

## Disease Modifying Therapies for Relapsing-Remitting and Primary Progressive Multiple Sclerosis: Effectiveness and Value

*Addendum to Draft Background and Scope*  
July 18, 2016

ICER has expanded the draft scope for its upcoming review of disease-modifying therapies (DMTs) for multiple sclerosis (MS) to include the use of ocrelizumab and rituximab for patients with primary-progressive multiple sclerosis (PPMS). The primary comparator will be best supportive care, as there is currently no drug with FDA approval for the treatment of PPMS. The decision to expand the scope of the MS review reflects feedback from patients, clinicians, and other stakeholders that an analysis of all DMTs for MS would be of greatest utility, as well as the Food and Drug Administration's (FDA) June 27 announcement that it had granted Priority Review Designation to ocrelizumab for both PPMS and relapsing-remitting multiple sclerosis (RRMS) indications with a decision date of December 28, 2016.<sup>1</sup> Rituximab has been studied for the treatment of PPMS although it is not labeled for this indication.<sup>2</sup>

This addendum will be open to public comment until **Friday, August 12, at 5:00 pm PT**. The public comment period for the draft scoping document released on July 1 will not be re-opened.

Approximately 10-15% of MS patients have PPMS, a clinical course that is characterized by steadily worsening neurologic function without remissions or acute episodes.<sup>3,4</sup> On average, the onset of PPMS occurs 10 years later than RRMS and patients with PPMS experience more severe disability.<sup>3,4</sup> While RRMS affects around three times as many women as men, PPMS affects both genders in approximately equal numbers.<sup>3</sup>

The modifications to the draft scope are as follows:

- **Population:** Expanded to include patients aged 18 and older with PPMS.
- **Interventions:** Modified to include PPMS indication of ocrelizumab and off-label use of rituximab for patients with PPMS.
- **Comparators:** The primary comparator for the use of ocrelizumab and rituximab in patients with PPMS will be best supportive care.
- **Outcomes:** We will look for the same outcomes identified for the RRMS scope with the exception of advancement to secondary-progressive MS.

We will develop a simulation model to assess the lifetime cost-effectiveness of ocrelizumab and rituximab for patients with PPMS. In an additional analysis, we will explore the potential budgetary impact of each treatment over a five-year time horizon.

### References

1. FDA Grants Priority Review for Genentech's OCREVUS (Ocrelizumab) Biologic's License Application [press release]. June 27 2016.
2. Hawker K, O'Connor P, Freedman MS, et al. Rituximab in patients with primary progressive multiple sclerosis: results of a randomized double-blind placebo-controlled multicenter trial. *Annals of neurology*. 2009;66(4):460-471.
3. Goodin DS. The epidemiology of multiple sclerosis: insights to disease pathogenesis. *Handbook of clinical neurology*. 2014;122:231-266.
4. National Multiple Sclerosis Society. Primary progressive MS (PPMS). <http://www.nationalmssociety.org/What-is-MS/Types-of-MS/Primary-progressive-MS>. Accessed July 13, 2016.