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Dear Meindert

Prasugrel with percutaneous coronary intervention for treating acute coronary syndrome (review of TA182) [ID648]: Daiichi Sankyo UK Ltd / Eli Lilly and Company Ltd response to Assessment Report

Thank you for the opportunity to respond to the Assessment Report consultation for prasugrel with percutaneous coronary intervention for treating acute coronary syndrome.

We agree with the findings in the Assessment Report.

Please see table 1 below which addresses some minor points of factual accuracy, none of which will have a significant impact on the overall conclusion of the report.

In addition, please see our comment on the executable model in the format requested (table 2).

If you have any questions, please do not hesitate to contact me.

Yours sincerely,

[redacted] **– Lilly UK**

Table 1 General comments on the Assessment Report

Section	Page number	Comment
2.5 Summary of risks and benefits	p.10	Currently reads: "This review focussed on the health outcomes of the subgroup of patients discussed in TA182, and for whom the full dose of prasugrel is licensed, namely the core clinical cohort i.e. patients without a history of transient ischaemic attach (TIA) or stroke, those with body weight **less** than 60kg or those aged **over** 75 years." The core clinical cohort discussed in TA182 includes patients without a history of transient ischaemic attack (TIA) or stroke, those with body weight **more** than 60kg or those aged **under** 75 years.
2.6 Summary of the Assessment Group's cost-effectiveness results	p. 11	Regarding the point: "(iii) the AG considered it appropriate to develop an economic model using the most reliable clinical evidence available and therefore preferred to use 3-year clinical data from the CAPRIE trial instead of 15 month data from the TRITON-TIMI 38 trial". We felt that this point implied that the TRITON-TIMI 38 trial data was not used in the AG's economic model, whereas the AG's model accepted the manufacturer's statistical model for the initial phase (up to 12 months) but used the CAPRIE trial data as a source for extrapolating long-term vascular events.
Table 5 Summary of trial characteristics	p.29	Currently reads under Inclusion criteria (main): "Moderate- to high-risk UA or NSTEMI patients: ischaemic symptoms of 10 minutes or longer within 72 hours **of** randomisation" This specific inclusion criterion would be better described as: ischemic symptoms lasting 10 minutes or longer and occurring within 72 hours **before**[1] randomisation.
5.2.2 Assessment of clinical effectiveness	p.30	One of the summary information points reads: "outcomes for people older than 70 years or weighing less than 60kg". This should this be **75** years instead of **70** years.
Table 10 Safety endpoints in the core clinical cohort	p.35	P-value for "TIMI major or minor bleeding - 30 days to 15 months" should be **0.097**[2] (not 0.97)

Section	Page number	Comment
Table 27 Annual transition matrix between health states due to events occurring during the year	p.79	In the column 'MI, 2 prior events, ND', row 'Nonfatal MI', we believe that there is a typo, and this should read MI (3+) ND rather than MI (2) ND.
6.3.8 Resource use estimation – Unit cost estimation	p.83	Currently reads: "Unit costs used in the AG's report for **TA182** have been uplifted…." We believe that this should read: "Unit costs used in the AG's report for **TA210** have been uplifted…."
8.1.1 Clinical effectiveness	p. 111	Currently reads: "This review focussed on the health outcomes of the subgroup of patients discussed in TA182,21 and for whom the full dose of prasugrel is licensed, namely the core clinical cohort i.e. patients without a history of TIA or stroke, those with body weight **less** than 60kg or those aged **over** 75 years." The core clinical cohort discussed in TA182 includes patients without a history of transient ischaemic attach (TIA) or stroke, those with body weight **more** than 60kg or those aged **under** 75 years.

1. Wiviott SD, Braunwald E, McCabe CH, Montalescot G, Ruzyllo W, Gottlieb S*, et al.* Prasugrel versus clopidogrel in patients with acute coronary syndromes. New Engl J Med. 2007; 357:2001-15.
2. Wiviott SD, Desai N, Murphy SA, Musumeci G, Ragosta M, Antman EM*, et al.* Efficacy and safety of intensive antiplatelet therapy with prasugrel from TRITON-TIMI 38 in a core clinical cohort defined by worldwide regulatory agencies. AmJC. 2011; 108:905-11.

Table 2: Comment on the executable model

Issue 1 Updating the PSA results

Description of problem	Description of proposed amendment	Result of amended model or expected impact on the result (if applicable)
PSA runs were carried out according to the supplied instructions. We noted that the results in the red PSA tab weren't being updated with each run and we saw that with shorter time horizons, the ICER decreased, which was unexpected.		While we had difficulties with the PSA, our testing in the deterministic mode and one way sensitivity analysis indicated that the model was robust. As the ranges of ICERs presented in one way sensitivity analyses were tight for all parameters, it is unlikely that an amendment to the PSA would impact the outcome or any conclusions about uncertainty.