Cover Page

Official Title:	A Multicenter, Postmarketing Study of Dimethyl Fumarate (Tecfidera; BG00012) in Relapsing Forms of Multiple Sclerosis (RMS) Participants in China.
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Name of Sponsor/Company:	Biogen MA Inc./Biogen Idec Research Limited
Name of Finish Product:	Tecfidera; BG00012
Name of Active Ingredient:	Dimethyl Fumarate
Study Indication:	Relapsing Forms of Multiple Sclerosis

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2. STUDY SYNOPSIS

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Title of Study:

A Multicenter, Postmarketing Study of Dimethyl Fumarate (Tecfidera; BG00012) in Relapsing Forms of Multiple Sclerosis (RMS) Participants in China.

Principal Investigator/Coordinating Investigator:

[redacted] MD, PhD, [redacted] – China

Study Period:	**Phase of Development:** 4
Date of first treatment: 28 June 2023 End of Study Date: 12 April 2025	

Study Objectives:

Primary Objectives:

- To assess the efficacy of dimethyl fumarate (DMF) in Chinese participants with RMS at Week 48.

Secondary Objectives:

- To assess the efficacy of DMF in Chinese participants with RMS.
- To assess the safety of DMF in Chinese participants with RMS.

[redacted]

Study Design:

This was an interventional, open-label, single-arm, study to evaluate efficacy and safety of DMF (Tecfidera) in Chinese participants with RMS in the postmarketing setting in China. Participants who met the study entry criteria received DMF for a duration of up to 48 weeks, followed by a safety follow-up period of 2 weeks. There were 60 participants enrolled in the study at a total of 15 sites.

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Number of Participants (Planned and Analyzed):

Planned:

Approximately 50 participants were planned to be enrolled.

Analyzed:

Overall, 60 participants were enrolled and received study treatment.

Study Population:

Main Inclusion Criteria:

- Confirmed RMS diagnosis (including clinically isolated syndrome, relapsing-remitting multiple sclerosis [RRMS], and active secondary progressive MS) per 2017 McDonald's criteria
- Age between 18 and 65 years (both inclusive) at the time of informed consent
- Expanded Disability Status Scale (EDSS) score between 0.0 and 5.0, inclusive, at baseline Visit (pre-dose on Day 1)
- Experienced at least 1 documented relapse within the 12 months before screening, with a prior brain magnetic resonance imaging (MRI) demonstrating lesion(s) consistent with multiple sclerosis (MS), or showed evidence of gadolinium-enhancing (GdE) lesion(s) of the brain on an MRI performed within the 6 weeks prior to screening.

Main Exclusion Criteria:

- An MS relapse that occurred within the 30 days prior to screening and/or the participant had not stabilized from a previous relapse prior to screening.
- Any of the following abnormal blood tests at screening:
  - Alanine aminotransferase (ALT), aspartate aminotransferase (AST), or gamma glutamyl transferase (GGT) $\geq 3 \times$ upper limit of normal (ULN) or bilirubin $> 2 \times$ ULN
  - Lymphocyte count < lower limit of normal (LLN)
  - Estimated glomerulus filtration rate (eGFR) ≤ 60 mL/min/1.73 m^2 (using the Chronic Kidney Disease Epidemiology Collaboration equation)
- Had abnormal urine test for albumin to creatinine ratio > 22.6 mg/mmol at Screening and confirmed by a second urinalysis 2 weeks later.
- History of a suicide attempt within the 5 years prior to Screening or had suicidal ideation in the past 6 months as indicated by a positive response ("Yes") to either Question 4 or Question 5 of the "Screening/baseline" version of the Columbia Suicide Severity Rating Scale (C-SSRS) at Screening.

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Study Treatment, Dose, Mode of Administration:

DMF was supplied as a drug product formulated as white to off white capsules with micro-tablets for oral administration. Capsules containing 120 mg and 240 mg DMF were used and dispensed to participants for self-administration. The study treatment was administered orally with a gap of at least 6 hours between the doses. A total of 2 lots of DMF were used in the study.

DMF was administered orally as 120 mg twice a day (BID) for the first 7 days, followed by 240 mg BID (maintenance dose) after 7 days, for a total duration of 48 weeks. Dose reduction was allowed for tolerability.

Duration of Treatment and Follow-Up:

The total study duration for each participant was up to 54 weeks:

- Screening period up to 4 weeks
- Treatment period of 48 weeks
- Follow-up period of 2 weeks

The end of study was last participant, last visit for final collection of data.

Criteria for Evaluation:

Following is a description of all the efficacy and safety assessments that were originally planned for this study.

Efficacy:

- Recording of MS relapse information and relapse assessment
- Brain MRI measurements including, but not limited to:
  - T1-weighted MRI before Gd infusion
  - T1-weighted MRI after Gd infusion
  - T2-weighted MRI
- NEDA-3 (no evidence of disease activity-3)
- [redacted]
- EDSS scores

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Safety:

Clinical Safety Assessments

The following clinical assessments were performed to evaluate the safety profile of DMF:

- Collection of adverse events (AEs) and serious AEs (SAEs)
- Demographic and baseline disease characteristics, including MS relapse history and medical history
- Pregnancy status
- Concomitant treatment, including concomitant MS therapy and other concomitant medications
- Electrocardiograms (ECGs) - 12-lead ECG data
- Vital sign measurements (body temperature, pulse rate, systolic and diastolic blood pressure (BP), and respiratory rate)
- Physical examination (including weight)
- Columbia Suicide Severity Rating Scale (C-SSRS).

Laboratory Safety Assessments

The following laboratory assessments were performed to evaluate the safety profile of DMF:

- Hematology
- Blood chemistry
- Urinalysis

Statistical Methods:

Statistical analyses were generally descriptive and exploratory in nature. No formal statistical hypothesis testing was planned. [redacted]

Planned Analyses:

Analysis populations were defined as follows:

- Full analysis set (FAS): All enrolled participants who received at least 1 dose of DMF. The FAS was the primary population for efficacy endpoint analyses.
- Per-protocol set (PPS): Participants from the FAS population without any important protocol deviations in prespecified categories based on the protocol deviations category file. The PPS was used for supportive analysis of primary study endpoints.

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- Safety analysis set (SAS): All enrolled participants who received at least 1 dose of DMF.

Demographics and Baseline Disease Characteristics:

Participant demographic data, including age (years), age group in years (< 40, ≥ 40), sex, weight (kg), were summarized descriptively in the FAS.

The following baseline MS disease history characteristics were summarized for the FAS: Time since most recent relapse (days), total number of relapses experienced within the past 12 months, 2 years, 3 years (0, 1, 2, 3, and ≥ 4), time since MS diagnosis (days), and time since first MS symptoms (days).

The following baseline disease characteristics were summarized for the FAS: Prior MS treatment-procedure and MS-treatment-medication (Yes/No), baseline EDSS score and category (≤ 2, > 2), baseline GdE lesions, number of baseline GdE lesions (0, 1-2, 3-4, ≥ 5), and baseline T2 lesion volume.

Medical history and MS treatment history (procedures and medications) were coded using Medical Dictionary for Regulatory Activities (MedDRA) version 28.0 and were summarized separately by system organ class (SOC) and preferred term (PT). Listings were provided for demographic and baseline disease characteristics, medical history, and MS treatment history.

Efficacy:

MRI endpoints were assessed at Weeks 24 and 48. MRI endpoints are secondary endpoints. Baseline was defined as the closest available assessment at or prior to Day 1 (prior to any dose of study treatment). Unless an unscheduled MRI was performed after the Screening Visit, the screening MRI served as the baseline MRI.

The primary analysis was based on the FAS population.

Primary and secondary endpoints are presented below. [redacted]

Primary Endpoints:

For the primary estimand, the unadjusted annualized relapse rate (ARR) at Week 48 was summarized. ARR was also estimated from [redacted] The number of participants with relapse of 0, 1, 2, 3, ≥ 4 was summarized. Individual participant relapse rate and percentage were summarized by descriptive statistics.

For all sensitivity analyses, all relapses were analyzed by the same method described above. The primary endpoint was also analyzed in the PPS. The remaining sensitivity analyses were subgroup analyses. Subgroup analyses were performed for the primary efficacy endpoint (ARR at Week 48) only. The endpoint was analyzed, unadjusted and also presented as of model-based LS mean ARR for baseline EDSS score (≤ 2.0 versus > 2.0), age at baseline (< 40 versus

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≥ 40 years), gender, baseline number of relapses (≤ 1 versus ≥ 2, defined as the number of relapses in the 12 months prior to study entry), prior MS treatment (Yes versus No), and baseline GdE lesions (0, ≥ 1).

Secondary Endpoints:

- For change from baseline in the number of GdE lesions at Week 24, descriptive statistics were presented for baseline, Week 24, and Week 48 timepoints, and p-values were generated using the Wilcoxon Signed Rank test.
- The number of GdE lesions at Week 24 and Week 48 by MRI scan were summarized using descriptive statistics and the number and percentage of participants with 0, 1-2, 3-4, and ≥ 5 GdE lesions were summarized.
- The proportion of GdE lesion-free participants was summarized at Week 24 and Week 48 and the Clopper Pearson 95% CIs were calculated.
- For the proportion of participants relapsed at Week 48, if a participant did not experience a confirmed relapse (time from first dose to first confirmed relapse date) prior to study withdrawal, the participant was censored on the last visit date conducted on the study. The proportion of participants relapsed was estimated as the probability of relapses from the Kaplan-Meier curve of the time to the first relapse during the study (i.e., Kaplan-Meier product-limit estimator). The estimated proportion of participants relapsed and relapse-free at Week 24 and Week 48 was presented. A Kaplan-Meier plot of relapse-free survival was also provided.
- New T1 hypointense lesions and new/newly enlarging T2 hyperintense lesion count were collected at Week 24, Week 48, and Early Termination/Unscheduled Relapse Visits relative to the previous scheduled visit. The number of new T1 hypointense lesions and the number of new/newly enlarging T2 hyperintense lesions at Week 24 compared to baseline and at Week 48 compared to both Week 24 and baseline by MRI scan were summarized with descriptive statistics. The number and percentage of participants with 0, 1, 2, 3, ≥ 4 lesions were summarized.
- The total T2 lesion volume and change from baseline at Week 24 and Week 48 were summarized using descriptive statistics.

Safety:

All safety analyses were based on the SAS. All AEs were coded with the Medical Dictionary for Regulatory Activities using version 28.0.

- Statistical summaries were performed on general incidence of AEs, including: all treatment-emergent adverse event (TEAEs), TEAEs by severity, treatment-related TEAEs, SAEs, treatment-related SAEs, TEAEs leading to drug discontinuation (marked in the case report form as “drug withdrawal”), TEAEs leading to study withdrawal, TEAEs leading to drug interruption, TEAEs leading to drug dose reduction, and TEAEs leading to death.

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- Laboratory data were summarized using shift tables where appropriate. Hematology and blood chemistry values and quantitative urinalysis parameters, for each participant were flagged as "low", "normal", or "high" relative to the normal ranges of the central laboratory or as "unknown" if no result was available.
- In addition to the shift analyses, a summary of actual values and change from baseline values by visit were also presented for quantitative laboratory parameters.
- A summary of actual values and change from baseline values by visit were presented for each vital signs parameter (weight, systolic BP, diastolic BP, pulse rate, temperature, and respiratory rate).
- For ECG, shifts from baseline to worst postbaseline value were summarized according to the order of Abnormal – adverse event>Abnormal – no adverse event>normal>not done.
- Incidence of participants meeting one of the C-SSRS criteria at baseline and any postbaseline visit for suicidal behavior, suicidal ideation, and nonsuicidal self-injurious behavior were summarized.

Sample Size Calculations

The study was not powered for the primary endpoint. The sample size was primarily based on feasibility; the study was planned to enroll approximately 50 participants, with the goal of having approximately 45 evaluable participants at the Week 24 timepoint. This sample size was expected to provide approximately [redacted] power for the key secondary endpoint (i.e., change from baseline in number of GdE lesions at Week 24) and allow detection of an effect size (absolute mean difference between Week 24 and baseline number of GdE lesions, relative to the standard deviation of differences) of [redacted].

Results:

Participant Disposition:

All enrolled participants (60 participants [100%]) received at least 1 dose of study treatment.

A total of 56 participants (93.3%) completed the 48-week study treatment period. There were 4 participants (6.7%) who discontinued study treatment or withdrew from the study. The primary reasons for discontinuing the study treatment or withdrawing from the study were withdrawal by participant (3 participants [5.0%]), and disease relapse (1 participant [1.7%]).

Demographics and Baseline Disease Characteristics:

Demographics

Overall, the majority of participants were female (39 participants [65.0%]) while 21 (35.0%) participants were male. The mean (standard deviation or SD) age was 36.3 (10.53) years; 37 participants (61.7%) were < 40 years of age and 23 participants (38.3%) were ≥ 40 years of age. The mean (SD) weight was 62.96 (12.201) kg.

Baseline Disease Characteristics

Overall, the mean (SD) time since first MS symptoms was 1417.2 days (1630.61) and the mean time since MS diagnosis was 907.3 days (1409.39).

At baseline, the mean (SD) total number of relapses experienced within the past 12 months prior to the first dose of study treatment was 1.0 (0.55), and the mean (SD) time since the most recent relapse was 109.6 (78.46) days. The total number of relapses ranged from 0 to ≥ 4. The mean (SD) total number of relapses experienced within the past 2 and 3 years prior to the first dose of study treatment were 1.2 (0.76) and 1.4 (0.84), respectively. A total of 55 participants (91.7%) took MS medication prior to the study and 1 participant (1.7%) had prior MS procedures (acupuncture and cupping therapy).

At baseline, the majority of participants (44 participants [73.3%]) had an EDSS score ≤ 2. The mean (SD) EDSS score at baseline was 1.65 (1.293).

Baseline MRI evaluation showed the mean (SD) number of GdE lesions at baseline was 1.1 (2.76). At baseline, most participants (40 participants [66.7%]) had no GdE lesions. Thirteen participants (21.7%) had 1 or 2 GdE lesions, 3 participants (5.0%) had 3 or 4 GdE lesions, and 4 participants (6.7%) had ≥ 5 GdE lesions. The mean (SD) T2 lesion volume at baseline was 10.8 (10.83) mL.

Baseline Medical History

A total of 54 participants (90.0%) reported history of at least 1 other medical condition in addition to MS, of whom 23 participants (38.3%) had a medical history of Nervous system disorders.

Prior Treatments

A total of 40 participants (66.7%) reported 1 or more prior medications at baseline.

MS Treatment (Medication) History

A total of 55 participants (91.7%) received an MS treatment prior to study participation. Among the MS treatments (medications) used, the reported prior disease modifying therapies (DMTs) teriflunomide (4 participants [6.7%]), siponimod (3 participants [5.0%]), interferon beta (IFN-β) (1 participant [1.7%]) are approved DMTs for MS.

MS Treatment (Procedure) History

One participant (1.7%) underwent the MS procedures of acupuncture and cupping therapy prior to participating in the study.

Concomitant Treatments

A total of 50 participants (83.3%) reported 1 or more concomitant medication during the study.

The concomitant nondrug treatments included surgical and medical procedures. A total of 5 participants (8.3%) reported 1 or more concomitant nondrug treatment (surgical and medical procedures) during the study.

Protocol Deviations

Overall, important protocol deviations were reported in 23 participants (38.3%) during the study. The most commonly reported (≥ 10% of participants) were related to visit schedule or other protocol deviations (7 participants [11.7%] each), and IP (6 participant [10.0%]).

None of the protocol deviations were related to coronavirus disease 2019 (COVID-19).

Overall, none of the deviations affected the safety of the participants or were considered to have a meaningful impact on the study results or the overall analysis of the data.

Exposure and Compliance

Over all participants (n = 60), the mean (SD) duration of exposure to study treatment was 46.02 (8.556) weeks. The mean (SD) actual total DMF dose received was 150434.0 (29050.98) mg.

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Dose reduction of DMF was permitted at the discretion of the Investigator only for participants who were unable to tolerate DMF due to flushing and/or gastrointestinal disturbances.

One participant (1.7%) was reported to have a dose reduction due to an AE. Other dose reductions that were reported were the result of dosing errors by the participant (taken once a day [QD] rather than BID), and overall, compliance with treatment was high. Overall, the mean (SD) study treatment compliance was 98.33% (3.9), with most participants having a treatment compliance that ranged between 80% and 120% (59 participants [98.3%]). The remaining 1 participant (1.7%) had a treatment compliance of < 80%.

Efficacy:

Efficacy results are described for the FAS for all participants. The primary efficacy endpoint results (ARR at Week 48) are also described for the PPS.

- For the FAS, the majority of participants (54 participants [90.0%] [n = 60]) did not experience a protocol-defined relapse through Week 48. The model-based LS mean ARR was 0.13 (95% CI: 0.06, 0.28). The unadjusted ARR was 0.13. The mean ratio of the model-based ARR Week 48 compared to baseline) was 0.13 (95% CI: 0.06, 0.28). The mean (SD) ARR calculated at the participant level was 0.15 (0.525). The results of the PPS were consistent with the FAS.
- The estimated proportion of participants who relapsed at Week 48 was 0.10. The majority of participants (54/60 participants [90.0%]) did not experience a protocol-defined relapse from baseline through Week 48.
- At Week 24, over all evaluable participants (n = 57), the mean (SD) number of GdE lesions decreased to 0.4 (0.89), with a mean (SD) change from baseline of -0.7 (2.83) GdE lesions (p-value = 0.0273).
- The number of GdE lesions decreased from baseline to Week 48. The mean (SD) GdE lesions count at Week 24, and at Week 48 were 0.4 (0.89) and 0.4 (0.85), respectively, as compared to 1.1 (2.76) at baseline.
- An increased proportion of participants were GdE-lesion free at Week 48. The proportion of participants who were GdE-lesion free at baseline was 66.7% (40/60 participants), whereas the proportion of participants who were GdE-lesion free at Week 24 and Week 48 was 73.7% (42/57 participants) [95% CI: 60.3, 84.7] and 80.0% (44/55 participants) [95% CI: 67.0, 89.6], respectively.
- Few new T1 hypointense lesions (mean [SD] number of 2.9 [6.90] lesions) or new/newly enlarging T2 hyperintense lesions (mean [SD] number of 8.5 [14.59] lesions) developed relative to baseline.
- At Week 48, 26/55 participants (47.3%) had no new T1 hypointense lesions, 12/55 participants (21.8%) had 1 lesion, 1/55 participants (31.8%) had 2 lesions, 3/55 participants (5.5%) had 3 lesions, and 13/55 participants (23.6%) had ≥ 4 lesions compared to baseline.
- At Week 48, 13/55 participants (23.6%) had no new/ newly enlarging T2 hyperintense lesions, 1, 2, and 3 lesions were each reported in 5/55 participants (9.1%), and 27/55 participants (49.1%) had ≥ 4 lesions. compared to baseline.

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- There were small changes in mean T2 lesion volume from baseline to Week 48. The mean (SD) change in T2 lesion volume from baseline to Week 24 and Week 48 was 0.66 (2.260) mL and 0.66 (1.870) mL, respectively.
- The results of the efficacy endpoints were consistent with results of previous studies and demonstrated a reduction in clinical and radiological disease activity.

Safety:

All safety analyses were based on the SAS.

- There were no deaths reported during the study.
- 16 SAEs were reported in 13 participants (21.7%). One SAE of road traffic accident (1 participant [1.7%]) took place prior to the study on Day -4; the remaining 15 SAEs were treatment-emergent. By PT, the SAEs were MS relapse (7 participants [11.7%]), thyroid mass, large intestine polyp, gastroenteritis, clavicle fracture, road traffic accident, haemangioma of skin, uterine polyp, and pulmonary mass (1 participant [1.7%] each). None of the SAEs were considered related to the study treatment. One participant (1.7%) experienced 1 SAE of MS relapse that led to discontinuation of study treatment and withdrawal from the study. None of the SAEs lead to study treatment interruption or reduction.
- 50 participants (83.3%) experienced 197 TEAEs.
- There were no treatment-emergent adverse events of special interest (AESIs) reported.
- 5 participants (8.3%) experienced AEs that led to drug interruption. One participant (1.7%) experienced an AE that led to drug dose reduction during the study.
- 14 participants (23.3%) had AEs that were considered mild, 25 participants (41.7%) had moderate AEs, and 11 participants (18.3%) had 14 severe AEs. Twenty-six participants (43.3%) experienced AEs that were considered related to study treatment. One participant (1.7%) experienced 1 AE that led to discontinuation of study treatment and withdrawal from the study. Of the 14 severe AEs, 7 were severe events of MS relapse and the remaining events occurred only once each.
- The SOCs with the highest number of participants (> 20% participants) reporting AEs were Infections and infestations (22 participants [36.7%]), Investigations (21 participants [35.0%]), Nervous system disorders (17 participants [28.3%]), and Gastrointestinal disorders (16 participants [26.7%]).
- The most common AEs (≥ 5% of participants) by PT were MS relapse (11 participants [18.3%]); upper respiratory tract infection and ALT increased (10 participants [16.7%] each); AST increased (7 participants [11.7%]); cough (6 participants [10.6%]); hyperlipidaemia (5 participants [8.3%]); GGT increased, diarrhoea, and flushing (4 participants [6.7%] each); and COVID-19, gastroenteritis, influenza, nasopharyngitis, blood uric acid increased, headache, anxiety, sleep disorder, and leukopenia (3 participants [5.0%] each).
- The most common shifts from baseline to low, postbaseline, in hematology were in the categories of neutrophils (11/59 participants [18.6%]), leukocytes (10/59 participants [16.9%]), lymphocytes

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(10/59 participants [16.9%]), monocytes/total cells (9/59 participants [15.3%]), monocytes (8/59 participants [13.6%]), and hemoglobin (6/59 participants [10.2%]). The most common shifts from baseline to high postbaseline in hematology were in the category of eosinophils/total cells (10/59 participants [16.9%]) and eosinophils (7/59 participants [11.9%]).

- The most common shifts from baseline to low postbaseline in blood chemistry parameters were creatinine (23/59 participants [39.0%]); bicarbonate (7/59 participants [11.9%]); glucose (6/59 participants [10.2%]); and low density lipoprotein (LDL) (1/2 participants [50.0%]). The most common shifts from baseline to high, postbaseline were ALT (21/59 participants[35.6%]); cholesterol (18/59 participants [30.5%]); albumin (15/59 participants[25.4%]); protein (12/59 participants [20.3%]); AST, GGT, triglycerides, and urate (11/59 participants [18.6%] each); and LDL cholesterol calculated and urea nitrogen (8/59 participants [13.6%] each).
- For quantitative urinalysis laboratory tests, the only shift from baseline to low postbaseline was observed in creatinine for 3of 59 participants (5.1%). The most common shifts from baseline to high postbaseline were albumin (24/59 participants [40.7%]), followed by creatinine (19/59 participants [32.2%]), and albumin/creatinine (13/59 participants [22.0%]). For qualitative urinalysis laboratory tests, shifts in ketones (12/59 participants [20.3%]) and occult blood (16/59 participants [27.1%]), were seen from normal baseline levels to 3+ at postbaseline.
- For vital signs, the most common abnormal shifts from baseline were body temperature (2 participants [3.4%] with > 38°C), pulse rate (7 participants [11.9%] with > 120 bpm and 8 participants [13.6%] with < 50 bpm), systolic blood pressure (1 participant [1.7%] with > 180 mmHg or an increase from baseline of > 40 mmHg and 4 participants [6.8%] with < 90 mmHg) or a decrease from baseline of > 30 mmHg, and diastolic blood pressure (1 participant [1.7%] each with > 105 mmHg or an increase from baseline of > 30 mmHg and < 50 mmHg or a decrease from baseline of > 20 mmHg, respectively).
- Of 58 participants, 21 participants (36.2%) with a normal ECG at baseline had a postbaseline worst ECG reported “abnormal – no AE”. Of 58 participants, 1 participant (1.7%) with a normal ECG at baseline had a postbaseline worst ECG reported as "abnormal – AE", corresponding to an AE of sinus arrythmia. The event of sinus arrythmia was mild in severity and was considered not related to the study treatment by the Investigator.
- There were no clinically significant new or worsening physical examination findings reported as AEs or medical history during the study.
- There were no reports of suicidal ideation, suicidal behavior, or nonserious self-injurious behavior that emerged in any participant postbaseline, as assessed by C-SSRS.
- The safety profile of DMF was generally consistent with the known safety profile of DMF and with previous DMF studies.

Conclusions:

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This study was conducted at 15 sites in China. A total of 60 participants were enrolled in the study. All enrolled participants (60 participants [100%]) received at least 1 dose of study treatment. A total of 56 participants (93.3%) completed the 48-week study treatment period. There were 4 participants (6.7%) who discontinued study treatment or withdrew from the study. The primary reasons for discontinuing the study treatment or withdrawing from the study were withdrawal by participant (3 participants [5.0%]), and disease relapse (1 participant [1.7%]).

The study design limits the conclusions that can be drawn from this study in this open-label, unblinded, single-arm study of 48 weeks of treatment in 60 patients. The sample size of this study relative to the pivotal studies for DMF results in wide confidence intervals for endpoints that use exposure-years in the estimation process including AE incidence rate estimates. In addition, this study is limited in demonstrating long term effects of treatment beyond 48 weeks.

Results from efficacy assessments showed that the majority of participants (54 participants [90.0%]) did not experience a protocol-defined relapse from baseline through Week 48. At Week 24 and Week 48, 73.7% (42/57 participants) and 80.0% (44/55 participants) were GdE-lesion free, respectively. At Week 24, the mean (SD) number of GdE lesions decreased to 0.4 (0.89), with a mean (SD) change from baseline of -0.7 (2.83) GdE lesions (p-value = 0.0273). The number of GdE lesions decreased from baseline to Week 48. The mean (SD) GdE lesions count at Week 48 was 0.4 (0.85) as compared to 1.1 (2.76) at baseline. Few new T1 hypointense lesions or new or newly enlarging T2 lesions developed relative to baseline. There was a small mean change from baseline in T2 lesion volume, with a mean (SD) change from baseline to Week 24 and Week 48 of 0.66 (2.260) mL and 0.66 (1.870) mL, respectively.

Results from the safety assessments showed that DMF was well tolerated in Chinese participants. Thirteen participants (21.7%) experienced 16 SAEs. One SAE of road traffic accident (1 participant [1.7%]) took place prior to the study on Day -4; the remaining 15 SAEs were treatment-emergent. Of the 16 SAEs, 1 participant (1.7%) experienced an SAE of MS relapse that led to discontinuation of study treatment and withdrawal from study. None of the SAEs were considered related to the study treatment.

Fifty participants (83.3%) experienced 197 TEAEs. There were no treatment-emergent AESIs reported. Five participants (8.3%) experienced AEs that led to drug interruption. One participant (1.7%) experienced an AE that led to drug dose reduction during the study. Fourteen participants (23.3%) experienced mild AEs, 25 participants (41.7%) experienced moderate AEs, and 11 participants (18.3%) experienced 14 severe AEs. Of the 14 severe AEs, 7 were severe events of MS relapse and the remaining events occurred only once each.

The most common AEs (≥ 5% of participants) by PT were MS relapse (11 participants [18.3%]); upper respiratory tract infection and ALT increased (10 participants [16.7%] each); AST increased (7 participants [11.7%]); cough (6 participants [10.6%]); hyperlipidaemia (5 participants [8.3%]); GGT increased, diarrhoea, and flushing (4 participants [6.7%] each); and COVID-19, gastroenteritis, influenza, nasopharyngitis, blood uric acid increased, headache, anxiety, sleep disorder, and leukopenia (3 participants [5.0%] each).

Overall, the efficacy results from the Chinese participants this study were consistent with those of previous DMF studies. The safety profile of DMF in Chinese participants was generally consistent with the known safety profile of DMF and with previous DMF studies.

Name of Sponsor/Company: Biogen MA Inc./Biogen Idec Research Limited	**Individual Study Table Referring to Part <> of the Dossier** **Volume:** **Page:**	***(For National Authority Use only)***
Name of Finished Product: Tecfidera; BG00012	**Name of Active Ingredient:** Dimethyl Fumarate	**Study Indication:** Relapsing forms of multiple sclerosis (RMS)
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