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Appraisals Service

NHS

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National Institute for Health and Clinical Excellence

[redacted]

RE: Dapagliflozin in combination therapy for the treatment of type 2 diabetes

On behalf of the Commissioning Support Appraisals Service (CSAS), Solutions for Public Health, I would like to submit our comments on the appraisal consultation document for dapagliflozin in combination therapy for the treatment of type 2 diabetes. We are in agreement with the recommendation in the ACD not to recommend dapagliflozin due to considerable uncertainties regarding the clinical and cost effectiveness of this drug in real life clinical practice.

- **Combination therapy dapagliflozin (as either a metformin or insulin add-on) appears to offer weight loss benefits and to have similar effects as comparators in terms of glycaemic control.** However, the committee concluded that there are significant uncertainties regarding the selection of outcomes and the validity of the network meta-analyses used to assess the effectiveness of dapagliflozin versus UK relevant comparators.
- **Evidence on the effects of the licensed dose and treatment combinations for dapagliflozin comes from five clinical trials and three network meta-analysis.** The clinical trials included three metformin 'add-on' and two insulin 'add-on' studies, in which dual therapy was used. Effectiveness data for dapagliflozin as an add-on to sulfonylurea was not provided, despite the availability of such evidence. Evidence is less robust for triple therapy (dapagliflozin + metformin + suphonylurea) or other combinations with two oral drugs, as clinical trials were older or had not been completed for the relevant combinations.
- **There is significant uncertainty regarding the cost effectiveness of dapagliflozin**. There are concerns over the credibility and reproducibility of the economic model, e.g. the QALY gains were related to weight change rather than diabetic complications or other adverse events associated with any of the treatments. Removing the impact of BMI on utility increased the ICER of dapagliflozin plus insulin compared to DPP-4 inhibitors plus insulin from £19,094 per QALY gained to £105,511 per QALY gained.
- **NICE have requested further information from the manufacturer regarding their modelling.** Additional information has been requested regarding the network meta-analysis and cost-effective models submitted by the manufacturer as the Decision Support Unit (DSU) at NICE could not replicate the model.
- **The safety profile of dapagliflozin differs from other oral diabetic drugs.** The most common adverse events were urinary tract and genital infections, which were more common in women than men. The committee concluded that the manner in which these adverse events were accounted for in the economic model required consideration and adjustment.
- **The annual cost of dapagliflozin per patient is estimated at £476.92.** This is based on a patient receiving a daily dose of 10mg dapagliflozin.

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- **In England and Wales the incremental cost of adding dapagliflozin could total £10.8 million in the fifth year after implementation.** This cost assumes about 2.5 million patients being eligible for dapagliflozin and 4.3% of them receiving it in year five.