FAQ – Ocrelizumab (OCREVUS*)

1. **What is ocrelizumab?**

Ocrelizumab is a monoclonal antibody that specifically targets CD20, a protein that is found on the surface of white blood cells called B lymphocytes or B cells. Because of this property, ocrelizumab acts as an immunomodulatory drug by targeting and removing potentially harmful B cells in people living with MS. Ocrelizumab is developed by Hoffmann–La Roche's subsidiary Genentech.

2. **Has ocrelizumab been approved for use in multiple sclerosis (MS)?**

Genentech submitted drug marketing applications for ocrelizumab for the treatment of both primary progressive MS and relapsing forms of MS. In February 2016, the U.S. Food and Drug Administration (FDA) granted ocrelizumab "Breakthrough Therapy Designation" for primary progressive MS, which meant that review of the submission would be accelerated. In July of 2016 this designation was upgraded to "Priority Review Designation". On March 28, 2017 ocrelizumab was approved by the FDA for the treatment of primary progressive and relapsing forms of MS. This means that, at this time, only people with MS in the U.S. can access the treatment. With regards to approval in Canada, an application has been submitted to Health Canada and a decision is pending. The MS Society will continue to monitor the status of the submission to Health Canada.

3. **What data did the FDA use to form the basis of their approval of ocrelizumab for primary progressive MS?**

The FDA's decision was based on findings from a phase III clinical trial called ORATORIO. During the trial, 732 primary progressive MS patients were randomly selected to receive ocrelizumab at a dose of 600 mg (given as two 300 mg intravenous infusions 14 days apart) or a mock drug (placebo). The primary endpoint was the proportion of individuals who experienced disability progression sustained over 12 weeks, as determined by an increase in one point on the EDSS score. The results of the trial, which were published in the New England Journal of Medicine, found that treatment with ocrelizumab significantly reduced the percentage of patients with disability progression at 12 weeks (32.9% treated with ocrelizumab versus 39.3% with placebo). Additionally, ocrelizumab significantly reduced the proportion of patients with disability progression at 24 weeks (29.6% on ocrelizumab compared to 35.7% with placebo). Treatment with ocrelizumab resulted in improvements in a number of secondary outcomes, such as the Timed 25-foot Walk test which looks at mobility, and imaging measures like lesion volume and brain volume loss.

4. **What other MS trials for ocrelizumab have been conducted?**

Genentech previously conducted two other ocrelizumab phase III trials, called OPERA I and OPERA II. These trials were randomized, double-blind, crossover, global multi-centre studies evaluating the efficacy and safety of ocrelizumab compared with the standard MS treatment interferon beta-1a in people with relapsing-remitting and secondary-progressive MS with relapses. New data from these trials were also presented at ECTRIMS, demonstrating superior efficacy across clinical and imaging measures compared with interferon beta-1a, as well as a sound safety profile with infusion site reactions, upper respiratory infections and influenza reported.

5. **What do these outcomes mean for people living with progressive MS?**

The ORATORIO study, along with the results from OPERA I and OPERA II in relapsing MS, indicates that B cells are an important factor driving inflammation in all subtypes of MS. How B cells interact with other parts of the immune system, including T cells, is an area of ongoing research.

Based on the promising findings from all three-pivotal phase III ocrelizumab clinical trials, ocrelizumab will be the first ever disease-modifying therapy approved for treatment of primary progressive MS.

6. What are the side effects have been reported for ocrelizumab?

The most common adverse events reported in the ocrelizumab group in the ORATORIO trial were infusion-related reactions and infections (nasopharyngitis, urinary tract infections, influenza and upper respiratory track infections). Five deaths were reported in the ORATORIO trial, four of which were in the ocrelizumab group and included; pulmonary embolism, pneumonia, and pancreatic cancer. One participant from the placebo group died as a result of a non-medical reason.

In a phase II clinical trial involving 218 participants with relapsing-remitting MS, one participant taking high-dose ocrelizumab (2000mg) died from brain edema (swelling). The connection between this death and ocrelizumab is unclear. Ocrelizumab carries other serious side effects which will be made available through the product monograph once it is published. Progressive multifocal leukoencephalopathy (PML) has not been reported in individuals treated with ocrelizumab however there is still a potential risk of developing PML.

7. When will ocrelizumab be available in Canada?

Genetech has submitted a drug marketing application for ocrelizumab to Health Canada. Until the drug has received marketing approval the company cannot sell the drug in Canada. Once approved, individuals with private insurance may have access to the drug. Criteria for reimbursement under private plans vary, and individuals should check with their benefit providers. In terms of provincial drug coverage, the provincial governments will determine if they will reimburse the cost of the drug based on input from the Common Drug Review conducted by the Canadian Agency for Drugs and Technologies in Health (CADTH). Quebec conducts an independent review through the Institut national d'excellence en sante et en services sociaux (INESS). The MS Society will provide updates on Health Canada approval and drug access as they become available.

8. Why was ocrelizumab approved in the U.S. but not in Canada?

Each regulatory body conducts a separate review of new drugs. Timelines and approval criteria will vary from country to country. Health Canada must conduct its own review of all data submitted prior to deciding to market a new drug in Canada. The MS Society of Canada will provide updates on the status of ocrelizumab in Canada when they are made public by Health Canada.

9. Can Canadians travel to the U.S. for treatment with ocrelizumab?

Individuals are encouraged to discuss treatment options with their healthcare team. The MS Society of Canada does not provide a list of clinics in the U.S. who offer ocrelizumab infusions. There are a number of important considerations that one should be mindful of when considering traveling abroad for medical treatments. Click here to read through these considerations in more detail.

10. How much will ocrelizumab cost in Canada?

It is not known what the cost of ocrelizumab will be in Canada. Roche estimates the cost of ocrelizumab in the U.S. to be $65,000USD per year.