Drug-drug interactions between dicloxacillin/flucloxacillin and DOACs

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Study | Planned

Administrative details

Contact details

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PURI
https://redirect.ema.europa.eu/resource/38061

EU PAS number
EUPAS38060

Study ID
38061

DARWIN EU® study
No

Study countries
Denmark
Netherlands

Study description
Direct oral anticoagulants (DOACs) are a group of anticoagulants that include dabigatran, rivaroxaban, apixaban, and edoxaban. They are used to reduce the risk of stroke and systemic embolism (SE) in patients with non-valvular atrial fibrillation (NVAF) and as prophylaxis against deep vein thrombosis (DVT) and pulmonary embolism (PE). They were developed as alternatives to vitamin-K antagonists (VKA) such as warfarin, and studies have shown that they are just as safe and effective in prevention of stroke in patients with NVAF. DOACs are more convenient than warfarin due to wider therapeutic range meaning that routine blood tests are not required. Previous studies have investigated co-administration of dicloxacillin and warfarin, which leads to higher risk of strokes and SE. Wether or not a similar association between DOACs and dicloxacillin/flucloxacillin exists, has never been assessed. With this cohort study we aim to investigate if co-administration of dicloxacillin/flucloxacillin leads to increased risk of strokes or SE in patients using DOACs.

Study status
Planned

Research institution and networks

Institutions

University of Southern Denmark (SDU)
Denmark
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Last updated 27/03/2024
Institution
Educational Institution

Division of Pharmacoepidemiology & Clinical Pharmacology (PECP), Utrecht Institute for Pharmaceutical Sciences (UIPS), Utrecht University
Netherlands
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16/04/2024

Institution

Educational Institution

ENCePP partner

Pharmacoepi center, University of Southern Denmark

Denmark
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27/07/2023

Institution

Educational Institution

ENCePP partner

Study timelines

Date when funding contract was signed
Planned:
13/11/2020

Data collection
Planned:
01/01/2021

Date of final study report
Planned:
02/08/2021

Sources of funding

- Other

More details on funding

None

Study protocol

Protocol-EU-PAS.pdf(717.17 KB)

Regulatory

Was the study required by a regulatory body?
No

Is the study required by a Risk Management Plan (RMP)?
Not applicable

Methodological aspects

Study type

Study type list

Study type:
Non-interventional study

Scope of the study:
Assessment of risk minimisation measure implementation or effectiveness

Main study objective:
To investigate if co-administration of dicloxacillin/flucloxacillin leads to increased risk of strokes or systemic embolism in patients using DOACs

Study Design

Non-interventional study design
Cohort

Study drug and medical condition

Anatomical Therapeutic Chemical (ATC) code
100000094315
dabigatran etexilate
100000144760
rivaroxaban
100000144761
apixaban
100000170085
edoxaban

100000096141
phenoxymethylpenicillin
100000096152
dicloxacillin
100000096156
flucloxacillin

Medical condition to be studied
Ischaemic stroke
Embolism arterial

Population studied

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)

Special population of interest
Hepatic impaired
Immunocompromised
Pregnant women
Renal impaired

Estimated number of subjects
200000

Study design details

Outcomes
To estimated the hazard ratios (HR) for the four DOACs (dabigatran, rivaroxaban, apixaban, edoxaban) with a 95% CI comparing the group treated with dicloxacillin/flucloxacillin vs. group treated with phenoxymethylpenicillin, and vs. no treatment with antibiotics. - To calculate number needed to treat for one additional patient to be harmed (NNTH) - Performing subgroup analysis (age, sex, or intake of dicloxacillin or flucloxacillin) - Extend follow-up period from 5-20 days to 5-30 days - Analyze if indication for DOAC treatment had any influence - Subgroup analysis excluding specific patient groups

Data analysis plan
Risks, hazard ratio using Cox regression, odds ratio using conditional logistic regression

Data management

Data sources

Data source(s)
Danish registries (access/analysis)
PHARMO Data Network

Data source(s), other
Danish Registries (access/analysis), PHARMO Data Network

Data sources (types)
Administrative data (e.g. claims)
Drug dispensing/prescription data

Use of a Common Data Model (CDM)

CDM mapping
No

Data quality specifications

Check conformance
Unknown

Check completeness
Unknown

Check stability
Unknown

Check logical consistency
Unknown

Data characterisation

Data characterisation conducted
No