National Institute for Health and Care Excellence
Centre for Health Technology Evaluation

Canagliflozin, dapagliflozin and empagliflozin monotherapy for treating type 2 diabetes [ID756]

AstraZeneca Response

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AstraZeneca thank NICE for the opportunity to respond to the appraisal consultation document (ACD).

- We believe the ACD is a fair and robust reflection of the available evidence, the assessment group (AG) report and the Committee meeting, and support NICE's recommendation for the positioning of Sodium-glucose co-transporter-2 (SGLT2s) in monotherapy: *where a dipeptidyl peptidase-4 (DPP-4) inhibitor would otherwise be prescribed, and a sulfonylurea or pioglitazone is not appropriate*.

- Given the evidence base in monotherapy and challenges discussed during the process, AstraZeneca also agree with the Committee that the clinical and cost evidence submitted did not support any differences between SGLT2s.

- We wish to highlight that cost-effectiveness results for SGLT2s reported in the ACD (company results pages 20-22, and AG results pages 30-32) include the anomalous study Kaku *et. al.* 2014 which had different baseline characteristics to other included studies. Sensitivity analyses demonstrated this study had a significant negative effect on the results for dapagliflozin; we therefore request NICE clarify that the ICERs presented include this study and therefore may not be truly reflective of the cost-effectiveness of dapagliflozin.

Table of specific comments or responses to the ACD

Pg	AG comment in report	AstraZeneca comment
6	3.6: …an eGFR of less than 60 ml/min/1.73 m2) because its efficacy depends on renal function.	Reduced efficacy at lower eGFR is common for the class. Please alter the text to: "*because the efficacy of SGLT2s depends on renal function*", or include text on eGFR restriction for each flozin
19 … 25	The costs in the AstraZeneca model were higher than those assumed by the AG; the AG was not sure why there was a discrepancy. … the company had used the same source for the costs of complications of diabetes (blindness and amputation; UKPDS84) as the AG, but that the AG had derived lower values.	Please note data from the UKPDS84 (cost year 2012) were used but were inflated to 2014 using the hospital & Community health services (HCHS) index.
25	inpatient and outpatient costs appeared to be completely omitted if the patient did not experience a complication. It stated that if this was the case, it would be a serious omission....	AstraZeneca note that the difference in life years between the treatment arm and the control arm is <u>minor</u> meaning that patients in the treatment arm live at most 0.004 years longer; the impact therefore seems negligible.
36	However, it heard from the AG and AstraZeneca (the company for dapagliflozin) that the results for dapagliflozin were sensitive to the inclusion of a trial by Kaku et al. (2014), and when this was removed, results were similar to the other SGLT-2 inhibitors	AstraZeneca agree with this statement. We note that the reason for the removal of this trial was due to the differences in baseline characteristics versus all other SGLT2 studies including: 1. Lower baseline HbA1c; 7.5% vs. 7.9%-8.3% 2. Lower eGFR; 67.1 mL/min1.73m^2 vs. all studies >86 mL/min1.73m^2

38	BMI-2 scenario (in which weight gains were maintained and weight losses rebounded to natural history after 1 year) best reflected the treatment effect on weight loss.	AstraZeneca agree this is the most appropriate scenario listed; however we note that data have demonstrated SGLT2s in monotherapy maintain weight over two years (Ferrannini *et al. 2010*). As such, rebounding after two years would be considered better aligned to clinical data.

Abbreviations table

ACD	Appraisal Consultation Document
AG	Assessment Group
BMI	Body Mass Index
DPP4	Dipeptidyl peptidase-4
eGFR	estimated Glomerular Filtration Rate
HbA1c	Glycated haemoglobin (A1c)
ICER	Incremental Cost-Effectiveness Ratio
MTA	Multiple Technology Appraisal
NMA	Network Meta-Analysis
SGLT2	Sodium-glucose co-transporter-2
SU	Sulfonylurea