

## **Clinical Study Synopsis for Public Disclosure**

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The synopsis - which is part of the clinical study report - had been prepared in accordance with best practice and applicable legal and regulatory requirements at the time of study completion.

The synopsis may include approved and non-approved uses, doses, formulations, treatment regimens and/or age groups; it has not necessarily been submitted to regulatory authorities.

A synopsis is not intended to provide a comprehensive analysis of all data currently available regarding a particular drug. More current information regarding a drug is available in the approved labeling information which may vary from country to country..

Additional information on this study and the drug concerned may be provided upon request based on **Boehringer Ingelheim's Policy on Transparency and Publication of Clinical Study Data**.

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## 1. ABSTRACT

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| <b>Name of finished medicinal product:</b><br>Jardiance® (Empagliflozin) |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                              |                               |
| <b>Name of active ingredient:</b><br>Empagliflozin                       |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                              |                               |
| <b>Report date:</b><br>14-SEP-2021                                       | <b>Study number:</b><br>BI 1245.149                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | <b>Version/Revision: 0.3</b> | <b>Version/Revision date:</b> |
| <b>Title of study:</b>                                                   | Post-authorization safety study in patients with type 2 diabetes mellitus to assess the incidence of ketoacidosis, severe complications of urinary tract infection, volume depletion, and dehydration among patients treated with Empagliflozin or DPP-4 inhibitors in Saudi Arabia.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                              |                               |
| <b>Keywords:</b>                                                         | Dehydration, ketoacidosis, urinary tract infections (UTIs), post-authorization safety, volume depletion                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                              |                               |
| <b>Rationale and background:</b>                                         | Saudi Food and Drug Authority (SFDA) had requested a non-interventional study (NIS) to provide the supplementary data to monitor the safety of Jardiance® (Empagliflozin) in the country, including the Ramadan period.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                              |                               |
| <b>Research question and objectives:</b>                                 | <p>This NIS was conducted to collect new data with the following objectives:</p> <p><u>Primary objective</u></p> <p>To estimate the incidence of:</p> <ul style="list-style-type: none"><li>• Ketoacidosis</li><li>• Severe UTIs</li><li>• Volume depletion</li><li>• Dehydration</li></ul> <p>in type 2 diabetes mellitus (T2DM) patients initiating Empagliflozin compared with the incidence in T2DM patients initiating Dipeptidyl peptidase-4 (DPP-4) inhibitors.</p> <p><u>Secondary objective</u></p> <p>To estimate the risk of each primary outcome with respect to the following definition of exposure:</p> <ul style="list-style-type: none"><li>• the Ramadan period<sup>1</sup></li></ul> <p><sup>1</sup>Ramdan period is defined as the first day of Ramadan to 29<sup>th</sup> day of Ramadan based on the Islamic Hijri calendar:</p> <ul style="list-style-type: none"><li>○ Ramadan month 2019: 05 May to 04 Jun 2019 (± 1 to 2 days)</li><li>○ Ramadan month 2020: 23 Apr to 23 May 2020 (±1 to 2 days)</li></ul> <p>Both primary and secondary outcomes were followed up for 12 months from the Index date (defined as the date on which each identified new user received the index prescription for Empagliflozin or DPP-4 inhibitor).</p> |                              |                               |

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| <b>Study design:</b>                                                     | <p>This study was a NIS with new data collection from T2DM patients in Saudi Arabia. The study used a “new users” design and compared new users of Empagliflozin to new users of DPP-4 inhibitors in T2DM patients.</p> <p>A total of 1502 patients with T2DM of age ≥ 18 years who agreed to initiate Empagliflozin or DPP-4 inhibitors treatment during the study period according to the local label and at the discretion of investigator and had not used other sodium glucose co-transporter-2 (SGLT2) or DPP-4 inhibitors during the previous 12 months were enrolled into the study after signing the informed consent form. Patients with known hypersensitivity to Empagliflozin or DPP-4 inhibitors or any of their excipients or patients for whom Empagliflozin or DPP-4 inhibitors was contraindicated according to SFDA label or patients who were prescribed fixed dose combination of SGLT2 inhibitors with DPP-4 inhibitors were excluded from the study. Patients were managed according to the local practice guidelines. The choice of treatment was solely at the discretion of the investigator. Empagliflozin and the comparator DPP-4 inhibitor were administered according to the approved labels in Saudi Arabia. Since this is was a NIS, neither of the drugs were supplied by the sponsor.</p> <p>All the patients were followed up for 12 months after the index date or until any of the following conditions were met: death, specific exclusion criteria, the last continuous treatment of the index drug (Empagliflozin or DPP-4 inhibitor) (also defined as index period, i.e., from index date to end of treatment) plus a defined grace period (30 days after the end of the last prescription’s days’ supply in main analyses), or new treatment episode started with any of the other index drugs. Patients who discontinued an index drug and subsequently initiated another index drug were not allowed to re-enter the study.</p> <p>All patients were to attend the following 4 study visits:</p> <ul style="list-style-type: none"><li>• Visit 1/Baseline visit</li><li>• Visit 2/Week 16 ± 2 weeks</li><li>• Visit 3/Week 32 ± 2 weeks</li><li>• Visit 4/End of study/Week 52</li></ul> <p>The successive surveys were to be conducted over the follow-up visits (Visits 2 to 4) and the investigator recorded the information from surveys into the electronic case report forms. No interim analyses were conducted during the study.</p> <p>Propensity scores based on information prior to the index date was to be used to account for potential confounding.</p> |                              |                               |
| <b>Setting:</b>                                                          | <p>A total of 25 sites participated in this study. Of these, 18 sites enrolled patients where 1 site was terminated after collecting the baseline data for 8 patients. The remaining 7 sites did not screen or enroll any patients.</p> <p>The same inclusion criteria were applied to enroll patients in either of the study groups and included:</p> <ul style="list-style-type: none"><li>• Patients had signed on the informed consent form.</li></ul>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                              |                               |

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|                                                                          | <ul style="list-style-type: none"><li>Patients aged 18 years or above and diagnosed with T2DM in Saudi Arabia and initiated Empagliflozin or DPP-4 inhibitors treatment during the study period.</li><li>Patients who had not used other SGLT2 or DPP-4 inhibitors during the previous 12 months.</li></ul> <p>The treating physician/investigators were mainly general practitioners and/or specialists, including endocrinologists, diabetologists and internists.</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |                              |                               |
| <b>Patients and study size, including dropouts:</b>                      | <p>Planned study size: 1500 patients (750 patients each in Empagliflozin and DPP-4 inhibitors treatment group).</p> <p>Actual study size: 1502 patients (751 patients each in Empagliflozin and DPP-4 inhibitors treatment group).</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |                              |                               |
| <b>Variables and data sources:</b>                                       | <p><u>Primary variable/outcome</u></p> <ul style="list-style-type: none"><li>Incidence and occurrence of ketoacidosis<sup>1</sup>, severe UTIs<sup>2</sup>, volume depletion<sup>3</sup>, and dehydration<sup>4</sup></li></ul> <p><sup>1</sup>Ketoacidosis is defined as a serious complication of diabetes characterized by high level of ketones in the body due to lack of insulin and low food intake.</p> <p><sup>2</sup>Severe UTIs is defined as pyelonephritis or urosepsis.</p> <p><sup>3</sup>Volume depletion is defined as the reduction in the extracellular fluids.</p> <p><sup>4</sup>Dehydration is defined as the loss of total body water that leads to hypertonicity.</p> <p><u>Secondary variable/outcome</u></p> <ul style="list-style-type: none"><li>Incidence and occurrence of ketoacidosis, severe UTI, volume depletion and dehydration in the Ramadan periods</li></ul> <p><u>Data source</u></p> <p>Data on the period preceding the index date were collected at the time of first survey. The sites were primary care clinics, hospital clinics and other outpatient clinics. Data from hospitals were documented when needed, especially if there were cases of admission for one of the study outcomes. Discharge data were documented by the investigator when needed.</p> |                              |                               |
| <b>Results:</b>                                                          | <p>A total of 1502 patients were enrolled into the study where 751 patients each were on Empagliflozin and DPP-4 inhibitors. Majority (93.7%) of the patients completed 1 year on treatment and their treatment was also ongoing at the end of study. A total of 86 (5.7%) patients had early termination where 74 (4.9%) patients were lost to follow-up, 6 (0.4%) patients switched their therapy, 5 (0.3%) patients terminated the study due to other reasons, and 1 (0.1%) patient was terminated due to an adverse event (AE).</p> <p>The mean ± SD age of the enrolled patients was 52.5 ± 10.5 years (Empagliflozin group: 52.1 ± 10.3 years; DPP-4 inhibitors group: 52.9 ± 10.7 years). Majority (87.1%) of the patients were aged between 30 and 64 years. Males predominated</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                              |                               |

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| <p>females across both groups (Empagliflozin group: 63.6% versus 36.4%; DPP-4 inhibitors: 64.8% versus 35.2%, respectively). The demographic characteristics were well balanced between the 2 treatment groups.</p> <p>More than 90% of the patients in either treatment groups were not on any prior insulin intake or insulin use at baseline. Only 76 (5.1%) and 65 (4.3%) patients reported the prior and current use of insulin, respectively. The mean HbA1c and FBG was comparable between the 2 treatment groups (HbA1c: Empagliflozin group: 9.2 ± 1.6%; DPP-4 inhibitors: 8.8 ± 1.5%; and FBG: Empagliflozin group: 181.1 ± 58.3 mg/dL; DPP-4 inhibitors: 176.3 ± 59.9 mg/dL)</p> <p>A total of 602 (40.1%) patients received the study treatment with metformin and 900 (59.9%) patients did not receive the study treatment with metformin. More than 25% of the patients in both treatment groups were on dual (Empagliflozin: 45.7%; DPP-4 inhibitors: 52.3%) and triple (Empagliflozin: 30.8%; DPP-4 inhibitors: 27.8%) GLDs in addition to the study treatment.</p> <p>Primary Outcomes: The primary outcome of the study was to estimate the incidence and times to first occurrence of diabetic ketoacidosis (DKA), severe UTI, volume depletion, and dehydration between the 2 treatment groups.</p> <p><b>Diabetic ketoacidosis:</b> The incidence of DKA was comparable between the 2 treatment groups (Empagliflozin group: 1 [0.1%] patient; DPP-4 inhibitors: 1 [0.1%] patient) in index and follow-up periods. The time to first occurrence was 365 days in Empagliflozin group and 344 days in DPP-4 inhibitor group. The treatment-adjusted incidence rate ratio of DKA in Empagliflozin/DPP-4 inhibitors groups was 0.981 in the index period and 0.980 in the follow-up period.</p> <p><b>Severe UTI:</b> There was no severe UTI in either of the 2 treatment groups.</p> <p><b>Volume depletion:</b> The incidence of volume depletion was comparable between the 2 treatment groups (Empagliflozin group: 6 [0.8%] patient; DPP-4 inhibitors: 7 [0.9%] patient) in index period and follow-up period. The time to first occurrence of volume depletion was 169 ± 131 days in Empagliflozin group and 256.1 ± 110.5 days in DPP-4 inhibitors group in index and follow-up periods. The treatment-adjusted incidence rate ratio of volume depletion in Empagliflozin/DPP-4 inhibitors groups was 0.841 in the index group and 0.840 in the follow-up period.</p> <p><b>Dehydration:</b> There were no incidence of or dehydration in either of the 2 treatment groups.</p> <p><b>Secondary outcome:</b> There was no incidence of DKA, severe UTI, volume depletion or dehydration in either of the 2 treatment groups during the Ramadan period.</p> <p><b>Safety:</b> Overall, a total of 121 (8.1%) patients reported AEs during the index period (Empagliflozin group: 58 [7.7%]; DPP-4 inhibitors group: 63 [8.4%]). Of these, 3 (0.2%) patients reported severe AEs (Empagliflozin group: 2 [0.3%]; DPP-4 inhibitors group: 1 [0.1%]). A total of 8 (0.5%) patients reported 10 serious AEs (SAEs) in the index period where 6 (0.8%) patients in Empagliflozin group</p> |                                     |                              |                               |

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|                                                                          |                                     | reported 7 SAEs and 2 (0.3%) patients in DPP-4 inhibitors group reported 3 SAEs.<br><br>A total of 4 (0.3%) patients experienced 5 AEs of special interest (AESIs) in the index period during the study where 2 (0.3%) patients in each treatment group reported 2 AESIs (DKA and UTI) in Empagliflozin group and 3 AESIs (DKA, acute kidney injury and end stage renal disease) in DPP-4 inhibitors group.<br><br>During Ramadan, 4 (0.3%) patients reported AEs (Empagliflozin group: 3 [0.4%]; DPP-4 inhibitors group: 1 [0.1%]). None of the patients had severe AEs, SAEs or AESIs during Ramadan period.<br><br>There was a comparable decline in glycated hemoglobin (HbA1c) from baseline to Visits 2, 3 and 4 in both treatment groups. There were no major changes in vital signs across different visits. There were no deaths reported in either of the treatment groups during the study.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                               |
| <b>Discussion:</b>                                                       |                                     | The present NIS was conducted to further monitor the safety of Jardiance® (Empagliflozin) in Saudi Arabia, including Ramadan period as per request of the SFDA.<br><br>Saudi Arabia has the second highest rate of diabetes in the Middle East and ranks seventh in the world. In Saudi Arabia, Empagliflozin (a SGLT2 inhibitor) is indicated for treatment of T2DM as a monotherapy or add on combination therapy with other glucose lowering drugs (GLDs), including insulin when these agents do not provide adequate glycemic control. However, Empagliflozin is associated with some common adverse reactions like vaginal moniliasis, vulvovaginitis, balanitis, and other genital infection, thirst, pruritus (generalized), rash, increased urination, and serum lipids increased, UTI (including urosepsis and pyelonephritis), and hypoglycemia (Empagliflozin prescribing information).<br><br>In the study, the “new users” design has been used where new users of Empagliflozin were compared to new users of DPP-4 inhibitors in T2DM patients. The DPP-4 inhibitors were considered as the comparator group as it is one of the new groups of hypoglycemic agents to treat patients with T2DM and had similar indications to Empagliflozin. Patients with T2DM aged at least 18 years who had agreed to initiate Empagliflozin or DPP-4 inhibitors treatment during the study period (according to the local label and at the discretion of investigator) and had not used other SGLT2 and DPP-4 inhibitors during the previous 12 months were enrolled into the study after signing the informed consent form. The study sample size of 1502 patients with T2DM (751 patients each group receiving Empagliflozin or DPP-4 inhibitors) was based on the SFDA requirements.<br><br><b>Limitations:</b><br><br>This study has few limitations: <ul style="list-style-type: none"><li>• The study findings were restricted to patients in Saudi Arabia and hence the findings were not generalizable to all patients with T2DM.</li></ul> |                               |

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| <b>Name of finished medicinal product:</b><br>Jardiance® (Empagliflozin) |                                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                               |
| <b>Name of active ingredient:</b><br>Empagliflozin                       |                                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                               |
| <b>Report date:</b><br>14-SEP-2021                                       | <b>Study number:</b><br>BI 1245.149 | <b>Version/Revision: 0.3</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | <b>Version/Revision date:</b> |
|                                                                          |                                     | <ul style="list-style-type: none"><li>• The incidences of DKA, severe UTI, volume depletion and dehydration were not analyzed across different age groups, males versus females, duration of disease, and varying doses of study treatment.</li><li>• Considering the anticipated incidences of outcomes, the sample size in this study seems limited.</li><li>• No laboratory data was collected for subsequent visits, which further limited the assessment of the impact of study treatment on laboratory parameters.</li></ul> <p><b><u>Interpretation:</u></b></p> <p><b>Diabetic Ketoacidosis:</b> DKA, a serious complication associated with diabetes mellitus where ketone bodies are increased in the body has been reported with the use of SGLT2 inhibitors. However, DKA is a rare side-effect of Empagliflozin (Empagliflozin prescribing information). In our study, 1 (0.1%) patient each developed DKA after 1-year treatment with Empagliflozin and DPP-4 inhibitors. Both cases of DKA were considered as not related to the study treatment and resolved. The similar results were reported in the Cardiovascular outcome trial for Empagliflozin (EMPA-REG™), where the incidence of DKA in patients on Empagliflozin was reported as 0.1%. In a number of cases, the presentation of the condition was atypical with only moderate blood glucose values below 14 mmol/L (250 mg/dL).</p> <p>There was no incidence of DKA during Ramadan period.</p> <p><b>Volume Depletion and Dehydration:</b> Empagliflozin and other SGLT2 inhibitors are known to cause transient increase in sodium excretion and urine output, which leads to reduced extravascular volume. The placebo-controlled and post-marketing data reported overall frequency of volume depletion (including blood pressure [ambulatory] decreased, dehydration, hypovolemia, orthostatic hypotension and syncope) was similar in patients treated with Empagliflozin (Empagliflozin 10 mg: 0.6% and 25 mg: 0.4% and placebo (0.3%). The frequency of volume depletion events was increased in patients 75 years and older treated with empagliflozin 10 mg (2.3%) or empagliflozin 25 mg (4.3%) compared to placebo (2.1%). This mechanism may result in symptomatic hypotension, particularly in vulnerable patient groups such as elderly, those with renal impairment, and individuals on diuretics (Empagliflozin prescribing information). In our study, &lt;1% of the study population on Empagliflozin or DPP-4 inhibitors reported the incidence of volume depletion. The reason for low occurrence of volume depletion cases in our study may be explained by exclusion of patients for whom Empagliflozin or DPP-4 inhibitors was contraindicated according to SFDA approved label, including patients with renal or hepatic impairment or elderly population. There was no incidence of volume depletion during Ramadan.</p> <p>No cases of dehydration (loss of total body water) were observed during this study.</p> <p><b>Urinary tract infection:</b> The use of SGLT2 inhibitors such as Empagliflozin results in increased urinary glucose concentration, which is a potential exacerbating factor to high incidence of UTI with the use of Empagliflozin. The</p> |                               |

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| <b>Name of company:</b><br>Boehringer Ingelheim                          |                                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                               |
| <b>Name of finished medicinal product:</b><br>Jardiance® (Empagliflozin) |                                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                               |
| <b>Name of active ingredient:</b><br>Empagliflozin                       |                                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                               |
| <b>Report date:</b><br>14-SEP-2021                                       | <b>Study number:</b><br>BI 1245.149 | <b>Version/Revision: 0.3</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | <b>Version/Revision date:</b> |
|                                                                          |                                     | <p>placebo-controlled and post-marketing data reported UTI as AE was similar in patients treated with Empagliflozin 25 mg and placebo (7.0% and 7.2%) and higher in Empagliflozin 10 mg (8.8%). In our study, only 1 (0.1%) event of UTI was reported in Empagliflozin group, which was nonserious, not related to study treatment, and was resolved.</p> <p>There have been post-marketing reports of serious UTIs including urosepsis and pyelonephritis, requiring hospitalization in patients receiving SGLT2 inhibitors (Empagliflozin). In our study, no serious UTI was reported.</p> <p><b>Safety:</b> A total of 121 (8.1%) patients reported 157 AEs in the index period where 58 (7.7%) patients in the Empagliflozin group reported 70 AEs and 63 (8.4%) patients in the DPP-4 inhibitors group reported 87 AEs. Eight Empagliflozin-related AEs (3 events of hypoglycemia, 2 events each of thirst and fungal infection, and 1 event of genital infection fungal) were reported by 8 (1.1%) patients in the study. None of the AEs were present in &gt; 0.5% of the patients.</p> <p><b>Hypoglycemia:</b> The SGLT2 inhibitors are not expected to increase the risk of hypoglycemia, as they have no direct effect on insulin release and do not impair endogenous glucose production in response to hypoglycemia. Data from Phase III trials have confirmed that Empagliflozin is associated with low risk of hypoglycemia when given as monotherapy or as add-on therapy with most other GLDs. This decline in HbA1c was comparable between the 2 treatment groups.</p> <p><b>Conclusion:</b></p> <p>Administration of Empagliflozin was found to be safe and effective with respect to lowering blood glucose levels in T2DM management when administered according to local prescribing information in T2DM patients with at least 18 years of age. None of the serious AESIs were related to study treatment. Overall, no safety concerns were identified, thereby reinforcing the established safety profile of Empagliflozin. The benefit/risk ratio of Empagliflozin remains favorable and no update of the Empagliflozin prescribing information is deemed necessary.</p> |                               |
| <b>Marketing Authorisation Holder(s):</b>                                | Boehringer Ingelheim Saudi Arabia   |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                               |
| <b>Names and affiliations of principal investigators:</b>                | [REDACTED]                          |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                               |