TG1101-RMS404 - A Post-Authorization Study to Characterize the Safety of BRIUMVI (ublituximab) Use in Pregnant Patients with Multiple Sclerosis Using Data from a US Administrative Healthcare Claims Database

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Study | Ongoing

Administrative details

EU PAS number

EUPAS1000000612

Study ID

1000000612

DARWIN EU® study

No

Study countries

United States

Study description

The objective of this retrospective cohort study is to assess pregnancy and infant outcomes among pregnant individuals with multiple sclerosis (MS) who were exposed to BRIUMVI during pregnancy, compared to two unexposed patient groups:
(a) Disease-matched pregnant individuals exposed to other MS therapies and
(b) Disease-matched pregnant individuals who were not exposed to any treatment for MS at the time of the
estimated start of pregnancy (estimated date of conception (EDC)) or at any time during pregnancy.

Study status

Ongoing

Research institutions and networks

Institutions

Neuraxpharm Pharmaceuticals, S.L.

Contact details

Study institution contact

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Study contact

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Primary lead investigator

Diego Wyszynski

Primary lead investigator

Study timelines

Date when funding contract was signed
Planned: 29/01/2023

Actual: 03/05/2023

Study start date
Planned: 01/04/2024

Actual: 18/12/2024

Data analysis start date
Planned: 29/01/2034

Date of interim report, if expected
Planned: 29/01/2034

Date of final study report
Planned: 01/01/2036

Sources of funding

- Pharmaceutical company and other private sector

Study protocol

TG1101-RMS404 V1.0 Draft 4 in EMA.pdf (876.13 KB)

tg1101-rms404-protocol-v2.0_10Jul2025.pdf (813.66 KB)

tg1101-rms404-protocol-v2.0_10Jul2025.pdf (813.66 KB)

Regulatory

Was the study required by a regulatory body?

Yes

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

EU RMP category 3 (required)

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)

Data collection methods:

Combined primary data collection and secondary use of data

Study design:

The study will involve a retrospective analysis of pregnant subjects diagnosed with MS who were exposed to BRIUMVI at the time of the EDC or at any time during pregnancy.

The retrospective analysis will include three cohorts for comparison.

Main study objective:

The objective of this retrospective cohort study is to assess pregnancy and infant outcomes among pregnant individuals with multiple sclerosis (MS) who were exposed to BRIUMVI during pregnancy, compared to two unexposed patient groups:

(a) Disease-matched pregnant individuals exposed to other MS therapies and

(b) Disease-matched pregnant individuals who were not exposed to any treatment for MS at the time of the

estimated start of pregnancy (estimated date of conception (EDC)) or at any time during pregnancy.

Study Design

Non-interventional study design

Cohort

Study drug and medical condition

Medicinal product name

BRIUMVI

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

UBLITUXIMAB

Anatomical Therapeutic Chemical (ATC) code

(L04AG14) ublituximab

ublituximab

Medical condition to be studied

Relapsing-remitting multiple sclerosis

Population studied

Short description of the study population

Female, between the ages of 15 and 50, and pregnant during the study period.

Age groups

- Adolescents (12 to < 18 years)
- Adults (18 to < 65 years)
    - Adults (18 to < 46 years)
    - Adults (46 to < 65 years)

Special population of interest

Pregnant women

Estimated number of subjects

1688

Study design details

Setting

Eligible subjects for the exposed cohort and two comparison groups will be identified from the administrative claims data, using the following criteria:
Subjects must be female, between the ages of 15 and 50, and pregnant during the study period.
Pregnancies will be identified through claims data, and validated algorithms will be employed to estimate the first day of the last menstrual period (LMP) and the EDC.
Additionally, the end of the pregnancy will be determined through this process (18).
The LMP will be estimated based on diagnosis and procedure codes that record the trimester or
gestational age as of the date of service.
For example, ICD-10-CM code Z3A.xx captures the weeks of gestation. In the absence of codes that inform the trimester or gestational age, the algorithm will use an established number of days prior to the end of pregnancy, depending on the type of pregnancy outcome.
The EDC will be computed as date of LMP plus 14 days. The EDC will be used as the index date for each pregnancy.

Comparators

Other DMTs

Outcomes

Major congenital malformations (MCMs):An abnormality of body structure or function that is present at birth, is of prenatal origin (i.e., birth defect), has significant medical, social, or cosmetic consequences for the affected individual, and typically requires medical intervention.
Major structural birth defects will include ICD-10-CM codes for specific organ

systems, as defined in validated claims algorithms (20).
Minor congenital malformations will be excluded from consideration. MCMs will be reported in aggregate, and for each system organ class, as sample size permit.

Data analysis plan

To create comparable BRIUMVI-exposed and non-BRIUMVI-exposed pregnancy and live birth cohorts, we will use propensity score (PS) methods.
We will use inverse probability of treatment weighting (IPTW) to adjust for confounding of baseline factors and to preserve sample size.
For the proposed cohort comparison of pregnancies in Cohort 1 compared to those in Cohorts 2 and 3, PS models will be fit including maternal demographics, treatment, and all baseline characteristics with standardized differences >0.1 or <-0.1 in the eligible cohorts and any variable determined to be associated with pregnancy outcomes a priori.
Baseline covariates with more than 5% missingness will not be considered for inclusion in the propensity score models, to avoid limiting the PS population based on data availability rather than the PS value itself.
The PS model will be a logistic regression model run on eligible pregnancies in the BRIUMVI exposed and each comparison cohort, with BRIUMVI-exposure as the outcome in each model and the baseline covariates as the predictors.
The predicted probability of each individual receiving their treatment will be predicted from the model and will be used as the propensity score. The inverse of the probabilities from the PS model will be used as weights for each pregnancy in the analysis.
Separate PS models and IPTW weights will be constructed for the comparison of the BRIUMVI-exposed cohort to Cohort 2 and for the comparison of the BRIUMVI-exposed cohort to Cohort 3.Separate PS models and corresponding IPTW weights will be computed for each comparison of interest (BRIUMVI

exposed vs. Cohort 2 and BRIUMVI-exposed vs. Cohort 3) on the subset of live births, from among the linkable eligible pregnancies, for the analyses of infant outcomes.

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

MarketScan data

Data sources (types)

Drug registry

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

Unknown