Budget Impact Analysis of Empagliflozin in Type-2 Diabetes Patients with High Cardiovascular Risk in South Korea Based on EMPA-REG OUTCOME® Trial – HIRA (HEALTH INSURANCE REVIEW & ASSESSMENT SERVICE) - NPS (NATIONAL PATIENTS SAMPLE) Database

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Introduction

Type 2 diabetes mellitus (T2DM) is the most common metabolic disorder in the world. In South Korea, 14.4% of adults over the age 30 are suffering from this disease [1]. There is well established evidence that diabetes is associated with an increased risk of cardiovascular events. Diabetes patients have a two- to three-fold greater risk of heart failure compared to people without diabetes and cardiovascular disease (CVD) is the leading cause of death in people with diabetes across the world [2].

Sodium-glucose co-transport 2 (SGLT-2) inhibitors are a class of drugs indicated for the treatment of T2DM. By blocking glucose transport via SGLT-2, these drugs reduce glucose reabsorption in the kidney. Korean treatment guidelines recommend that SGLT-2 inhibitors are given priority for T2DM patients with atherosclerotic cardiovascular diseases [3].

In the class of SGLT-2 inhibitors, empagliflozin (Jardiance®) has been reimbursed in South Korea since May 2016. Through the EMPA-REG OUTCOME® trial, empagliflozin demonstrated significantly reduced rates of the primary composite cardiovascular outcome and death from any cause on top of standard of care in T2DM patients at high risk of cardiovascular events [4].

Following this finding, this study aims to assess the financial impact of adding empagliflozin to standard of care for T2DM patients at high cardiovascular risk in South Korea from a Korean health care perspective.

Methods

A Microsoft Excel-based budget impact model was used to compare direct medical costs arising from treatment with and without empagliflozin on top of standard of care (SoC) over a 3 year period. The model considered T2DM patients with high CV risk based upon EMPA-REG OUTCOME ®. The model calculated the number of high-risk patients with T2DM adding empagliflozin in South Korea. This was done by multiplying the number of T2DM adults patients in South Korea by 1) the proportion of T2DM patients with increased CV risk, 2) proportion of SGLT2-i patients assumed, and 3) proportion of empagliflozin patients in SGLT2-I patients (Table 1). All adult (age ≥20 years) T2DM patients were collected from HIRA Healthcare Big-data hub [5]. Empagliflozin patients share in SGLT2-I patients was estimated based on UBIST (UBIquitous System Technology) market trend data for the 3-year time horizon.

Table 1: Population input of the model

	Year 1	Year 2	Year 3
Number of T2DM adults* patients [5]	2,661,786	2,873,051	3,060,506
Proportion of T2DM patients with increased CV risk [6]	32.2%	32.2%	32.2%
Proportion of SGLT2-i patients assumed	9.0%	11.8%	14.8%
Proportion of empagliflozin patients in SGLT2-I patients	27.0%	36.0%	40.0%
Total population with empagliflozin	**20,712**	**39,133**	**58,222**

* Age ≥20 years

The annual drug acquisition costs were calculated as a weighted-average of the annual cost of all drugs within the class, based on data from the 2017 HIRA weighted-average price [7] and WHO Defined Daily Doses of each substance. We assumed no annual increase in costs. The model tracked the use of antiglycemic medication by class under SoC and the scenario with empagliflozin. The fraction of patients using each drug was extracted from the Asian patient subpopulation of EMPA-REG OUTCOME® trial [Boehringer Ingelheim data on file]. For insulin, mean dosage was assessed by EMPA-REG OUTCOME® trial data. Table 2 shows the annual drug acquisition costs, utilization per drug class and mean insulin dosage under SoC and with empagliflozin.

Table 2: Annual drug acquisition costs and Drug utilization

	Annual drug acquisition costs, KRW	Drug utilization, proportions of patients	
		Standard of Care (SoC)	SoC + Empagliflozin
Empagliflozin	275,210	0.0%	100.0%
Metformin	120,988	6.0%	2.9%
Sulphonylurea	60,985	6.4%	4.0%
Glitazone	402,778	6.0%	2.5%
Alpha-glucosidase inhibitor	202,088	5.1%	4.4%
Glinide	308,151	2.2%	0.9%
DPP-4 inhibitor	352,391	9.3%	7.3%
GLP-1 agonist	1,450,621	0.4%	0.1%
Other antidiabetics	120,988	0.0%	0.0%
Insulin (per I.U.)	36.1	10.7%	5.5%
Mean insulin dosage	-	69.1 IU	60.0 IU

The model encompasses the EMPA-REG OUTCOME® clinical endpoints. Results of pooled empagliflozin vs. placebo from the Asian patient sub-population data in the clinical trial report were used to characterize mean clinical events rates inputs for the model [Boehringer Ingelheim data on file]. As the clinical event rates were an average of three years, event rates in the model were assumed to be the same for each year. Clinical event management costs were derived from the 2017 HIRA National Patients Sample (HIRA-NPS) data (Table 3). Annual direct medical cost and number of treated patients related with each clinical events were extracted from HIRA-NPS dataset. Mean direct medical cost per each clinical event was calculated by dividing total cost by number of treated patients and used as inputs for the annual cost for each clinical event.

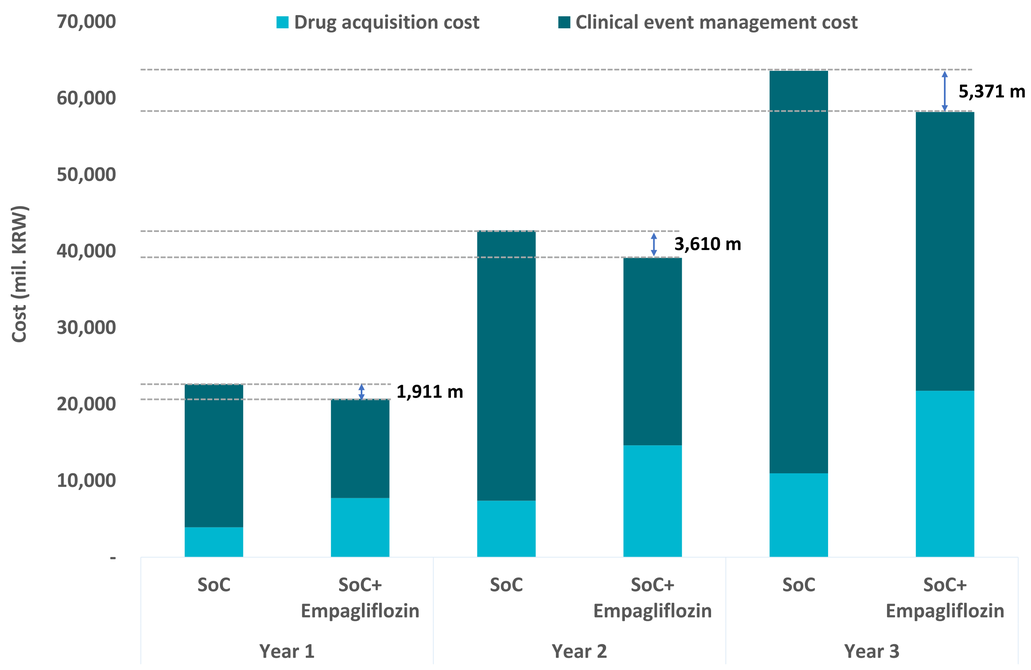
Table 3: Mean Clinical Event Rates (Per Person-Years) from the EMPA-REG OUTCOME® trial and related costs.

Event	Annual cost (KRW)	Mean clinical events rates (per person-years)	
		Standard of Care (SoC)	SoC + Empagliflozin
Non-fatal myocardial infarction	3,779,471	0.015	0.010
Non-fatal stroke	3,046,973	0.013	0.012
Unstable angina	7,439,022	0.010	0.009
Heart failure	7,695,334	0.011	0.007
Transient ischemic attack	1,084,865	0.002	0.001
Revascularization	11,298,287	0.020	0.020
CV death	19,548,629	0.016	0.007
Development of macroalbuminuria	1,300,023	0.065	0.042
Renal injury	472,362	0.006	0.003
Renal failure	8,396,995	0.003	0.002

Results

Results focused on total cost per year for both arms of the model, stratified by drug acquisition cost and clinical event management cost (Figure 1). The model predicted a cumulative budget saving of 10,892 mil KRW over three years in favor of empagliflozin. The addition of empagliflozin to SoC reduced direct medical costs with 1,911 million KRW in year 1 (Y1), 3,610 million KRW in Y2 and 5,371 million KRW in Y3. There was 31% reduction in event management cost every year. Major management cost reduction was driven by improved CV mortality of patients with empagliflozin (56% reduction in Asian population). The additional drug acquisition costs for empagliflozin were more than offset by the reductions in the costs of managing clinical events.

Figure 1: Annual cost of treating patients with SoC of T2DM with or without empagliflozin



Conclusion

The increase in drug acquisition costs by the addition of empagliflozin on top of SoC would be more than offset by the reduction in clinical event management costs. Consequently, the use of empagliflozin in T2DM patients at high CV risk would reduce overall direct medical costs in South Korea. These budget savings were driven by the reduction in clinical events.

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Reference

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* This data is based on the Health Insurance Review & Assessment Service National Patient Sample (HIRA-NPS-2017-0009) and the study results are not related to the Health Insurance Review & Assessment Service and Minister of Health and Welfare.