

Real-World Safety and Efficacy Outcomes in RMS Patients Initiating Ublituximab in the Phase 4 Observational Study ENABLE

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CONCLUSIONS

The real-world safety, efficacy, and tolerability of ublituximab are consistent with the pivotal trials.

On-treatment annualized-relapse rate (ARR) was 0.014, with 99.2% of participants reporting no relapses on ublituximab.

The largest category of patients starting ublituximab in ENABLE are treatment naïve followed by transitions from prior B-cell therapies.

Significantly improved tolerability was observed in the real-world compared to pivotal trials. First-dose infusion-related reactions (IRRs) were significantly lower compared to pivotal trials.

Most IRRs were Grade 1 or Grade 2, resolved completely, and decreased in frequency over time.

Overall safety profile remained consistent with the pivotal trials.

As an observational study, an inherent limitation is that participants are treated per standard of care at sites with heterogeneous data collection, thus leading to missing inputs for some categories (e.g., MRI).

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- BRIUMVI® (ublituximab-xiyy) Prescribing Information. TG Therapeutics, Inc. 2026

DISCLOSURES:

Carrie M. Hersh has received speaking, consulting, and advisory board fees from Genentech, Genzyme, Biogen, Novartis, EMD-Serono, Bristol Myers Squibb, TG Therapeutics, Horizon Therapeutics, and Alexion. She has received research support paid to her institution by Biogen, Novartis, Bristol-Myers Squibb, National MS Society, and Patient-Centered Outcomes Research Institute (PCORI). Angel R Chinea has received advisory/consulting fees from Biogen, Genentech, Novartis, Sanofi-Genzyme, and Teva Neuroscience; research support from Biogen, Novartis, and Sanofi-Genzyme; speaker fees from Biogen, Genentech, Novartis, Sanofi-Genzyme, and Teva. Sidarth Dasari is a speaker for TG Therapeutics. Susan Anzalone has done ad boards for TG Therapeutics, Genentech, Biogen, Sanofi and has been a speaker for Teva, Biogen, Genentech, BMS, Sanofi. Matthew C Carraro has received consulting fees and/or Speaking fees on behalf of Biogen, Sanofi, Novartis, TG Therapeutics, EMD Serono, Octave Bioscience. Andrew Bouley has received research funding and/or honoraria for consulting/speaking engagements for the following companies: Biogen, EMD Serono, Genentech, Novartis, Sanofi, TG Therapeutics. Jacqueline Rosenthal is a consultant for Speaker's Bureaus, steering committees, and/or advisory boards at TG Therapeutics, Amgen, EMD Serono, and Biogen. Bhupendra Khatri is a consultant and a paid speaker for Bristol-Meyer Squibb, Sanofi, Genentech, Biogen, Alexion, TG Therapeutics, EMD Serono, UCB, Argenx, Terumo BCT. Diana Andino has received consulting and/speaking fees from Genentech, Amgen, Merck-EMD Serono, TG Therapeutics, Multiple Sclerosis Association of America, and DKB Med. Jean-Raphael Schneider is a speaker and consultant for Bristol Myers Squibb and Argenx. Jeanie Cote has received speaking/consulting fees from TG Therapeutics, Biogen, EMD Serono, BMS. Jonathan Calkwood has received honorarium or financial support for promotional speaking, advisory board services and funding for research from TG Therapeutics, AstraZeneca, Biogen, Genentech, Octave Bio, Sanofi and Zenas BioPharma. Emily Riser has received speaker fees from TG Therapeutics and received research support from TG Therapeutics, Alexion, Genentech, Novartis, Sanofi, and Corvitas. Jackie Parker, Karthik Bodhinathan, Peter Sportelli, Hari Miskin, and Edward Fox are employees of TG Therapeutics.

BACKGROUND

- Ublituximab targets a unique epitope of CD20 and is glycoengineered for enhanced antibody-dependent cellular cytotoxicity (ADCC) and enhanced Fcγ-receptor (FcγR) binding.^{1,2}
- Ublituximab demonstrated significant clinical benefit vs teriflunomide in ULTIMATE I and II, sustained for 6 years during the open-label extension (OLE).^{3,4,5} The overall safety and efficacy profile remained consistent over 6 years of continuous treatment.
- ENABLE is an ongoing Phase 4 observational study for patients with RMS treated with ublituximab. The study is designed to yield valuable real-world clinical evidence on the effectiveness, safety, and tolerability of ublituximab.
- Results from an interim analysis of the ongoing study are presented here.

RESULTS

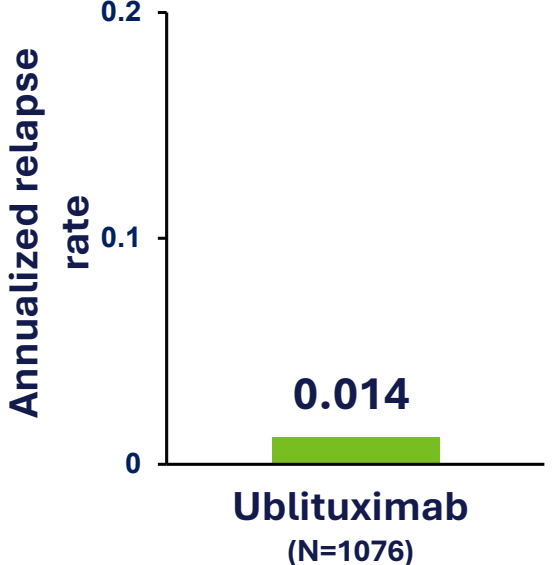
Table 1. Baseline Demographics	
Characteristic, Mean ± SD or n(%)	Ublituximab (N=1076)
Age (years)	43.1 ± 11.47
Gender, Female, n (%)	814 (75.7)
Race, n (%)	
White or Caucasian	763 (70.9)
Black or African American	197 (18.3)
Other	62 (5.8)
Unknown or Not Reported	41 (3.8)
Ethnicity, n (%)	
Hispanic or Latino	139 (12.9)
Not Hispanic or Latino	821 (76.3)
Unknown or Not Reported	116 (10.8)
Weight (kg)	85.1 ± 24.84
Height (cm)	167.61 ± 9.56
BMI (kg/m ²)	30.26 ± 8.24
BMI Category	
<30 kg/m ²	552 (51.3)
≥30 kg/m ²	409 (38.0)
Unknown or Not Reported	115 (10.7)

Baseline population included as of data cutoff on 1-July-2026; participants are actively enrolling.

- The average age of ENABLE participants (43.1 years) is higher than that of ULTIMATE I and II participants (35.4 years).
- 75.7% of participants are female, a higher proportion than in ULTIMATE I and II (~63%).
- 70.9% and 18.3% of participants are White/Caucasian and Black/African American, respectively. In ULTIMATE I and II, Black/African American participants were 1.5% of the trial population, owing to most sites being in Eastern Europe. Hispanic/Latino participants represented 12.9% of the overall ENABLE cohort.
- The number of participants with body mass index (BMI) ≥30 kg/m2 is 38.0%, which is relatively higher compared to ULTIMATE I/II participants (11.3%).

Figure 3. Summary of On-Treatment ARR and Relapses

ARR

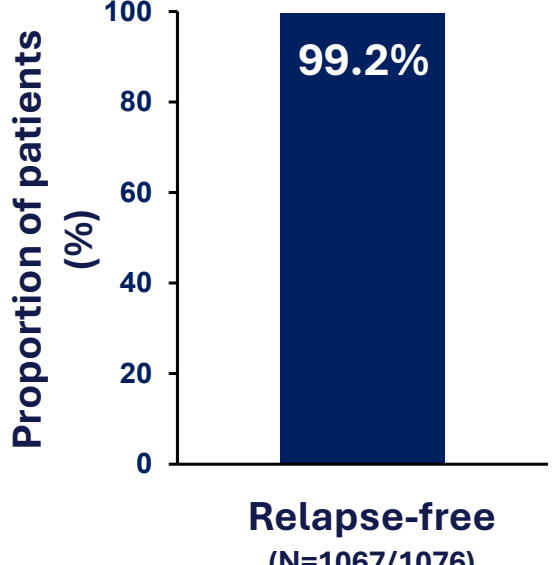


Annualized relapse rate

Ublituximab (N=1076)

0.014

Proportion relapse-free



Proportion of patients (%)

Relapse-free (N=1067/1076)

99.2%

ARR = Annualized relapse rate.

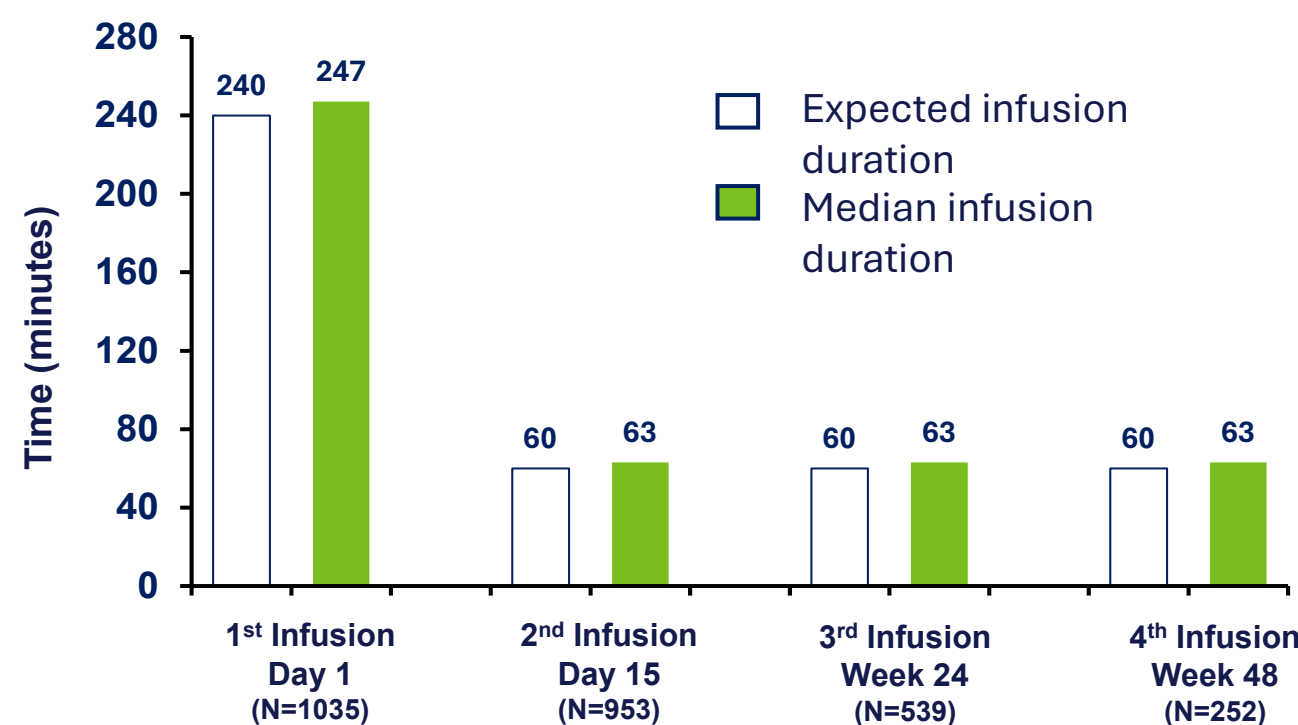
- On-treatment annualized relapse rate was 0.014, with cumulative treatment time of 848.2 patient-years.
- On-treatment relapses were rare, and 99.2% of participants reported no relapses during treatment with ublituximab.

Table 2. Baseline Disease History	
Characteristic, Mean ± SD or n (%)	Ublituximab (N=1076)
Time Since First MS Symptoms (years)	8.70 ± 9.09
Number of Relapses in the 2 Years Prior to Screening	0.7 ± 0.84
Number of Relapses in the 2 Years Prior to Screening, n (%)	
0	421 (39.1)
1	293 (27.2)
2	81 (7.5)
≥3	20 (1.8)
Unknown or Not Reported	261 (24.3)
Number of Baseline Gadolinium-enhancing (Gd+) Lesions	1.3 ± 5.16
Number of Baseline Gd+ Lesions, n (%)	
0	552 (51.3)
≥1	186 (17.3)
Unknown or Not Reported	338 (31.4)
Number of New and/or Enlarging T2 Hyperintense Lesions (compared to previous MRI scan)	1.5 ± 4.57
Number of New and/or Enlarging T2 Hyperintense Lesions, n (%)	
0	510 (47.4)
≥1	204 (19.0)
Unknown or Not Reported	362 (33.6)

Baseline population included as of data cutoff on 1-July-2026; participants are actively enrolling.

- ENABLE participants had slightly longer duration since onset of MS symptoms (8.70 years) vs ULTIMATE I and II (~7.4 years).
- Most of the participants were relapse-free (39.1%) or experienced 1 relapse (27.2%) in the 2 years prior to screening.
- At baseline, 51.3% of participants starting ublituximab had no Gd+ lesions and 47.4% did not have new/enlarging T2 lesions. However, approximately a third of the participants did not have MRI data to report at baseline.

Figure 4. Infusion Times in Ublituximab-Treated Participants from ENABLE

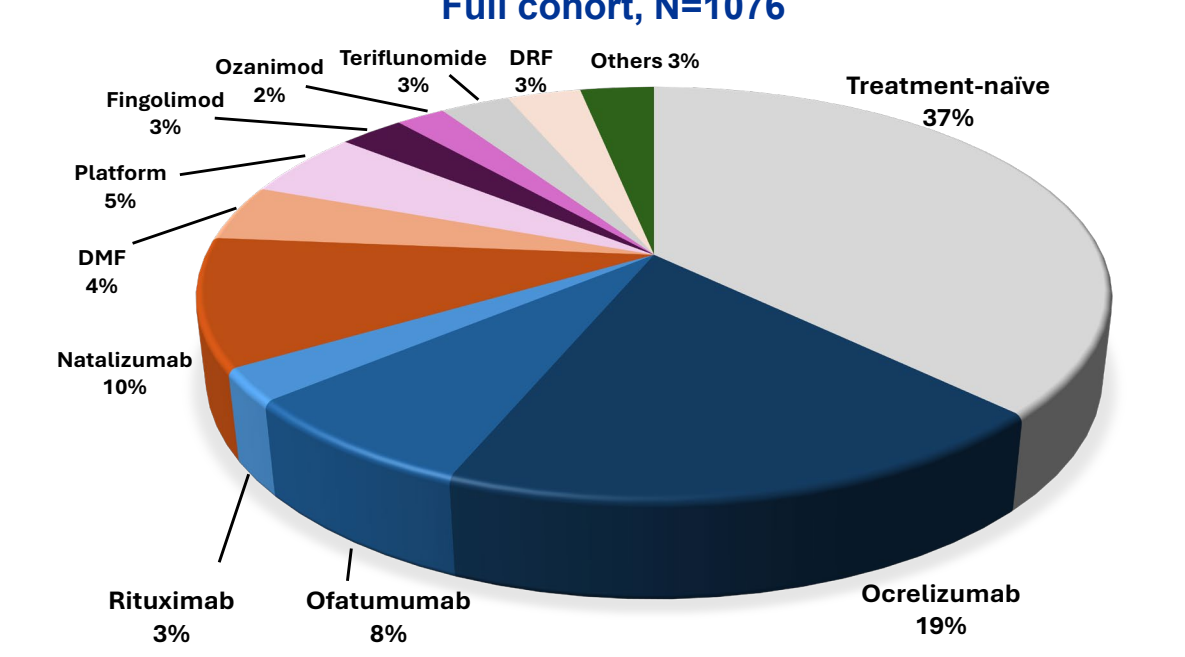


Infusion	Expected infusion duration (minutes)	Median infusion duration (minutes)
1 st Infusion Day 1 (N=1035)	240	247
2 nd Infusion Day 15 (N=953)	60	63
3 rd Infusion Week 24 (N=539)	60	63
4 th Infusion Week 48 (N=252)	60	63

IRR = Infusion-related reaction. Duration of infusion (in minutes) was defined as time between the start and end of infusion.

- Most infusions were completed within the specified time. The median infusion duration was 247 minutes for the 1st infusion and 63 minutes for the 2nd, 3rd, and 4th infusions, thus closely tracking the expected infusion durations.

Figure 1. Prior DMT Treatment History for MS Patients Starting Ublituximab on ENABLE

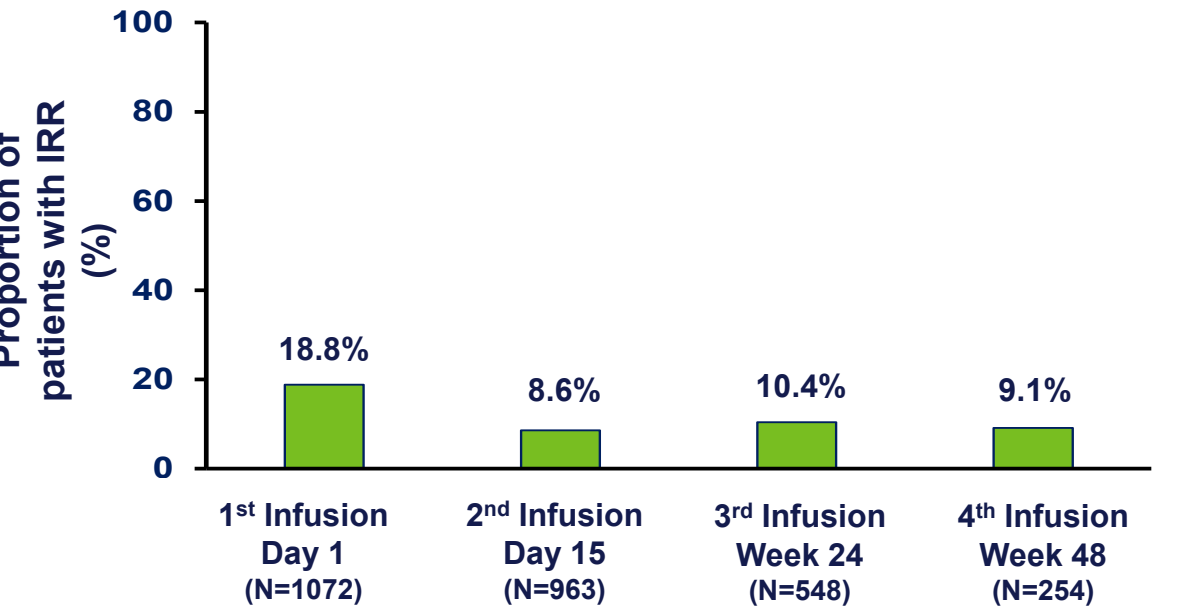


DMT	Percentage
Treatment-naïve	37%
Natalizumab	10%
Ocrelizumab	19%
Ofatumumab	8%
Rituximab	3%
DMF	4%
Platform	5%
Fingolimod	3%
Ozanimod	2%
Teriflunomide	3%
DRF	3%
Others	3%

Listed DMT's are immediately prior to start of ublituximab. DMF = dimethyl fumarate, DMT = disease-modifying treatment, DRF = diroxime fumarate. Missing input not included; N=22 (3.3%)

- Majority of patients (36%) was treatment-naïve at the start of ENABLE.
- A large proportion of patients (29%) transitioned to ublituximab from prior B-cell therapy (ocrelizumab, ofatumumab or rituximab) followed by patients who transitioned from natalizumab (12%).

Figure 5. IRRs in Ublituximab-Treated Participants



Infusion	Proportion of patients with IRR (%)
1 st Infusion Day 1 (N=1072)	18.8%
2 nd Infusion Day 15 (N=963)	8.6%
3 rd Infusion Week 24 (N=548)	10.4%
4 th Infusion Week 48 (N=254)	9.1%

IRR = Infusion-related reaction. Events assessed as IRRs by the treating physician.

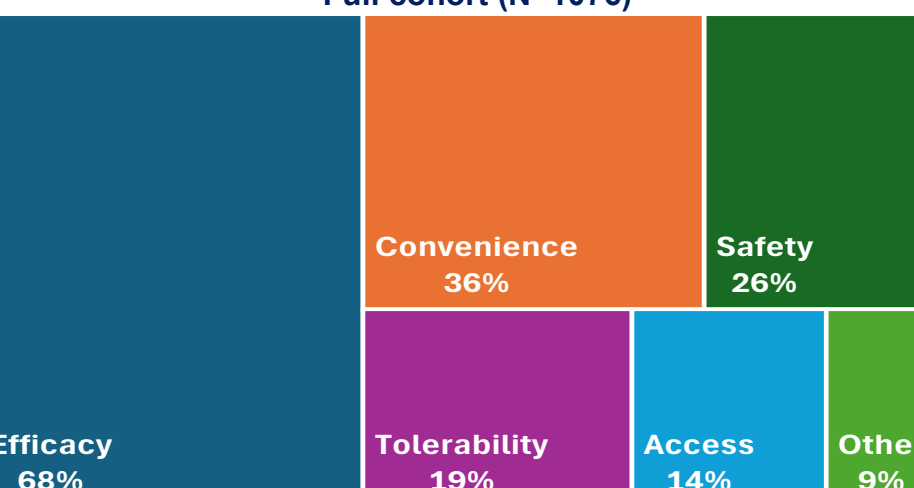
- IRRs were most frequently observed at the 1st infusion (18.8% of participants) and decreased in frequency during subsequent infusions.
- Most IRRs were Grade 1 or Grade 2 and resolved completely.

Table 3. Infusion-Related Adverse Events with an Incidence of at Least 2%

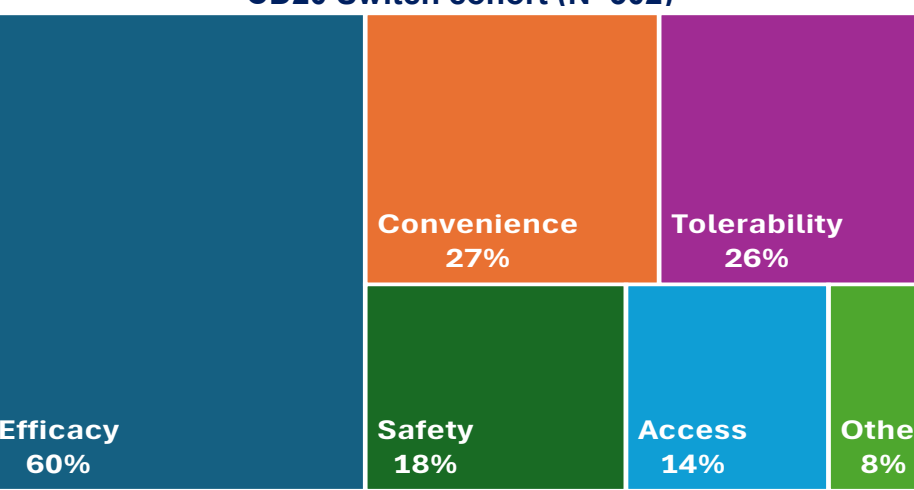
	Ublituximab, (n=658) n (%)
Headache	39 (5.9)
Nausea	26 (4.0)
Throat irritation	25 (3.8)
Pruritus	24 (3.6)
Flushing	18 (2.7)
Fatigue	14 (2.1)

Data cutoff: 1-July-2026.

Figure 2. Reasons for Starting Ublituximab in ENABLE



Reason	Percentage
Efficacy	68%
Convenience	36%
Safety	26%
Tolerability	19%
Access	14%
Other	9%



Reason	Percentage
Efficacy	60%
Convenience	27%
Tolerability	26%
Safety	18%
Access	14%
Other	8%

N=1076. Among the participants who provided a reason, prior DMT status was unknown for N=22. Each participant can submit multiple reasons for switch.

- Perceived efficacy of the prior DMT was the leading reason for initiating ublituximab treatment, reported by 68% and 60% of patients in the full and CD20 switch cohorts, respectively.
- In the full cohort, patients' decisions to start ublituximab included convenience (36%), safety (26%), tolerability (19%), and access (14%) of the prior DMT compared to ublituximab.
- In the CD20 switch cohort, the top reasons for switch to ublituximab included convenience (27%), tolerability (26%), and safety (18%).

Table 4. Adverse Events with an Incidence Rate of at Least 1%

Adverse event	Ublituximab, (n=1076) n (%)
Any TEAE	408 (37.9)
IRR	255 (23.7)
Headache	48 (4.5)
Fatigue	35 (3.3)
Pain	18 (1.7)
Insomnia	17 (1.6)
Urinary tract infection	17 (1.6)
Arthralgia	15 (1.4)
Nausea	15 (1.4)
Upper respiratory tract infection	15 (1.4)
Dizziness	11 (1.0)

Data cutoff: 1-July-2026. IRR = Infusion-related reaction, TEAE = Treatment emergent adverse event.

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