31 (0)88 781 6000 An agency of the European Union

DIVERGENT POSITION DATED 13 November 2025

Teizeild EMEA/H/C/005496/0000

The undersigned member of the CHMP did not agree with the CHMP's positive opinion recommending the granting of the marketing authorisation of Teizeild indicated for:

Teizeild is indicated to delay the onset of stage 3 type 1 diabetes (T1D) in adult and paediatric patients 8 years of age and older with stage 2 T1D.

The reasons for the divergent opinion were the following:

We do not consider the efficacy and safety of Teizeild established based on study TN-10. This is based on the size of the trial (n = 76) and the high number of early events in the placebo group (inconsistent with the expected natural history). In case of an application based on one pivotal trial, in the context of first in class treatment, we would expect trial data to be robust and compelling. Therefore, we would expect a replication of study findings, considering the small sample size, baseline imbalances, and the non-negligible risks associated with the treatment. While we welcome the hope that is conferred to (potential) patients with T1D, this is insufficient for significantly lowering the bar for MAA.

Additionally, we consider that the risk of diabetic ketoacidosis (DKA) should be addressed in a warning, beyond glucose monitoring. Although in all cases well-known precipitating factors are described and time-to-onset argues against direct causality, for a disease modifying treatment long-term effects on safety are a reasonable possibility. DKA should be labelled as it is potentially fatal, considering the uncertainties in the safety profile based on the limited pivotal study size, and that there were 21 DKA cases in the total teplizumab safety population (2.1%; i.e., including the population studied to claim a delay in the progression of Stage 3 T1D), but only 1 case in the control group (0.3%) during a mean follow-up of 1.8 years.

CHMP Member(s) expressing a divergent opinion:

Peter Mol