Non-Interventional Postmarketing Safety Study of the COMIRNATY 2025-2026 Formula (LP.8.1) in the United States

First published: 19/02/2026

Last updated: 26/03/2026

Study Ongoing

Administrative details

EU PAS number

EUPAS1000000932

Study ID

1000000932

DARWIN EU® study

No

Study countries

☐ United States

Study description

The study will be conducted in two phases, each with its own specific objectives.

Phase 1 will be designed to sequentially monitor the occurrence of pre-specified AESIs in near real-time following vaccination.

Primary objective:

• To estimate the incidence of pre-specified AESIs in a risk window following vaccination with the COMIRNATY 2025-2026 Formula compared to the incidence of these events during a control window (ie, expected rates of these events).

Phase 2 will be designed to compare the incidence of pre-specified AESIs for up to 1 year among individuals who receive the COMIRNATY 2025-2026 Formula to individuals with no recorded coronavirus disease 2019 (COVID-19) vaccination.

Primary objective:

• To estimate the incidence of pre-specified AESIs among individuals who receive the COMIRNATY 2025-2026 Formula compared to the incidence among individuals with no recorded COVID-19 vaccination.

Secondary objective:

• To estimate the incidence of pre-specified AESIs among individuals who receive the COMIRNATY 2025-2026 Formula compared to the incidence among individuals with no recorded COVID-19 vaccination within subgroups of individuals with prior SARS-CoV-2 infection; individuals with prior COVID-19 vaccination; individuals with administration of non-COVID-19 vaccines; children 5 through 17 years of age; adults 65 years of age and older; and individuals 5 years through 64 years of age with at least one underlying condition that puts them at high risk for severe outcomes from COVID-19, if sample size permits.

Study status

Ongoing

Research institutions and networks

Institutions

Pfizer

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Institution

Optum - United States

Contact details

Study institution contact

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Study contact

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Primary lead investigator

Jenny Sun

Primary lead investigator

Study timelines

Date when funding contract was signed

Planned: 29/08/2025

Study start date
Planned: 02/03/2026

Actual: 17/03/2026

Date of interim report, if expected
Planned: 30/06/2026

Date of final study report
Planned: 28/02/2028

Sources of funding

- Pharmaceutical company and other private sector

More details on funding

Pfizer

Study protocol

C4591077_COMBINED PROTOCOL AND SAP_23OCT2025.pdf (1.16 MB)

C4591077_COMBINED PROTOCOL AND SAP V2 AMENDMENT 1_05MAR2026.pdf (992.45 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 topic:

Human medicinal product

Study type:

Non-interventional study

Scope of the study:

Safety study (incl. comparative)

Study design:

This study will be conducted in two phases. Phase 1 will include a study of self-controlled risk interval (SCRI) design conducted using pre-adjudicated claims databases for the interim report. Phase 2 will be a comparative safety cohort design and will be included in the final report

Main study objective:

Primary Objective: To estimate the incidence of pre-specified AESIs among individuals who receive the COMIRNATY 2025-2026 Formula compared to the incidence among individuals with no recorded COVID-19 vaccination.
Secondary Objective: To estimate the incidence of pre-specified AESIs among individuals who receive the COMIRNATY 2025-2026 Formula compared to the

incidence among individuals with no recorded COVID-10 vaccination within subgroups of individuals with prior SARS-CoV-2 infection; individuals with prior COVID-19 vaccination; individuals with administration of non-COVID-19 vaccines; children 5 through 17 years of age; adults 65 years of age and older; and individuals 5 years through 64 years of age with at least one underlying condition that puts them at high risk for severe outcomes from COVID-19, if sample size permits.

Study Design

Non-interventional study design

Cohort

Study drug and medical condition

Medicinal product name

COMIRNATY

Medicinal product name, other

COMIRNATY 2025-2026 Formula (LP.8.1)

Anatomical Therapeutic Chemical (ATC) code

(J07BN01) covid-19, RNA-based vaccine

covid-19, RNA-based vaccine

Medical condition to be studied

COVID-19 prophylaxis

Population studied

Short description of the study population

The source population will be drawn from nationwide healthcare insurance claims databases. It will include individuals with at least one medical or pharmacy claim from 27 August 2025 (the date of product approval) through 31 March 2026. The end date of 31 March 2026 was chosen based on the assumption that the timing of vaccine uptake will be similar to the timing of uptake in previous vaccine seasons. During prior COVID-19 seasons, the end of March reflected the time when uptake of the COVID-19 vaccine was no longer increasing (ie, most individuals who received the COVID-19 vaccine had done so prior to March), and COVID-19 cases declined substantially from their fall/winter peak.

In Phase 1, individuals age ≥ 5 years will be eligible for inclusion if they receive at least one dose of the COMIRNATY 2025-2026 Formula from 27 August 2025 (the date of the COMIRNATY 2025-2026 US approval for marketed use) through 31 March 2026, have continuous medical and pharmacy insurance coverage in the 365 days prior to their vaccination date, experience a safety outcome of interest during a risk interval or control period, and do not experience the safety outcome of interest during the clean period prior to vaccination.

In Phase 2, individuals age ≥ 5 years will be eligible for inclusion if they receive at least one dose of the COMIRNATY 2025-2026 Formula from 27 August 2025 (the date of the COMIRNATY 2025-2026 US approval for marketed use) through 31 March 2026, have continuous medical and pharmacy insurance coverage in the 365 days prior to their vaccination date.

Individuals aged ≥ 5 years will be eligible for inclusion in the unexposed cohort if they have a healthcare encounter (outpatient physician visit or receipt of a non-COVID-19 vaccine) from 27 August 2025 through 31 March 2026 and if they have continuous medical and pharmacy insurance coverage in the 365 days prior to their outpatient healthcare encounter. Individuals in the unexposed cohort will be matched to those in the exposed cohort if their outpatient

healthcare encounter is within the same 14-day calendar period as the exposed individual’s vaccination date and if they are in the same age group

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Age groups

- Children (2 to < 12 years)
- Adolescents (12 to < 18 years)
- **Adult and elderly population (≥18 years)**
    - Adults (18 to < 65 years)
        - Adults (18 to < 46 years)
        - Adults (46 to < 65 years)
    - Elderly (≥ 65 years)
        - Adults (65 to < 75 years)
        - Adults (75 to < 85 years)
        - Adults (85 years and over)

Study design details

Outcomes

In both the SCRI and cohort studies, the pre-specified AESIs will include the following:

• Acute disseminated encephalomyelitis (ADEM)

• Anaphylaxis

• Bell’s palsy

• Cerebral venous sinus thrombosis (CVST)

• Convulsions/seizures (non-febrile)

• Encephalitis/myelitis/encephalomyelitis [not ADEM or transverse myelitis (TM)]

• Glomerulonephritis

• Guillain-Barré syndrome
• Herpes zoster
• Immune-mediated myositis
• Immune thrombocytopenia
• Kawasaki disease
• Multi inflammatory syndrome (in children and adults)
• Multiple sclerosis (MS)*
• Myocardial infarction (MI)
• Myocarditis/pericarditis
• Pulmonary embolism (PE)
• Stroke, hemorrhagic
• Stroke, ischemic
• Subacute thyroiditis
• Transverse myelitis (TM)

*The cohort analysis will include MS, but the AESI will be excluded from the SCRI analysis due to its chronic nature.

Data analysis plan

Phase 1: The observed incidence rates of the pre-specified AESIs will be estimated in the risk window and the control window. Among the individuals who experience an AESI in either the risk window or the control window (but not both), an exact conditional Poisson regression model with the natural logarithm of the person-time as the offset will be used to calculate the relative incidence (rate ratio) and corresponding 95% confidence interval (CI) of events occurring during the risk interval relative to the control period.

The results from the SCRI utilizing the Optum Pre-Adjudicated Claims Databases will be presented in the interim report, while results from the SCRI utilizing the Optum Research Database (ORD) and the Medicare Advantage and Medicare Part D (MA-PD) will be presented in the final report.

Please see the protocol for a description of the data analysis plan for the phase

2 cohort study.

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), other

Optum Pre-Adjudicated Claims Databases

Optum Research Database

Medicare Advantage and Medicare Part D Data

Data sources (types)

Administrative healthcare records (e.g., claims)

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