# A Multicenter, Global, Observational Study to Collect Information on Safety and to Document the Drug Utilization of Tecfidera™ (Dimethyl Fumarate) When Used in Routine Medical Practice in the Treatment of Multiple Sclerosis (ESTEEM)

**First published:** 19/12/2014

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

Study | Finalised

## Administrative details

**EU PAS number**

EUPAS6782

**Study ID**

46164

**DARWIN EU® study**

No

**Study countries**

- [ ] Argentina
- [ ] Australia
- [ ] Austria
- [ ] Canada
- [ ] Denmark
- [ ] France
- [ ] Germany
- [ ] Hungary
- [ ] Ireland
- [ ] Italy
- [ ] Netherlands
- [ ] New Zealand
- [ ] Norway
- [ ] Poland
- [ ] Portugal
- [ ] Puerto Rico
- [ ] Slovakia
- [ ] Spain
- [ ] Switzerland
- [ ] United Kingdom
- [ ] United States

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**Study description**

The primary objective of the study is to determine the incidence, type, and pattern of serious adverse events (SAEs), including but not limited to infections (including opportunistic infections), hepatic events, malignancies, and renal events, and of adverse events (AEs) leading to treatment discontinuation in patients with MS treated with dimethyl fumarate (DMF). Secondary objectives of this study in this population are as follows: To determine dimethyl fumarate

(DMF) prescription and utilization patterns in routine clinical practice in patients with multiple sclerosis (MS), To assess the effectiveness of dimethyl fumarate (DMF) on multiple sclerosis (MS) disease activity and disability progression in routine clinical practice as determined by the Expanded Disability Status Scale (EDSS) score and multiple sclerosis (MS) relapse information, and To assess the effect of dimethyl fumarate (DMF) on health-related quality of life, healthcare resource consumption, and work productivity.

**Study status**

Finalised

# Research institutions and networks

## Institutions

### Biogen

**First published:** 01/02/2024

**Last updated:** 01/02/2024

**Institution**

### Multiple centres: 468 centres are involved in the study

## Contact details

**Study institution contact**

Study Director Biogen ctrr@biogen.com

Study contact

ctrr@biogen.com

**Primary lead investigator**

Study Director Biogen

Primary lead investigator

## Study timelines

**Date when funding contract was signed**

Planned: 31/12/2013

Actual: 04/06/2013

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**Study start date**

Planned: 31/12/2013

Actual: 19/11/2013

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**Date of final study report**

Planned: 30/11/2024

Actual: 21/08/2023

## Sources of funding

- Pharmaceutical company and other private sector

## More details on funding

Biogen

## Study protocol

109MS401 Protocol V3 (EU) Final 15Aug14_Redacted.pdf(1.98 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

109MS401

https://clinicaltrials.gov/ct2/show/NCT02047097?term=109ms401&rank=1

# 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:**

Primary data collection

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**Main study objective:**

The primary objective of the study is to determine the incidence, type, and pattern of serious adverse events (SAEs), including but not limited to infections (including opportunistic infections), hepatic events, malignancies, and renal events, and of adverse events (AEs) leading to treatment discontinuation in patients with Multiple Sclerosis (MS) treated with dimethyl fumarate (DMF).

## Study Design

**Non-interventional study design**

Cohort

Other

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**Non-interventional study design, other**

Prospective, global, observational study

## Study drug and medical condition

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

DIMETHYL FUMARATE

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**Medical condition to be studied**

Multiple sclerosis

# Population studied

**Short description of the study population**

The study population included patients aged 18 years or older diagnosed with multiple sclerosis (MS) newly prescribed with treatment of dimethyl fumarate (DMF) under routine clinical practice.

Inclusion criteria:

- Patients must be naïve to DMF, Fumaderm®, and compounded fumarates at the time of enrollment, but need not be naïve to other MS treatments, and must not be currently enrolled in any other clinical trial or study except for the DMF Pregnancy Registry or other studies that, according to the study Medical Director, do not conflict with this observational study (e.g., health economic studies).

Exclusion criteria:

- Patients with previous exposure to DMF, Fumaderm®, and compounded fumarates are excluded so as not to introduce bias; these patients may be more or less likely to experience AEs and may fail to report AEs that occurred before study enrollment.
- Patients participating in other clinical studies are excluded so as not to unduly confound causality assessments when a concomitant experimental agent’s safety profile has yet to be established and/or the physician is blinded to the

patient’s treatment assignment.

**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**

Other

**Special population of interest, other**

Patients with multiple sclerosis

**Estimated number of subjects**

5496

## Study design details

**Outcomes**

The number of participants that experience Adverse Events (AEs) that lead to discontinuation of dimethyl fumarate (DMF) and the number of participants that experience Serious Adverse Events (SAEs). DMF prescription and utilization patterns, Effectiveness of DMF on MS disease activity and disability progression, Changes in health-related quality of life measures will be evaluated over time.

**Data analysis plan**

Statistical analyses will be based on all patients who enroll in the study and take at least 1 dose of DMF. Statistical analyses will generally be descriptive

and exploratory in nature. No formal statistical hypothesis testing is planned. Ninety-five percent CIs for incidence and incidence rate point estimates will be calculated using the binomial distribution and the Poisson distribution, respectively. Analyses of clinical laboratory parameters may include summaries of actual values over time, change from baseline over time, percent change from baseline over time, shift tables, and/or summaries of worst post-baseline values. Annualized relapse rate will be analyzed using a negative binomial model, adjusted for appropriate prognostic factors, and time-to-event endpoints will be analyzed using Kaplan-Meier estimates. Summary statistics will be presented for health-related quality of life, healthcare resource consumption, and work productivity outcomes over time.

## Documents

**Study results**

109MS401_CSR Synopsis 21Aug2023_Redacted.pdf(293.54 KB)

# Data management

## Data sources

**Data sources (types)**

Other

**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

**Check completeness**

Unknown

**Check stability**

Unknown

**Check logical consistency**

Unknown

# Data characterisation

**Data characterisation conducted**

No