

Electronic Supplementary Material 1

**COST-EFFECTIVENESS OF CANAGLIFLOZIN ADDED TO STANDARD OF CARE FOR TREATING
DIABETIC KIDNEY DISEASE (DKD) IN PATIENTS WITH TYPE 2 DIABETES MELLITUS (T2DM) IN
ENGLAND:
ESTIMATES USING THE CREDEM-DKD MODEL**

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Search Strategy for Targeted Literature Review for UK Health Related Quality of Life Data

In order to identify additional, potentially suitable HRQoL studies and utility studies, targeted searches of the following databases were performed in March 2020:

- Google Scholar
- MEDLINE®, searched via the PubMed platform
- The School of Health and Related Research Health Utilities Database (SchARRHUD)
- EQ-5D database
- Cost Effectiveness Analysis (CEA) database

The SchARRHUD, EQ-5D and CEA databases were searched for “diabetic kidney disease”, “DKD”, “chronic kidney disease” or “CKD”.

Three prior NICE appraisals in renal indications were also reviewed for relevant HRQoL and utility data:

- TA481 (immunosuppressive therapy for kidney transplant in adults)
- TA482 (immunosuppressive therapy for kidney transplant in children and young people)
- TA358 (tolvaptan for treating autosomal dominant polycystic kidney disease [ADPKD])

ESM Table 1: Treatment Effects for Canagliflozin 100mg + SoC vs. SoC Alone

	Canagliflozin 100mg	Source
	HR	
Start of Dialysis	0.74	Perkovic et al.[11]
Doubling of serum creatinine	0.60	Perkovic et al.[11]
Non-fatal MI	0.81	Mahaffey et al.[19]
Non-fatal stroke	0.80	Mahaffey et al.[19]
HHF	0.61	Perkovic et al.[11]
ACM	0.83	Perkovic et al.[11]
CV Cause of Death	0.85*	Estimated
	Mean	
<u>eGFR Progression (absolute change)</u>		
Initial effect (vs. placebo)	-3.17	Perkovic et al.[11]
Slope effect per year (vs. placebo)	2.74	Perkovic et al.[11]
<u>UACR Progression (proportional change)</u>		
Initial effect	-0.31	Perkovic et al.[11]

*Odds Ratio

eGFR estimated glomerular filtration rate, HHF hospitalization for heart failure, MI myocardial infarction, SoC standard of care, UACR urine albumin:creatinine ratio

ESM Table 2: Standard of Care Costs, by Treatment Arm

Drug Class	Examples of agents available / in common usage in UK	Cheapest and/or most commonly used agent	Pack Price	Pack size (tablets unless specified)	Days treatment	Treatment Cost	Treatments per year	Annual cost	% patients using the drug with SoC Alone*	% patients using the drug with Canagliflozin 100mg*	Notes Costs Sourced from the BNF on 15/07/2020
Anti-thrombotics (including aspirin)	Multiple classes and agents	Aspirin	£1.38	28	28	£1.38	13.04	£18.00	58.3%	60.9%	Drug Tariff (Part VIIIA Category M) price 75 mg OD dose
Beta-blocker	atenolol; bisoprolol; metoprolol; propranolol	Bisoprolol	£0.99	28	28	£0.99	13.04	£12.91	40.3%	40.1%	Drug Tariff (Part VIIIA Category M) price 10 mg OD dose
Calcium channel blocker	Amlodipine; diltiazem; felodipine; lacidipine; nifedipine; nimodipine; verapamil	Amlodipine	£0.84	28	28	£0.84	13.04	£10.96	49.1%	47.8%	Drug Tariff (Part VIIIA Category M) price 5 mg OD dose
Diuretic loop	Bumetanide; Furosemide; Torsemide	Furosemide	£0.80	28	28	£0.80	13.04	£10.44	21.7%	21.7%	Drug Tariff (Part VIIIA Category M) price 40 mg OD dose
Diuretic non-loop	Bendroflumethiazide; Chlortalidone; Hydrochlorothiazide; Indapamide	Bendroflumethiazide	£0.76	28	28	£0.76	13.04	£9.91	29.4%	28.3%	Drug Tariff (Part VIIIA Category M) price 2.5 mg OD dose
MRA	Eplerenone; spironolactone	Spironolactone	£1.24	28	28	£1.24	13.04	£16.18	0.6%	0.5%	Drug Tariff (Part VIIIA Category M) price 25 mg OD dose
Statins	Atorvastatin; rosuvastatin; simvastatin	Atorvastatin	£0.89	28	28	£0.89	13.04	£11.61	68.1%	69.9%	Drug Tariff (Part VIIIA Category M) price 10 mg OD dose
Biguanides	metformin	Metformin hydrochloride	£2.30	84	28	£2.30	13.04	£30.00	57.7%	58.0%	Metformin 500mg tablets (Crescent Pharma Ltd) NHS indicative price 500 mg TDS dose
DPP-4 inhibitors	Alogliptin; linagliptin; saxagliptin; sitagliptin; vildagliptin	Alogliptin	£26.60	28	28	£26.60	13.04	£346.99	17.0%	17.2%	Vipidia NHS indicative price 25 mg OD dose
GLP-1 agonist	Dulaglutide; Exenatide; Liraglutide; Lixisenatide; Semaglutide	Lixisenatide	£57.93	600 ug / 6 ml	30	£57.93	12.18	£705.30	4.3%	4.0%	Lyxumia NHS indicative price 20 ug / 0.2ml OD dose Despite being an injection, no administration costs are included as it is self-administered by the patient at home Abasaglar 100units/ml solution for injection 3ml cartridges (Eli Lilly and Company Ltd) NHS indicative price Insulin is a very complex class with more than 70 formulations available in UK and dosing that is tailored to each individual patient Typically, patients with T2DM would begin insulin treatment with a basal (long acting) insulin, of which abasaglar is the cheapest. Days treatment assumes 20 units per day, which is a reasonably conservative dose
Insulin	See notes		£35.28	1500 units / 15 ml	75	£35.28	4.87	£171.81	65.1%	66.0%	Drug Tariff (Part VIIIA Category M) price 40mg OD dose
Sulfonylurea	Gliclazide; glimepiride; glipizide	Gliclazide	£1.51	28	28	£1.51	13.04	£19.70	29.9%	27.8%	Drug Tariff (Part VIIIA Category M) price 15 mg OD dose
Thiazolidinediones	pioglitazone	pioglitazone	£1.41	28	28	£1.41	13.04	£18.39	3.0%	3.2%	
Total cost per year									SoC Alone £259.18	SoC in addition to Canagliflozin 100mg £259.40	Total costs calculated as % using multiplied with annual cost

*CREDENCE trial data, baseline use for each arm

ESM Table 3: Estimated Event Rates (per 100 Patient-Years), by Treatment Arm

	Estimated Event Rates (per 100 Patient-Years)		
	Canagliflozin + SoC	SoC	HR
<u>Mortality</u>	4.06	5.41	0.75
Due to CVD	2.93	4.14	0.71
Due to other causes	1.12	1.26	0.89
<u>Kidney</u>			
Stage 4	4.72	14.94	0.32
Stage 5, pre-RRT	0.35	5.77	0.06
Dialysis	1.99	3.60	0.55
Transplant	0.13	0.91	0.15
<u>CV</u>			
HHF	1.86	2.78	0.67
Nonfatal MI	1.17	1.38	0.85
Nonfatal Stroke	0.99	1.16	0.86
<u>Adverse Events*</u>			
UTI	0.30	--	--
GMI Males	0.43	--	--
GMI Females	0.22	--	--
DKA	0.18	--	--
LEA	0.10	--	--

*Incremental vs. SoC for canagliflozin + SoC

CVD cardiovascular disease, DKA diabetic ketoacidosis, GMI genital mycotic infections, HHF hospitalization for heart failure, MI myocardial infarction, LEA lower extremity amputation SoC standard of care, RRT renal replacement therapy, UTI urinary tract infection

ESM Figure 1: Mean eGFR Evolution, by Treatment Arm

