Appeal re: Ocrevus

To Whom It May Concern:

This is a request for (re-consideration of your denial of coverage OR exception to the formulary) for my patient _____ (insert name______) who has a diagnosis of (primary progressive OR a relapsing form of) multiple sclerosis.

_____ (Insert name)_____ is an appropriate candidate for treatment with Ocrevus, which I believe offers her/him the best treatment outcome at this time due to:

(choose one or more of the following and fill in the relevant information):

✓ (Her/his) past benefit from this therapy as suggested by (DESCRIBE e.g., no relapses/slower relapse rate, little/no evidence of disease activity on MRI scans, other). There is no clinical indication for changing treatments for this patient now stabilized on Ocrevus.

✓ the established risk-benefit profile of Ocrevus, which my patient and I have discussed and agree is the most appropriate first-line treatment for his/her multiple sclerosis.

✓ [his/her] inability to tolerate the side effects associated with previously prescribed medications (LIST side effects, e.g., flu-like symptoms, injection site reactions)

✓ ...a suboptimal response to previously prescribed disease modifying therapies that have a different mechanism of action than Ocrevus.

○ (list each medication and describe, e.g., additional relapses, MRI activity, disease progression

✓ ... contraindications associated with other disease-modifying therapies (LIST for example, allergies or hypersensitivities to active ingredients, depression, JC virus antibody status, history of prior treatment with chemotherapy) that would make alternative treatment unsustainable or unsafe for (him/her).
Please refer to the consensus paper by the Multiple Sclerosis Coalition entitled *The Use of Disease-Modifying Therapies in Multiple Sclerosis: Principles and Current Evidence* for evidence in support of early and ongoing access to the full range of therapy options for patients with MS.

**If patient has primary progressive disease, include the following paragraph:**

The ORATORIO study involving people with primary progressive MS, which compared Ocrevus to inactive placebo, met its primary endpoint, showing treatment with Ocrevus significantly reduced the risk of progression of clinical disability by 24% compared with placebo in 732 people. Compared to placebo, Ocrevus also reduced the time required to walk 25 feet by 29%, and decreased the volume of brain lesions.¹

**If patient has a relapsing form of MS, include the following paragraph:**

In the OPERA I and OPERA II studies involving people with relapsing MS, which compared ocrelizumab to interferon beta-1a (Rebif, ® EMD Serono and Pfizer), Ocrevus significantly reduced the annualized relapse rate by up to 47% compared with Rebif over two years in a total of 1,656 people with relapsing MS. In addition, Ocrevus significantly delayed confirmed progression of disability on the EDSS scale by 40% compared with Rebif. Ocrevus also significantly reduced active inflammation observed on MRI scans by up to 95%, and total damage on MRI scans by up to 83% compared with Rebif.²

For additional information about this patient, please contact (__________insert clinical practice contact info____________).

Sincerely,

John Doe, MD


Ocrelizumab versus Placebo in Primary Progressive Multiple Sclerosis.

Montalban X1, Hauser SL1, Kappos L1, Arnold DL1, Bar-Or A1, Comi G1, de Seze J1, Giovannoni G1, Hartung HP1, Hemmer B1, Lublin F1, Rammohan KW1, Selmaï K1, Traboulsee A1, Sauter A1, Masterman D1, Fontoura P1, Belachew S1, Garren H1, Mairon N1, Chin P1, Wolinsky JS1; ORATORIO Clinical Investigators. Collaborators (206)


BACKGROUND:
An evolving understanding of the immunopathogenesis of multiple sclerosis suggests that depleting B cells could be useful for treatment. We studied ocrelizumab, a humanized monoclonal antibody that selectively depletes CD20-expressing B cells, in the primary progressive form of the disease.

METHODS:
In this phase 3 trial, we randomly assigned 732 patients with primary progressive multiple sclerosis in a 2:1 ratio to receive intravenous ocrelizumab (600 mg) or placebo every 24 weeks for at least 120 weeks and until a prespecified number of confirmed disability progression events had occurred. The primary end point was the percentage of patients with disability progression confirmed at 12 weeks in a time-to-event analysis.

RESULTS:
The percentage of patients with 12-week confirmed disability progression was 32.9% with ocrelizumab versus 39.3% with placebo (hazard ratio, 0.76; 95% confidence interval [CI], 0.59 to 0.98; P=0.03). The percentage of patients with 24-week confirmed disability progression was 29.6% with ocrelizumab versus 35.7% with placebo (hazard ratio, 0.75; 95% CI, 0.58 to 0.98; P=0.04). By week 120, performance on the timed 25-foot walk worsened by 38.9% with ocrelizumab versus 55.1% with placebo (P=0.04); the total volume of brain lesions on T2-weighted magnetic resonance imaging (MRI) decreased by 3.4% with ocrelizumab and increased by 7.4% with placebo (P<0.001); and the percentage of brain-volume loss was 0.90% with ocrelizumab versus 1.09% with placebo (P=0.02). There was no significant difference in the change in the Physical Component Summary score of the 36-Item Short-Form Health Survey. Infusion-related reactions, upper respiratory tract infections, and oral herpes infections were more frequent with ocrelizumab than with placebo. Neoplasms occurred in 2.3% of patients who received ocrelizumab and in 0.8% of patients who received placebo; there was no clinically significant difference between groups in the rates of serious adverse events and serious infections.

CONCLUSIONS:
Among patients with primary progressive multiple sclerosis, ocrelizumab was associated with lower rates of clinical and MRI progression than placebo. Extended observation is required to determine the long-term safety and efficacy of ocrelizumab. (Funded by F. Hoffmann-La Roche; ORATORIO ClinicalTrials.gov number, NCT01194570.).
Background: B cells influence the pathogenesis of multiple sclerosis. Ocrelizumab is a humanized monoclonal antibody that selectively depletes CD20+ B cells.

Methods: In two identical phase 3 trials, we randomly assigned 821 and 835 patients with relapsing multiple sclerosis to receive intravenous ocrelizumab at a dose of 600 mg every 24 weeks or subcutaneous interferon beta-1a at a dose of 44 μg three times weekly for 96 weeks. The primary end point was the annualized relapse rate.

Results: The annualized relapse rate was lower with ocrelizumab than with interferon beta-1a in trial 1 (0.16 vs. 0.29; 46% lower rate with ocrelizumab; P<0.001) and in trial 2 (0.16 vs. 0.29; 47% lower rate; P<0.001). In prespecified pooled analyses, the percentage of patients with disability progression confirmed at 12 weeks was significantly lower with ocrelizumab than with interferon beta-1a (9.1% vs. 13.6%; hazard ratio, 0.60; 95% confidence interval [CI], 0.45 to 0.81; P<0.001), as was the percentage of patients with disability progression confirmed at 24 weeks (6.9% vs. 10.5%; hazard ratio, 0.60; 95% CI, 0.43 to 0.84; P=0.003). The mean number of gadolinium-enhancing lesions per T1-weighted magnetic resonance scan was 0.02 with ocrelizumab versus 0.29 with interferon beta-1a in trial 1 (94% lower number of lesions with ocrelizumab, P<0.001) and 0.02 versus 0.42 in trial 2 (95% lower number of lesions, P<0.001). The change in the Multiple Sclerosis Functional Composite score (a composite measure of walking speed, upper-limb movements, and cognition; for this z score, negative values indicate worsening and positive values indicate improvement) significantly favored ocrelizumab over interferon beta-1a in trial 2 (0.28 vs. 0.17, P=0.004) but not in trial 1 (0.21 vs. 0.17, P=0.33). Infusion-related reactions occurred in 34.3% of the patients treated with ocrelizumab. Serious infection occurred in 1.3% of the patients treated with ocrelizumab and in 2.9% of those treated with interferon beta-1a. Neoplasms occurred in 0.5% of the patients treated with ocrelizumab and in 0.2% of those treated with interferon beta-1a.

Conclusions: Among patients with relapsing multiple sclerosis, ocrelizumab was associated with lower rates of disease activity and progression than interferon beta-1a over a period of 96 weeks. Larger and longer studies of the safety of ocrelizumab are required. (Funded by F. Hoffmann-La Roche; OPERA I and II ClinicalTrials.gov numbers, NCT01247324 and NCT01412333, respectively.)

Comment in

- **B-Cell Depletion - A Frontier in Monoclonal Antibodies for Multiple Sclerosis.** [N Engl J Med. 2017]