# Protocol

# Ocrelizumab (Ocrevus®) treatment of multiple sclerosis (MS)

## 1 Scope

Neurology patients in Addenbrooke's Hospital.

## 2 Purpose

Treatment of patients with a diagnosis of multiple sclerosis by the MS team at Cambridge University Hospitals NHS Foundation Trust (CUH).

## 3 Undertaken by (staff groups)

Consultant neurologists with special interest and expertise in the use of therapy for multiple sclerosis, registered nurses who are competent and trained in the administration of intravenous medication and medical staff with appropriate training and expertise, MS specialist nurses and MS support nurses.

## 4 Eligibility

Eligible patients are to be assessed only by consultant neurologists who have special interest and expertise in using therapy for multiple sclerosis. This will be in the disease modifying therapies clinic. NICE technology appraisal guideline TA533 'Ocrelizumab for treating relapsing-remitting multiple sclerosis' (2018) will be followed for patients with relapsing-remitting multiple sclerosis (RRMS). For patients with primary progressive MS (PPMS) NICE technology appraisal guideline TA585 'Ocrelizumab for treating primary progressive multiple sclerosis' (2019) will be followed.

Patients falling outside NICE eligibility criteria, but in whom it is clinically appropriate to treat, eg patients under 18 years of age, will require funding through exceptional circumstances agreement, and agreement to treat beyond protocol which may be sought by a consultant neurologist.

## 5 Before treatment

### 5.1 Pre-treatment screening

At assessment clinic appointment:

- Risks and benefits of ocrelizumab are discussed with neurologist and MS nurse, and the patient receives an information leaflet.
- Screening blood tests are sent as outlined in the Multiple Sclerosis (MS) disease modifying therapy (DMT) Initiation and Monitoring Standard Operating Procedure.
- Vaccine advice given as per Multiple Sclerosis (MS) disease modifying therapy (DMT) Initiation and Monitoring Standard Operating Procedure.
- MS nurse advises that hypotension can occur as a symptom of infusion related reaction during ocrelizumab infusions. MS nurse advises withholding of antihypertensive treatments the night before and the morning of infusion. Patients should be advised to bring their anti-hypertensive medication to the appointment for the ocrelizumab infusion.
- Patients with active malignancy, active hepatitis B or who are severely immunocompromised should not be treated with ocrelizumab.
- Complete required vaccinations at least six weeks before treatment initiation.

At the consenting clinic appointment:

- Doctor/MS specialist nurse to go through consent process, including sending a letter to the patient after the clinic with the ocrelizumab smartphrase summary of risks.
- Women of child bearing potential should agree to use contraception while receiving ocrelizumab and for 12 months after the last infusion of ocrelizumab. Patients should not breast feed.

# 6 Treatment

## 6.1 Prescribing

After consent the following should be completed:

- Doctor/admin staff to request funding from NHS England by Blueteq
- Doctor/MS prescribing nurse to prescribe the EPIC therapy plan and check that the following is prescribed:
    - Pre-medication for all ocrelizumab infusions:
        - Cetirizine 10mg PO 30-60 minutes before ocrelizumab
        - Paracetamol 1g PO 30-60 minutes before ocrelizumab
        - Methylprednisolone 100mg in 100ml 0.9% sodium chloride given IV infusion over 15min, to be given and completed 30min before ocrelizumab
    - Initial doses of ocrelizumab for visit 1a and 1b:
        - Two 300mg doses (given two weeks apart)
    - Subsequent doses of ocrelizumab for visit 2 onwards:
        - 600mg dose once every 6 months:
    - As required medication list for all infusions:
        - Paracetamol 1g PO/IV QDS PRN (max TDS if IV)
        - Chlorphenamine 4mg PO QDS PRN
        - Salbutamol 2.5mg nebuliser

- Anaphylaxis PRNs with note 'ONLY TO BE USED FOR ANAPHYLAXIS'
  - Intramuscular Adrenaline 1:1000 adrenaline 500 micrograms (0.5 mL)
  - Chlorphenamine 10mg IV slow infusion
  - Hydrocortisone 200mg IV slow infusion

## 6.2 Supply and initiation arrangements

MS specialist nurse will undertake responsibility for pre ordering ocrelizumab for named patient before admission/ booking to unit/ advising relevant ward managers of intended admission so that staff with appropriate skill level are on duty.

MS specialist nurse will liaise with pharmacy regarding ocrelizumab dispensing.

The pharmacist will release ocrelizumab from the therapy plan and communicate with inpatient pharmacy to dispense.

## 6.3 Cautions and contraindications

- Hypersensitivity to the active substance or to any of the excipients
- Patients in a severely immunocompromised state
- Known active malignancy
- Current active infection – ocrelizumab administration must be delayed until the infection is resolved.
- Infusion rate reactions (IRRs) – may occur during any infusion but have been more frequently reported during the first infusion. IRRs can occur within 24 hours of the infusion. These reactions may present as pruritus, rash, urticaria, erythema, throat irritation, oropharyngeal pain, dyspnoea, pharyngeal or laryngeal oedema, flushing, hypotension, pyrexia, fatigue, headache, dizziness, nausea and tachycardia
- Hypotension – can occur as a symptom of infusion related reaction. Therefore, withholding of antihypertensive treatments should be considered for 12 hours prior to and throughout each ocrelizumab infusion.
- Complete required vaccinations at least six weeks before treatment initiation

## 6.4 Side effects

**Very common and common side effects**:

- Infections and infestation: upper respiratory tract infection, nasopharyngitis, influenza, sinusitis, bronchitis, oral herpes, gastroenteritis, respiratory tract infection, viral infection, herpes zoster, conjunctivitis, cellulitis. **During the COVID-19 pandemic the ABN Guidance On The Use Of Disease-Modifying Therapies In Multiple**

**Sclerosis In Response To The COVID19 Pandemic will be followed** (Date: August 2021, published 26/10/21).

- Cough and catarrh
- Blood immunoglobulin M and G decreased
- Neutropenia
- Infusion related reactions

## 7 Switching to ocrelizumab from other therapies

When switching disease modifying treatment the following breaks in treatment are required prior to commencing ocrelizumab. If the current MS drug is not listed this is because information is not available, or is limited, and it should be discussed at MDT.

- **Beta interferon and Glatiramer acetate** – start immediately, or after wash-out of one month, provided total lymphocyte count normal

- **Dimethyl fumarate** – start immediately or after wash-out of one month, provided total lymphocyte count normal

- **Fingolimod** – ideally lymphocyte count should be greater than 0.8. However, patients should not wait more than 6 weeks from stopping fingolimod to starting Ocrevus irrespective of lymphocyte count due to the increased risk of a disabling relapse with a longer washout period.

- **Natalizumab** –
    - If JCV negative: wash-out 1-2 months and ensure lymphocyte count greater than 0.8. MRI brain within 3 months of starting Ocrevus to act as a new baseline.
    - If JCV positive: wash-out approx. 2 months (no longer than 12 weeks) months and ensure lymphocyte count greater than 0.8. MRI with last natalizumab infusion **and** repeated before starting ocrelizumab. CSF for JCV DNA prior to starting ocrelizumab.

## 8 Treatment day

Infusion nurse follows the following checklist and steps (EPIC smartphrase .OCRELIZUMABCHECKLIST)

| **Checklist and steps to be completed by infusion nurse for Ocrelizumab (Ocrevus)** |
|---|
| 1. Patient arrives to the infusion unit, is correctly identified, admitted on EPIC and given a wristband |
| 2. Infusion nurse checks baseline observations (vital observations: BP, Temp, SpO2, pulse recorded) |
| 3. Urinalysis done:<br>• to exclude urine tract infections [UTI] see step 5 for action on abnormal results<br>• and in all female patients urine pregnancy test done (ocrelizumab and pre- |

| |
|---|
| medications not be given if pregnant) |
| **4. Infusion nurse asks patient if they have any symptoms of infection.**<br>• A doctor/MS nurse review is not necessary if the patient is well and afebrile<br>• Ocrelizumab should NOT be given if there is any possibility of an active infection<br>• **If patient has symptoms of infection contact the MS team** on 01223 596319 (if no answer email add-tr.msnurses@nhs.net) and contact the on call neurology registrar.<br>• If the patient is well without symptoms of a UTI but has on urine dipstick:<br>○ Leucocytes and nitrites (without fever or urinary symptoms) urine should be sent to microbiology for microscopy, culture and sensitivity. The infusion can go ahead but the on call neurology registrar should prescribe an antibiotic to cover the possibility of a urine infection (see trust antibiotic policy).<br>○ Leucocytes 2+ or more and no nitrites (without fever or urinary symptoms) urine should be sent to microbiology for microscopy, culture and sensitivity. The infusion can go ahead but the on call neurology registrar should prescribe an antibiotic to cover the possibility of a urine infection (see trust antibiotic policy).<br>○ If well, no symptoms and leucocyte 1+ only (nitrite negative) infusion can go ahead and culture not needed. |
| 5. Peripheral cannula to be inserted |
| 6. Nursing staff to follow the EPIC therapy plan, with pre medications including IV methylprednisolone followed by ocrelizumab<br>• Reconstitute and administer the ocrelizumab in accordance with IV drug monograph found via here. Wear protective (latex or nitrile) gloves and ensure protective eyewear is worn.<br>• Aseptic non-touch technique principles must be followed at all times (refer to the ANTT for administering drugs and fluids by intravenous devices procedure).<br>• This drug should not be handled by pregnant women or those wishing to become pregnant.<br>• Record BP, temp, pulse and respiratory rate before methylprednisolone and before ocrelizumab then for:<br>○ Infusion 1a and 1b (ocrelizumab 300mg) vitals done every 15min for the first half hour of the ocrelizumab infusion, then every 30min<br>○ Infusion 2 and subsequent infusions (ocrelizumab 600mg) vitals done every 30min during the ocrelizumab infusion |
| 7. Inform neurology on call SpR of any concerning side effects as they occur and manage with PRN medications. |
| 8. Patients should be observed for one hour after ocrelizumab infusion with vital signs measured once just before discharge. |
| 9. If well, patient will go home and be advised that an infusion reaction can occur anytime within 24 hours and to seek medical attention if required. Discharge letter for GP completed daily by unit staff. |

## 9 Discharge

- If well, patient will go home and be advised that an infusion reaction can occur anytime within 24 hours and to seek medical attention if required.
- Follow up appointment will have been booked by MS specialist/ MS support nurse
- Discharge letter for GP completed by unit staff.

## 10 Follow up and monitoring visits

Patients are to be monitored after treatment, in a clinic setting, by consultant neurologist and team with special interest in MS, follow-up is tailored to the needs of the patient, the minimum clinic monitoring is as follows:

- Patients may benefit from a month 3 review after starting ocrelizumab (optional)
- Month 11 nurse clinic review pre-infusion
- Year 2 Dr review before infusion (EDSS)
- Then continues to alternate nurse/Dr if stable

Blood monitoring, to identify neutropaenia, lymphopaenia and hypogammaglobulinaemia, is done as outlined below (none required at visit 1b).

- FBC, Immunoglobulins and if possible lymphocyte phenotypes prior to infusion
- Ocrevus infusions will be scheduled every 6 months, however, if there is inadequate capacity in the infusion unit, patients with a CD19 count of 1% or more will be prioritised. Patients with a CD19 count of 1% or more should be highlighted to the MS nurses for prioritisation.

Following treatment female patients should comply with routine breast cancer screening.

Progressive multifocal leukoencephalopathy (PML) has occurred with other anti-CD20 monoclonal antibodies. There have been a small number of cases of carry-over PML in MS patients treated with ocrelizumab after natalizumab or fingolimod.

- Physicians should be vigilant for the early signs and symptoms of PML, which can include any new onset, or worsening of neurological signs or symptoms, as these can be similar to MS disease.
- If PML is suspected, dosing with ocrelizumab must be withheld. Evaluation including magnetic resonance imaging (MRI) scan preferably with contrast (compared with pre-treatment MRI), confirmatory cerebro-spinal fluid (CSF) testing for John Cunningham (JC) viral deoxyribonucleic acid (DNA) and repeat neurological assessments, should be considered. If PML is confirmed, treatment must be discontinued permanently.

Vaccination with live-attenuated or live vaccines is not recommended during treatment and not until B-cell repletion.

Women of child bearing potential should use contraception while receiving ocrelizumab and for 12 months after the last infusion of ocrelizumab.

## 11 Monitoring compliance with and the effectiveness of this document

(a) Process for Monitoring compliance and Effectiveness

- Patients will be assessed in clinic by consultant neurologist or MS specialist nurse
- Patients will agree before starting treatment to comply with treatment protocol, keep appointments and contact relevant health professionals in the event of changes in their underlying MS condition.
- Ongoing maintenance of database of patients offered treatment, undergoing treatment and stopping treatment, including reason for stopping treatment, will be kept by the MS specialist nurse to audit against NICE guidelines
- The prescription of ocrelizumab to be sensitive to pre and post marketing safety data.

(b) Standards/ key performance indicators

- The audit department will request evidence of compliance with NICE Technical Appraisal.
- Internal checks on safety, compliance and efficacy will be undertaken by the MS team.

## 12 References

Cambridge University Hospitals (2019) Ocrelizumab monograph, Pharmacy monographs.

Roche Products Limited (2018) Ocrevus 300 mg concentrate for solution for infusion - Summary of Product Characteristics. Retrieved from: https://www.medicines.org.uk/emc/product/8898

National Institute for Health and Care Excellence (2018). Ocrelizumab for treating relapsing-remitting multiple sclerosis [TA533]. Manchester: NICE. https://www.nice.org.uk/guidance/ta533

National Institute for Health and Care Excellence (Jun 2019). Ocrelizumab for treating primary progressive multiple sclerosis [TA585]. Manchester: NICE. https://www.nice.org.uk/guidance/ta585

ABN Guidance On The Use Of Disease-Modifying Therapies In Multiple Sclerosis In Response To The COVID19 Pandemic (Date: August 2021, published 26/10/21).

https://cdn.ymaws.com/www.theabn.org/resource/collection/6750BAE6-4CBC-4DDB-A684-116E03BFE634/21.10.26_ABN_Guidance_on_DMTs_for_MS_and_COVID-19.pdf

Treatment Algorithm for Multiple Sclerosis Disease-modifying Therapies NHS England Reference: 170079ALG Date Published: 4 September 2018 Gateway reference: 07603 https://www.england.nhs.uk/commissioning/wp-content/uploads/sites/12/2018/09/Treatment-Algorithm-for-Multiple-Sclerosis-Disease-modifying-Therapies.pdf

## Equality and diversity statement

This document complies with the Cambridge University Hospitals NHS Foundation Trust service equality and diversity statement.

## Disclaimer

It is **your** responsibility to check against the electronic library that this printed out copy is the most recent issue of this document.

## Document management

| | | | |
|---|---|---|---|
| Approved by: | R Roberts | | |
| Approval date: | 25 November 2021 | | |
| JDTC approval date: | n/a | | |
| Owning department: | Neurology | | |
| Author(s): | Claire McCarthy | | |
| Pharmacist: | Frances Smith | | |
| File name: | Ocrelizumab protocol v4 Nov 21 | | |
| Supersedes: | Ocrelizumab (Ocrevus®) treatment of relapsing-remitting multiple sclerosis (MS) version 3, November 2021 and document id 101303 Ocrelizumab (Ocrevus®) treatment of primary progressive multiple sclerosis version 1, August 2019 | | |
| Version number: | 4 | | |
| Local reference: | | Document ID: | 101124 |