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AstraZeneca

24th April 2014

Dear Nicole,

Thank you for the opportunity to submit comments for the Appraisal Consultation Document (ACD) of the appraisal: Prasugrel with percutaneous coronary intervention for treating acute coronary syndrome (review of TA182) [ID648].

AstraZeneca would like to comment on the draft recommendation (1.2) that prasugrel, in combination with aspirin, be recommended as an option for patients with **NSTEMI or UA with diabetes** (of appropriate age and weight).

- The Appraisal Committee's consideration of the evidence for clinical-effectiveness contemplated all patients with diabetes (4.3.8), rather than considering patients in line with the defined subgroups for the appraisal (STEMI with diabetes, NSTEMI or UA with diabetes). AstraZeneca recognises that the TRITON-TIMI 38 trial showed additional benefit for patients with diabetes but would argue that the findings for the NSTEMI or UA with diabetes cohort (in particular) are not generalisable to routine clinical practice in England and Wales. The recently updated SmPC for prasugrel states "In NSTEMI/UA patients, where coronary angiography is performed within 48 hours after admission, the loading dose should only be given at the time of PCI." (1). Data from the most recent UK BCIS Audit (2) shows that, in UK real world practice, the median delay from first hospital arrival to PCI in NSTEMI patients is 2.6 days (for those who are admitted directly to a PCI centre) or 4.3 days for those who undergo an inter-hospital transfer. Therefore prasugrel use is appropriate in only a minority of UK NSTEMI patients undergoing PCI, and any recommendation from the appraisal should be reflective of this point. In NSTEMI patients in the TRITON study (3, 4), the loading of prasugrel anti-platelet therapy occurred only after the coronary anatomy was known to be suitable for PCI. Therefore the timing of prasugrel loading (as extrapolated from the TRITON trial) is not

representative of the current treatment pathways for many patients presenting with NSTEMI/UA and potentially delays the initiation of dual anti-platelet therapy where an earlier diagnosis of NSTEMI/UA has already been made.

- In accordance with the above, the findings of the TRITON-based cost-effectiveness analysis should not be considered generalisable to patients in England and Wales with NSTEMI or UA with diabetes, given real world treatment practice.

If you require any further clarification, please let me know.

Best regards,

AstraZeneca UK Ltd

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References

1) Summary of Product Characteristics Efient 5 and 10mg tablets. Available from http://www.medicines.org.uk/emc/medicine/21504/SPC
2) BCIS National Audit of Percutaneous Coronary Interventional Procedures Public Reports Available at http://www.bcis.org.uk/pages/page_box_contents.asp?pageid=697&navcatid=11
3) Wiviott SD *et al.* Evaluation of prasugrel compared with clopidogrel in patients with acute coronary syndromes: design and rationale for the TRial to assess Improvement in Therapeutic Outcomes by optimizing platelet InhibitioN with prasugrel Thrombolysis In Myocardial Infarction 38 (TRITON-TIMI 38). Am Heart J. 2006; 152:627-35.
4) Wiviott SD *et al.* Prasugrel versus clopidogrel in patients with acute coronary syndromes. New Engl J Med. 2007; 357:2001-15.