Media Release

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People with highly disabling form of multiple sclerosis denied access to first and only proven treatment due to inflexible medicine assessment system

- *NICE has rejected NHS access for OCREVUS® ▼ (ocrelizumab) for people with early primary progressive multiple sclerosis (PPMS) after being unable to consider the indication-specific price offered by Roche in order to make ocrelizumab cost-effective to the NHS*[1]
- *PPMS, a highly disabling form of multiple sclerosis (MS), affects around 10-15,000 people in the UK often impacting mobility, employment and families*[2]
- *Roche remains committed to working with the MS community, NICE, NHS England and the Department of Health and is confident a solution can be found so people with early PPMS have access to the first and only licensed disease-modifying treatment*

10 September 2018, Welwyn Garden City – The assessment body that decides which treatments are made available to NHS patients today announced it has not recommended ocrelizumab, the first and only licensed disease-modifying treatment, for people with early PPMS.[1] In clinical trials ocrelizumab has shown it could delay the need for a wheelchair by seven years in people with early PPMS.[3]

Ocrelizumab is licensed for both relapsing-remitting multiple sclerosis (RRMS) and PPMS in over 65 countries globally, with over 50,000 people having been treated with this first-in-class treatment. Ocrelizumab is currently approved for use on the NHS for people living with active RRMS when alemtuzumab is contraindicated or otherwise unsuitable.[4,5]

In other diseases, such as cancer and ultra-rare diseases, the National Institute for Health and Care Excellence (NICE) has additional flexibility in the assessment of medicines. As this flexibility is not granted for neurological conditions, such as MS, the system cannot assess the true value ocrelizumab brings to people with PPMS. The Department of Health does not allow medicines to have different confidential prices for different indications which meant NICE could not even consider the indication-specific price offered by Roche in order to make ocrelizumab cost-effective to the NHS for people with early PPMS. Failure to resolve this technicality between NHS England and NICE ultimately means that people with PPMS are denied access to the only effective treatment available for

their condition. Within the NHS the different MS indications are already monitored, therefore allowing flexibility should not cause additional burden to the system.

"This is devastating news for people with PPMS who urgently deserve access to the first and only licensed treatment which has been proven to slow the progression of this highly disabling disease. The committee has recognised ocrelizumab as an innovative treatment that provides a step change in the treatment of PPMS with a substantial effect on the lives of patients and their families," said Richard Erwin, General Manager, Roche UK.

"We ask that NICE are given the flexibility to consider an indication-specific price for ocrelizumab in PPMS. The challenge with ocrelizumab for people with PPMS could also have huge implications for future access to innovative medicines for people in the UK. We are unwavering in our commitment to people with PPMS and, as we have done with other disease areas, want to work together with NICE and NHS England to find a solution so this decision can be overturned."

PPMS affects around 10-15,000 people in the UK and people with this highly disabling form of MS often end up in a wheelchair, are unable to work and rely on carers or family members to look after them.[2]

"There are currently no approved treatments for PPMS and people with this form of MS experience disability significantly quicker than those with other forms. The lack of treatments that can modify their disease often forces them to rely on wheelchairs and mobility aids sooner, impacting on their independence. They are the forgotten people with MS and it is critical that NICE overturn the decision for ocrelizumab as soon as possible," said Jo Sopala, Director of Health Professional Programmes, MS Trust. "Before preparing our appraisal submission to the committee, we conducted a survey to gather the views of those affected by PPMS. We received nearly 500 responses from people with PPMS, their families and specialist MS health professionals. These people have been desperately waiting years for a licensed treatment that can slow the progression of their disease, they should not be deprived of the hope a disease modifying drug offers when there is a licensed treatment."

In the Phase III clinical trial ORATORIO, ocrelizumab was shown to slow disability progression and reduce signs of disease activity in the brain (MRI lesions) in people with PPMS, compared with placebo, with a median follow-up of three years. A similar proportion of people in both groups experienced adverse events and serious adverse events.[6]

In addition, an exploratory analysis from the extended control period of the ORATORIO study in PPMS demonstrated that ocrelizumab may significantly delay the time to need a wheelchair by seven years, as measured by the Expanded Disability Status Scale, a common measure of disability.[3] Another exploratory analysis showed ocrelizumab more than tripled the proportion of people with PPMS who maintained No Evidence of Progression or Active Disease (NEPAD) compared with placebo at 120 weeks.[3]

"As doctors, we are left feeling powerless when we deliver the devastating diagnosis of PPMS to people because we know there is currently no disease-modifying treatment available to help them. It is even more frustrating that an effective treatment that can help slow the disease has been developed and made available across the globe yet people in England and Wales will continue to suffer disability worsening because of an archaic and inflexible medicine assessment system," said Professor Gavin Giovannoni, Consultant Neurologist at Barts and the London School of Medicine and Dentistry. "Everyone must work together to resolve this situation as soon as possible so we can finally offer our patients the hope they deserve. Ocrelizumab is the first therapy to slow-down worsening of both leg and arm function in people with PPMS and not being able to use it on the NHS puts us in a very difficult situation."

Roche is further continuing its commitment to people with progressive MS by initiating new studies that will evaluate the efficacy of ocrelizumab in a broad range of people with progressive forms of MS using novel endpoints to evaluate upper limb function and disease progression. A first of its kind study, ORATORIO-HAND, will evaluate the long-term safety and efficacy of ocrelizumab in people with PPMS, including those later in their disease course. For the first time ever, the Nine-Hole Peg Test (9-HPT) – a measure of arm, wrist and hand function – is intended to be used as the primary measure of efficacy.

ENDS

Editor's Notes

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NICE assessment

The current NICE assessment process does not allow ocrelizumab in early PPMS to be effectively assessed for several reasons:

- Earlier this year ocrelizumab was recommended by NICE for people with RRMS, a form of MS for which there are several other treatments already available.[4] The Department of Health does not allow medicines to have different confidential prices for different indications which meant NICE could not consider the indication-specific price offered by Roche, differing to that for RRMS, in order to make it cost-effective to the NHS for ocrelizumab for people with early PPMS.

- NICE does not formally take severity of disease and unmet need into consideration in their decision making. NICE bases its decision to recommend a medicine on its cost effectiveness by establishing the incremental difference in cost between the new treatment and the current treatment, and assesses this against the additional benefit the treatment provides. When no current treatment is available, such as in PPMS, the incremental difference is between the cost of treatment and no treatment, which impacts the incremental cost, giving a skewed and grossly undervalued assessment of the value of the treatment.

- Many people with PPMS eventually transition into a wheelchair, meaning that maintaining the ability to use their hands and arms is of utmost importance. This is true for themselves but also to remain in work and reduce the need for a carer, reducing the financial burden on families and having wider societal benefits. When the benefit of MS medicines is assessed, the emphasis is placed on the preservation of leg function; however this approach is less appropriate to people with PPMS, as some loss of leg function is likely to have already occurred by the time they are diagnosed due to the progressive nature of the disease.[2] The value of maintaining independence and quality of life in people with PPMS by retaining use of their hands and arms isn't valued highly enough in the NICE assessment of MS medicines.

About Multiple Sclerosis

Multiple sclerosis (MS) is a chronic disease for which there is currently no cure. It affects an estimated 2.3 million people around the world, of whom approximately 100,000 live in the UK. [7,8,9] MS occurs when the immune system mistakenly attacks the insulation and support around nerve cells (myelin) in the central nervous system (CNS), causing inflammation and consequent damage.[10]

The myelin sheath helps insulate nerves so that messages are able to travel quickly and smoothly.[11] The damage caused by MS can cause a wide range of symptoms, including muscle weakness, fatigue and sight problems, and may eventually lead to disability.[12,13] MS is typically diagnosed in young adults between 20-40 years old, when they may be building their careers or planning their future, making the disease the leading cause of non-traumatic disability in younger adults.[8,14]

There are several types of MS, which are categorised by the rate of progression and pattern of symptoms experienced. Primary progressive multiple sclerosis (PPMS) is a debilitating form of the disease which is characterised by the gradual worsening of symptoms from the outset.[15] Approximately 10-15 percent of people with MS are diagnosed with the primary progressive form of the disease.[2]

Relapsing-remitting MS (RRMS) is the most common type of MS and is characterised by episodes of new or worsening signs or symptoms (relapses) followed by periods of recovery.[16,17] Approximately 85 percent of people with MS are initially diagnosed with RRMS.[16] Many people who are diagnosed with RRMS will eventually transition to secondary progressive MS (SPMS), in which they experience steadily worsening disability over time.[18]

People with all forms of MS experience disease progression – inflammation in the nervous system and permanent loss of nerve cells in the brain – even when their clinical symptoms aren't apparent or don't appear to be getting worse.[16,19,20] An important goal of treating MS is to reduce disease activity as soon as possible to slow how quickly a person's disability progresses.[20]

About ocrelizumab

Ocrelizumab works by killing specific immune cells within the body known as B-cells which are thought to be a key contributor to myelin and axonal (nerve cell) damage.[6,21,22,23] Ocrelizumab is a humanised monoclonal antibody designed to target immune cells with CD20 antigens present on the surface of the cell, including B-cells. Based on preclinical studies, ocrelizumab binds to CD20 cell surface proteins expressed on certain immune cells, including B and T-cells but not on stem cells or plasma cells, and therefore important functions of the immune system may be preserved.[6,21,22,23]

By reducing the number of B-cells in the body, the strength of the immune system attacking the central nervous system is lowered, slowing down the rate at which the myelin is damaged and ultimately reducing the rate of disease progression.

Roche's ocrelizumab is now licensed for administration by intravenous infusion every six months.[5] The initial dose is given as two 300 mg infusions given two weeks apart and subsequent doses are given as single 600 mg infusions.[5] Prior to each ocrelizumab infusion, 100 mg intravenous methylprednisolone (or an equivalent) and antihistamine must be administered, to reduce the frequency and severity of infusion-related reactions.[5] Ocrelizumab does not require active monitoring, however, physicians should be vigilant for the early signs and symptoms of progressive multifocal leukoencephalopathy (PML).

Ocrelizumab is approved for relapsing forms of multiple sclerosis and primary progressive multiple sclerosis in over 65 countries across North America, South America, the Middle East, Eastern Europe, as well as in Australia, Switzerland and the European Union. Over 50,000 people worldwide have received treatment with ocrelizumab.

About the ORATORIO study in PPMS

ORATORIO is a Phase III, randomised, double-blind, global multi-centre study evaluating the efficacy and safety of ocrelizumab (600 mg administered by intravenous infusion every six months; given as two 300 mg infusions two weeks apart) compared with placebo in 732 adults with PPMS.[6] The blinded treatment period of the ORATORIO study continued until all patients had received at least 120 weeks of either ocrelizumab or placebo and a predefined number of confirmed disability progression (CDP) events was reached overall in the study.[6] A similar proportion of patients in both groups experienced adverse events and serious adverse events compared with patients in the placebo group in the PPMS study.[6]

About Roche in neuroscience

Neuroscience is a major focus of research and development at Roche. The company's goal is to develop treatment options based on the biology of the nervous system to help improve the lives of people with chronic and potentially devastating diseases. Roche has more than a dozen investigational medicines in clinical development for diseases that include multiple sclerosis, Alzheimer's disease, spinal muscular atrophy, Parkinson's disease and autism.

About Roche Products Limited

Roche is the world's largest biotech company, with truly differentiated medicines in oncology, immunology and infectious diseases. Roche is also the world leader in in-vitro diagnostics and tissue-based cancer diagnostics, and a frontrunner in diabetes management. Roche's personalised healthcare strategy aims at providing medicines and diagnostics that enable tangible improvements in the health, quality of life, safety and survival of patients. Twenty-eight medicines developed by Roche are included in the WHO Model Lists of Essential Medicines, among them life-saving antibiotics, antimalarials and chemotherapy. Roche employs over 2,000 people in pharmaceuticals and diagnostics in the UK.

For more information: www.roche.co.uk.

Adverse event reporting

▼This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme: website www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

Adverse events should also be reported to Roche Products Ltd. Please contact Roche Drug Safety Centre by emailing welwyn.uk_dsc@roche.com or calling +44(0)1707 367554.

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