

# Post-licensure observational safety study after meningococcal B vaccine 4CMenB (Bexsero®) vaccination in routine UK care

**First published:** 30/11/2015

**Last updated:** 26/03/2024

Study

Finalised

## Administrative details

### EU PAS number

EUPAS11728

### Study ID

41061

### DARWIN EU® study

No

### Study countries

United Kingdom

### Study description

The objective is to assess the safety of 4CMenB vaccination within the UK National Immunisation program (NIP). The study design is an observational descriptive study followed by a comparative self-controlled case series (SCCS) for primary outcomes based on THIN database of UK primary care records. The primary outcomes are seizures (all and febrile seizures), and Kawasaki disease. Acute disseminated encephalomyelitis (ADEM), Guillain-Barré syndrome (GBS), and anaphylaxis are secondary outcomes. The exposure of interest is meningococcal B vaccine 4CMenB (Bexsero®). The incidence of each outcome will be estimated during an outcome specific post-exposure risk period. The incidence after any immunisation dose in total and after each immunization dose (recommended as 2, 4 and 12-13 months) will be estimated. The risk period is the time frame when an outcome might be expected to occur if it was caused by the exposure based on known mechanisms, published studies or case reports. A plot will be produced to show the temporal distribution of episodes of outcomes around the date of the exposure. Relative incidence and 95% confidence intervals will be estimated using the self-controlled case series (SCCS) method. Within the SCCS, person time and outcomes for each individual will be assigned to the outcome specific post-exposure risk period or a control period outside this time. A relative incidence will then be calculated.

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### **Study status**

Finalised

## Research institutions and networks

### Institutions

[Gillian Hall](#)

United Kingdom

**First published:** 01/04/2022

**Last updated:** 05/04/2022

**Institution**

**Other**

**ENCePP partner**

## Contact details

### **Study institution contact**

Gillian Hall [gillian.hall@gchall.com](mailto:gillian.hall@gchall.com)

**Study contact**

[gillian.hall@gchall.com](mailto:gillian.hall@gchall.com)

### **Primary lead investigator**

Gillian Hall

**Primary lead investigator**

## Study timelines

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

Planned: 11/11/2014

Actual: 02/11/2011

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### **Study start date**

Planned: 31/12/2015

Actual: 08/12/2015

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

Planned: 31/12/2017

Actual: 30/01/2018

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

Planned: 12/06/2020

Actual: 12/03/2020

## Sources of funding

- Pharmaceutical company and other private sector

## More details on funding

GSK Vaccines s.r.l.

## Study protocol

[V72\\_360B-04 Trial Registration Form-ENCePP Registration-2015-08-24-76747267.pdf](#) (966.42 KB)

[V72\\_360B-04 Revised Protocol-v3-2015-11-13-77293343 pdf.pdf](#) (556.43 KB)

## 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)

## Methodological aspects

## Study type

**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:**

Combined primary data collection and secondary use of data

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**Main study objective:**

The objective is to assess the safety of 4CMenB vaccination within the UK National Immunisation program.

## Study Design

**Non-interventional study design**

Other

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**Non-interventional study design, other**

Self-controlled case series

## Study drug and medical condition

**Anatomical Therapeutic Chemical (ATC) code**

(J07AH09) meningococcus B, multicomponent vaccine

meningococcus B, multicomponent vaccine

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### **Medical condition to be studied**

Seizure

Febrile convulsion

Acute disseminated encephalomyelitis

Guillain-Barre syndrome

Anaphylactic reaction

Kawasaki's disease

## Population studied

### **Short description of the study population**

The baseline population will be those children permanently registered at a UK primary care practice which contributes data to The Health Information Network (THIN) database between a start date and an end date (observation period).

The start date for each child will be the most recent of 1st May 2015 (earliest data included), date of birth plus one month, or transfer from another practice plus three months. The first month of life is not included as part of this time is usually spent in secondary care. The three months after transfer in is not included so that prevalent events recorded at a registration visit during this period are not mistaken for incident episodes. The end date will be the earliest of date of birth plus 18 months, transfer out of the practice, last data collection or the study end.

There are no exclusion criteria.

Descriptive analysis – The study population will be all children in the baseline population who receive one or more vaccination with 4CMenB in their

observation period.

SCCS – For both primary outcomes the study population will be children in the baseline population who had a diagnosis of that outcome and had received at least one dose of 4CMenB vaccine.

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### **Age groups**

- Preterm newborn infants (0 – 27 days)
- Term newborn infants (0 – 27 days)
- Infants and toddlers (28 days – 23 months)

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### **Estimated number of subjects**

70000

## **Study design details**

### **Outcomes**

Seizures (all and febrile seizures) and Kawasaki disease. Acute disseminated encephalomyelitis, Guillain-Barré syndrome, and anaphylaxis

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### **Data analysis plan**

A post-exposure risk period has been assigned for each outcome as the time following vaccination during which an outcome would be expected to occur if it were caused by the vaccination. The incidence of each outcome in the post-exposure risk periods will be estimated for all vaccination doses and each dose. Plots will be produced for outcomes with at least one event to show the temporal distribution around exposure. Age-sex distributions will be reported. The self-controlled case series will analyse the primary outcomes of seizures and KD (first episodes). GBS, ADEM and anaphylaxis will be analysed if sufficient events are observed in the risk period to provide 80% power, relative incidence of 10. All exposures to 4CMenB will be treated as equivalent risk

periods. Outcomes and person-time during pre-defined pre-exposure periods will be excluded from baseline and analysed as a separate risk window. SCCS subgroup and sensitivity analyses have been outlined in a Statistical Analysis Plan.

## Documents

### Study results

[EPI-MENB REC 2ND GEN \(V72\)-007 EPI VS GB DB \(205512\) V72\\_360B \(205512\) Redacted Report \(20-Feb-2020\).pdf \(2.33 MB\)](#)

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### Study publications

[Hall, G. C., Douglas, I., Heath, P. T., Prabhakar, P., Rosillon, D., Khan, J. e...](#)

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## Data management

### ENCePP Seal

The use of the ENCePP Seal has been discontinued since February 2025. The ENCePP Seal fields are retained in the display mode for transparency but are no longer maintained.

## Data sources

### Data source(s)

[THIN® \(The Health Improvement Network®\)](#)

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## **Data sources (types)**

[Electronic healthcare records \(EHR\)](#)

[Other](#)

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## **Data sources (types), other**

Prospective patient-based data collection

# 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

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## Data characterisation

### **Data characterisation conducted**

No