Teriflunomide (Aubagio®) International Pregnancy Registry: Enrollment Update

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OBJECTIVE
• To provide the study design and updated enrolment for the International Teriflunomide Pregnancy Exposure Registry

INTRODUCTION
Teriflunomide is a once-daily oral immunomodulator approved for the treatment of patients with relapsing forms of MS in over 25 countries, including the United States and countries of the European Union. As of August 2018, over 95,000 patients were being treated with teriflunomide, with a total real-world exposure of approximately 186,000 patient-years as of December 2017.

In addition to a consistent, well-characterized safety and tolerability profile,1 teriflunomide has demonstrated consistent efficacy on clinical and MRI disease activity in patients with relapsing forms of MS1–5 and in those who experienced a first clinical episode suggestive of MS.1

Use of teriflunomide is contraindicated in pregnant women and in women of reproductive potential who are not using an effective contraception because of the potential for foetal harm and the observation of teratogenicity and embryo-fetal lethality in the offspring of teriflunomide-treated rats and rabbits.1

Rats exhibit greater sensitivity to the effects of teriflunomide than humans, which may explain why similar plasma exposures of teriflunomide have resulted in teratogenicity in animals but not, to date, in humans.2

Teriflunomide elimination can be accelerated in patients by the administration of cholestyramine or activated charcoal after stopping teriflunomide treatment.

Teriflunomide is the principal active metabolite of leflunomide (approved since 1998) and is a member of the pyrimidine antimitotic antineoplastic agents.1

The objective of the registry is to enrol 196 pregnant women, projected to result in 104 live births; this sample size is estimated to provide an 80% power to detect a 3.5-fold increase in the rate of birth defects associated with teriflunomide exposure versus EUROCAT®.

Analyses will be based on prospective cases of women with teriflunomide exposure during pregnancy prior to the knowledge, or perceived knowledge, of pregnancy outcome and assessed on a routine basis.2

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RESULTS
• Patient enrolment commenced in early 2015 and is planned to continue until December 2019.

– As of 23 July 2018, 22 patients have been recruited from 8 countries.

– Outcomes are available for 18 pregnancies at the interim analysis, with a cutoff date of 23 July 2018.

– There have been 16 live births.

– There were no abnormalities reported among 15 of the 16 live births.

One case of ectopic pregnancy identified prospectively.

– One patient in Spain had an elective termination that was motivated by the abnormal result of a prenatal test or by any suspicion of a potential birth defect.

One serious adverse event was reported in a retrospective case:

– Report as death of one of twin foetuses (in utero) as possibly related to teriflunomide exposure, with the spontaneous abortion of one fetus per physiopathology as not related to teriflunomide exposure

– The surviving twin was delivered prematurely, with no abnormalities reported to date.

Acknowledgments and Disclosures
The authors were reviewed by Dennis Fithian, PhD, Karen Lu, PhD, and Jonathan Valenzano, PhD, of Sanofi. Medical writing support for this paper was provided by Beth Wieland of Michael Fiddes Communications, end-of-study support provided by Seraphina Murphy, Onward, UK, and Sanofi for this paper.

DISCLOSURES
DC: Consulting fees Bayer Schering, Biogen, Medfly, Merck Serono, Novartis, Roche, Sanofi, Teva Neuroscience, research support Biogen Idec, Genzyme, Pfizer, Merck Serono, Merck-sharpe & Dohme, Merck, Teva Neuroscience. NS: Support for congress attendance, Sanofi, Genzyme. EE: Employees of Sanofi and Medfly. FD: Employees of Sanofi, with ownership interest. AG: Consulting fees Biogen, Genzyme, Pfizer, Merck, Schering-Plough, Salix, Sanofi, Novartis, Genzyme.

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