

Actively Advocating: An update
from MSNZ on Ocrelizumab

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Overview

This report has been developed to update Regional Societies about the progress and developments of MSNZ's advocacy work in relation to Ocrevus (Ocrelizumab) for people with MS (PwMS).

Ocrelizumab

In March 2017 the FDA in America approved Ocrelizumab as a treatment for RRMS and PPMS. MSNZ has reviewed the positive research and been in discussions with the pharmaceutical company Roche regarding the treatment since 2016. In August 2016 Roche submitted Ocrelizumab for Medsafe approval which can take over 12 months in most cases. This is still under review and we hope to receive further information by October 2017.

What is Ocrelizumab¹

OCREVUS is a humanised monoclonal antibody designed to selectively target CD20-positive B cells, a specific type of immune cell thought to be a key contributor to myelin (nerve cell insulation and support) and axonal (nerve cell) damage. This nerve cell damage can lead to disability in people with MS. Based on preclinical studies, OCREVUS binds to CD20 cell surface proteins expressed on certain B cells, but not on stem cells or plasma cells, and therefore important functions of the immune system may be preserved.

¹ <http://www.roche.com/media/store/releases/med-cor-2017-03-29.htm>

How is Ocrelizumab Administered?

OCREVUS is administered by intravenous infusion:

First & second infusions (day 1 and day 15):
Pre-medications 30-60 mins before infusion
Infusion 2.5 hours
Observe for at least one hour after infusion

Subsequent infusions
Pre-medications 30-60 mins before infusion
Infusion 3.5 hours
Observe for at least one hour after infusion

Side effects

Patients most commonly experienced mild to moderate infusion reactions and upper respiratory tract infections. There were also slight increased risks of oral herpes reactivation and neoplasms which should be considered when assessing treatment appropriateness.

Read more: [Safety of Ocrelizumab in Multiple Sclerosis: Updated Analysis in Patients with Relapsing and Primary Progressive Multiple Sclerosis - poster presented at the 69th American Academy of Neurology \(AAN\) Annual Meeting; April 22–28, 2017; Boston, MA, USA](#)

No cases of Progressive multifocal leukoencephalopathy (PML), a rare and potentially fatal viral brain disease were found during the trials. Since then one case in Germany has been found in an Ocrelizumab patient however causality has been assigned to the earlier use of Natalizumab (Tysabri). [Read more here about switching patients at high risk of PML](#).

More Information about Ocrelizumab

For more information about Ocrelizumab visit: <http://www.roche.com/media/store/releases/med-cor-2017-03-29.htm>

Ocrelizumab for Relapsing Remitting MS

Two identical trials involving 1656 people with RRMS, 821 of which received the proposed treatment, showed clear demonstrable evidence that relapses were reduced, the volume of brain lesions were significantly decreased and the reduction in disability progression. Trials OPERA 1 and OPERA 2 clearly showed in comparison to its Rebif (interferon beta-1a) trial comparator^{2 3}:

- 46% and 47% lower rate of relapses
- 40% lowered the risk of disability progression
- 33% higher disability improvement
- between 47.9% and 47.5% of the Ocrelizumab recipients had no evidence of disease activity over the trial period compared to 29.2% and 25.1% of those on the interferon.
- 94% and 95% lower number of T1 gadolinium enhancing lesions in those patients MRIs who were being administered Ocrelizumab than the interferon recipients

² [Hauser, S. L., et al, Ocrelizumab versus Interferon Beta-1a in Relapsing Multiple Sclerosis. N ENGL J MED \(2016\).](#)

³ [Calabresi, P. A., B-Cell Depletion — A Frontier in Monoclonal Antibodies for Multiple Sclerosis. N ENGL J MED \(2016\)](#)

- 77% and 83% lower number of new or growing T2 hyperintense lesion
- the longer the patients underwent treatment the number of new lesions decreased

Submission for funding for Ocrelizumab for Relapsing Remitting MS

In August 2016 Roche applied to Medsafe Ocrelizumab to be registered for use in New Zealand. We expect to hear by October 2017 on the progress of this application.

On 22nd May 2017 Roche applied to PHARMAC for Ocrelizumab to be listed on the Pharmaceutical Schedule for RRMS under the pre-existing MS Treatments Special Authority Criteria for review at the August meeting. Despite not yet having Medsafe approval this decision was made to speed the process along and have the treatment available in NZ at the earliest opportunity.

MSNZ wrote to PHARMAC in support of this application on Monday 22nd May. However, PHARMAC have advised on the 9th June 2017 that the application will not be considered until Medsafe approval is confirmed. This is likely to be at PTAC's February 2018 meeting if a positive Medsafe result is achieved by October 2017. While this is disappointing, we are unable to speed through this process.

Ocrelizumab for Primary Progressive

There has been a lot of media interest since Ocrelizumab was approved by the FDA as it is the first treatment in the world that has shown proven benefits for people with Primary Progressive MS.

A Phase III study (ORATORIO) involving 732 participants with PPMS was undertaken which showed evidence of reduce signs of disease activity in the brain (MRI lesions) compared with placebo with a median follow-up of three years.⁴ The results showed that at 120-weeks:

- on the timed 25-foot walk worsened by 38.9% with ocrelizumab versus 55.1% with placebo
- 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
- the percentage of brain-volume loss was 0.90% with ocrelizumab versus 1.09% with placebo

Should Ocrelizumab for PPMS be funded in NZ it will have its own special authority criteria developed. Roche has consulted with MSNZ and an Advisory Board around the potential criteria. We foresee that there will be special authority criteria based on the research findings. Roche is currently working on the application for funding for Ocrelizumab.

MSNZ is continuing to work with those involved to ensure people receive access based on the research evidence and will make a submission to PHARMAC for funding for PPMS as well as RRMS.

Ocrelizumab Global Compassionate Programme

MSNZ has been advised that there is a Global Compassionate Programme currently open for those with PPMS. A limited number of spaces are available and as at 13 June 2017 9 of the 20 places have been filled. Numbers are allocated based on DHB population. It is important to note that the Global Compassionate Programme is only open in NZ until the treatment is registered by Medsafe.

⁴ [Montalban, X, et al, Ocrelizumab versus Placebo in Primary Progressive Multiple Sclerosis. N ENGL J MED \(2016\).](#)

PwMS cannot self-register as this must be done by a neurologist based on their recommendation that the treatment will provide clinical benefit. PwMS who are successfully registered on the programme will continue to receive fully funded access to Ocrelizumab until either:

- a) PHARMAC agree to fund the treatment in NZ for PPMS, or if funding does not happen;
- b) until the patient chooses to discontinue or it is not clinically appropriate any longer on the advice of their neurologist.

Ocrelizumab Global Compassionate Programme Criteria

The criteria for the Compassionate Programme is:

- 1) A diagnosis of PPMS under the McDonald 2010 criteria. For some patients, an MRI and lumbar puncture for CSF may be required.
- 2) EDSS score 2-6.5
- 3) No history of Relapsing MS
- 4) The patient is considered by the physician to have a potential positive benefit/risk ratio for treatment with ocrelizumab. The clinician is likely to consider several patient factors in assessing whether the treatment is clinically appropriate.

More information for people with PPMS

If people with PPMS are interested in accessing Ocrelizumab we encourage them to contact their Neurologist or MS/Neurology Nurse. To access the programme a PwMS cannot self-refer, this must be done by a Neurologist. Those interested in the treatment should carefully review with their Neurologist whether the treatment is right for them, the potential side effects and risks involved and what the treatment involves.

More information for Neurologists

For more information about the Global Compassionate Programme and to find out more about registering patients, Neurologists are encouraged to contact the Roche NZ Medical Information Line:

- Phone: 0800 276 243 (8.30am-4.30pm)
- Email: aucklandmedinfon@roche.com

Potential Issues

While we appreciate the impact this will have on Neurology departments and infusion clinics we also see it as our ethical responsibility to advise PwMS that the treatment is accessible and available now through the Compassionate Programme. Issues that may restrict access include:

- 1) An application for Medsafe Registration was made in August 2016. The Programme will be open until the treatment is registered with Medsafe. This is expected to be until October.
- 2) There are only 20 spaces on the programme. An Advisory Board has allocated numbers based on DHB population. This means that most of the smaller DHBs have 1 allocated space. Should any spots be unused by 1st September 2017 these will be made open to any DHB. If your local Neurologist is not aware of the Programme you may encourage them to contact Roche.

- 3) We understand waiting times at many DHBs are currently extensive in some areas. Clients may wish to discuss with their Neurologist or MS Nurse over the phone in the first instance whether they will be a good candidate.
- 4) Many people with PPMS will not have seen a Neurologist in many years and so the total number of PPMS, is unknown. It is currently estimated that there are around 584 people with PPMS in NZ and around 33% who will be eligible under the criteria for treatment. These estimated figures are based on the Prevalence and Incidence Studies funded by MSNZ.

How can you be of assistance?

1. We would be interested in speaking to people who join the Compassionate Programme. If you are successfully registered onto the Programme and would like to update us on your progress please contact info@msnz.org.nz.
2. Provide feedback to MSNZ about the impacts of our advocacy to help demonstrate the positive outcomes of our work. Information we are interested may include but is not limited to: What has accessing treatments meant to you? How has it improved your life?
3. MSNZ is also interested to understand the issues impacting and restricting access to services and treatments.