

# Comparison of the Risk of Severe Complications of Urinary Tract Infections (UTI) Between Patients With Type 2 Diabetes Exposed to Dapagliflozin and Those Exposed to Other Antidiabetic Treatments

**First published:** 15/01/2016

**Last updated:** 02/07/2024

Study

Finalised

## Administrative details

### **PURI**

<https://redirect.ema.europa.eu/resource/50496>

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### **EU PAS number**

EUPAS12113

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### **Study ID**

50496

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## **DARWIN EU® study**

No

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### **Study countries**

United Kingdom

United States

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### **Study description**

The overall goal of this research study is to estimate the sex-specific incidence of hospitalization or emergency department visit for severe complications of urinary tract infections, defined as pyelonephritis and urosepsis, in patients who are prescribed dapagliflozin compared to patients prescribed other specific oral antidiabetic drugs. Dapagliflozin and other antidiabetic drugs are used to treat type 2 diabetes mellitus. Because of the mechanism of action for dapagliflozin and results from small safety monitoring studies, there is interest in further evaluating the safety of dapagliflozin in large populations. The study will be implemented in three administrative health care data sources in two countries: in the United Kingdom, the Clinical Practice Research Datalink (CPRD), and in the United States, the Centers for Medicare and Medicaid Services (CMS) Medicare databases and the HealthCore Integrated Research Database (HIRDSM). Individuals in the databases will be included in the study if they meet the following age criteria, 18 years and older (CPRD and HIRD), or 65 years or older (Medicare), and if they did not have type 1 diabetes, are new users of one of the study drugs and meet the criteria of at least 180 days of electronic data before their first prescription of the study drug. The study period starts July 1, 2013 in CPRD and January 9, 2014 in the United States data sources, and will end at the latest available data at each database at the time of analysis.

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### **Study status**

Finalised

## **Research institutions and networks**

## Institutions

### RTI Health Solutions (RTI-HS)

- France
- Spain
- Sweden
- United Kingdom
- United Kingdom (Northern Ireland)
- United States

**First published:** 21/04/2010

**Last updated:** 13/03/2025

**Institution**

**Not-for-profit**

**ENCePP partner**

### Healthcore United States

## Contact details

### Study institution contact

Catherine Johannes

**Study contact**

[cjohannes@rti.org](mailto:cjohannes@rti.org)

### Primary lead investigator

Catherine Johannes

## Study timelines

### **Date when funding contract was signed**

Planned: 12/02/2015

Actual: 12/02/2015

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### **Study start date**

Planned: 29/01/2016

Actual: 02/02/2016

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### **Date of interim report, if expected**

Planned: 30/12/2016

Actual: 22/11/2016

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### **Date of final study report**

Planned: 30/11/2020

Actual: 23/12/2020

## Sources of funding

- Pharmaceutical company and other private sector

## More details on funding

Astra Zeneca

## Study protocol

[DAPA UTI\\_final\\_23June2014\\_redacted.pdf\(1.16 MB\)](#)

[DAPA UTI\\_Protocol\\_Revisions 28Feb2017\\_redacted.pdf\(1.28 MB\)](#)

## Regulatory

### **Was the study required by a regulatory body?**

Yes

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### **Is the study required by a Risk Management Plan (RMP)?**

EU RMP category 3 (required)

## Other study registration identification numbers and links

D1690R00008

## Methodological aspects

### Study type

### Study type list

#### **Study topic:**

Disease /health condition

Human medicinal product

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**Study type:**

Non-interventional study

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**Scope of the study:**

Assessment of risk minimisation measure implementation or effectiveness

**Data collection methods:**

Secondary use of data

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**Main study objective:**

To compare, by insulin use at the index date, the sex-specific incidence of hospitalization or emergency department visit for severe complications of UTIs among patients with type 2 diabetes mellitus who are new users of dapagliflozin with those who are new users of antidiabetic drugs in classes other than SGLT2 inhibitors, insulin monotherapy, metformin monotherapy, or sulfonylurea monotherapy.

## Study Design

**Non-interventional study design**

Cohort

## Study drug and medical condition

**Name of medicine**

FORXIGA

XIGDUO

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**Name of medicine, other**

farixga, xigduo xr

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**Study drug International non-proprietary name (INN) or common name**

DAPAGLIFLOZIN

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**Anatomical Therapeutic Chemical (ATC) code**

(A10BD15) metformin and dapagliflozin

metformin and dapagliflozin

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**Medical condition to be studied**

Urosepsis

Pyelonephritis

## Population studied

**Short description of the study population**

The study focused on risk of urinary tract infections (UTI) in patients with type 2 diabetes aged 18 years or more exposed to dapagliflozin and other antidiabetic (ADs) treatments identified from CPRD, HIRD and Medicare database in the US.

Inclusion criteria:

- 1) receive newly prescribed dapagliflozin (with or without other ADs) or a newly prescribed AD (with or without other ADs) in a class other than SGLT2 inhibitors, insulin monotherapy, metformin monotherapy, or sulfonylurea monotherapy;
- (2) do not have evidence of type 1 diabetes;
- (3) are aged 18 years or older at the index date for CPRD patients, 18-64 years for HIRDSM patients, or 65 years or older for Medicare patients; and
- (4) have been enrolled in the data source for at least 180 days before the first prescription or dispensing dapagliflozin or eligible index comparator AD.

Exclusion criteria:

Patients with a previous diagnosis of chronic pyelonephritis will be excluded.

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### **Age groups**

Adults (18 to < 46 years)

Adults (46 to < 65 years)

Adults (65 to < 75 years)

Adults (75 to < 85 years)

Adults (85 years and over)

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### **Special population of interest**

Other

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### **Special population of interest, other**

Patients with type 2 diabetes mellitus

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### **Estimated number of subjects**

459636

## Study design details

### **Outcomes**

urosepsis, pyelonephritis, Hospitalization, ED visit, or outpatient diagnosis of pyelonephritis

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### **Data analysis plan**

Descriptive statistics will be calculated to compare baseline characteristics at cohort entry between dapagliflozin users versus comparator antidiabetic users. Propensity scores will be estimated by using logistic regression, with measured potential confounders and predictors of complications of UTI as independent



variables in the regression model and actual exposure group (dapagliflozin or comparator) as the outcome. Sex-specific incidence rates of complications of UTI will be estimated during exposure time at risk for dapagliflozin initiators and comparators. Unadjusted sex-specific incidence rate ratios (IRRs) of the outcome of interest with 95% confidence intervals in dapagliflozin users versus other AD users will be calculated, and adjusted using propensity score-stratified analysis. Analyses will be conducted in each data source separately, and a pooled estimate will be calculated if deemed appropriate.

## Documents

### Study results

[0304030\\_Dapa UTI Final Report\\_Final\\_9Nov2020\\_Abstract\\_Redacted.pdf](#)(190.87 KB)

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### Study publications

[Danysh HE, Johannes CB, Beachler DC, Layton JB, Ziemiecki R, Arana A, Dinh J, L...](#)

[Johannes C, Layton JB, Beachler DC, Ziemiecki RM, Li L, Danysh HE, Dinh J, Hunt...](#)

[Johannes C, Beachler D, Ziemiecki R, Yin R, McGrath L, Jemison J, Lanes S, Gils...](#)

[Layton JB, Zhou CK, Danysh HE, Beachler DC, Ziemiecki R, Dinh J, Yin R, Calinga...](#)

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## Data management

### Data sources

**Data source(s)**

Clinical Practice Research Datalink

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**Data sources (types)**

Administrative healthcare records (e.g., claims)

Drug dispensing/prescription data

Electronic healthcare records (EHR)

## Use of a Common Data Model (CDM)

**CDM mapping**

No

## Data quality specifications

**Check conformance**

Unknown

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**Check completeness**

Unknown

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**Check stability**

Unknown

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**Check logical consistency**

Unknown

## Data characterisation

## **Data characterisation conducted**

No