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

Final Addendum to Background and Scope
September 6, 2016

Stakeholder Input

This updated scoping document addendum reflects input gathered from patient advocacy organizations, clinical societies, and pharmaceutical manufacturers during a four-week public comment period. We have updated the background section to clarify our rationale for including ocrelizumab and rituximab in the review while excluding other disease-modifying therapies that have been studied for use in primary-progressive multiple sclerosis (PPMS). We have also removed relapses as an outcome of interest and have updated our description of the clinical course of PPMS.

Background

Based on input from patients, clinicians, and other stakeholders on the original scope focusing on relapsing-remitting multiple sclerosis (RRMS), ICER has expanded the scope to include the use of ocrelizumab and rituximab for patients with PPMS. The expansion reflects feedback from these stakeholders that to fully understand the value that ocrelizumab represents to patients and the health care system, its utility for both PPMS and RRMS should be evaluated. In addition, the Food and Drug Administration (FDA) announced on June 27 that it had granted Priority Review Designation to ocrelizumab for both PPMS and RRMS, with a decision date of December 28, 2016. The same stakeholders recommended the inclusion of rituximab because it has been studied for the treatment of PPMS although it is not labeled for this indication. While other DMTs have been studied for use in PPMS and are currently used off-label, stakeholders expressed greatest interest in the inclusion of rituximab because its mechanism of action is similar to that of ocrelizumab.

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

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, as there is currently no drug with FDA approval for the treatment of PPMS.
- **Outcomes**: We will look for the same outcomes identified for the RRMS scope with the exception of advancement to secondary-progressive MS and relapse rates. Though relapses may occur in PPMS, they have not been included as outcomes in studies of the disease course.

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