Protocol

Ofatumumab (Kesimpta®) treatment of relapsing-remitting 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 Abbreviations used

CUH	Cambridge University Hospitals NHS Foundation Trust
CSF	cerebrospinal fluid
DNA	deoxyribonucleic acid
EDSS	
FBC	full blood count
JCV	John Cunningham virus
MRI	magnetic resonance imaging
MS	multiple sclerosis
NICE	National Institute for Health and Care Excellence
PML	progressive multifocal leukoencephalopathy

4 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.

5 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 TA699 'Ofatumumab for treating relapsing multiple sclerosis' (2021) 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.

6 Before treatment

6.1 Pre-treatment screening

At assessment clinic appointment:

- Risks and benefits of ofatumumab are discussed with neurologist and 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.
- Patients with active malignancy, active hepatitis B or who are severely immunocompromised should not be treated with ofatumumab.

At the consenting clinic appointment, either virtual or in person (at least 24 hours from assessment visit):

- Doctor or nurse specialist to go through consent process, including sending a letter to the patient after the clinic with the ofatumumab smartphrase summary of risks.
- Women of childbearing potential should agree to use contraception while receiving ofatumumab and for six months after the last infusion of ofatumumab.

7 Treatment

7.1 Prescribing

After consent, the following should be completed:

- Doctor/ MS administrator to request funding from NHS England by Blueteq
- Doctor to prescribe the drug (Homecare prescription)

Dosage:
20mg week 0, 1, 2 and 4 then 20mg monthly by subcutaneous injection.

7.2 Supply and initiation arrangements

MS specialist nurse will undertake responsibility for communicating with the Homecare support nurses prior to initial prescription being ordered.

MS specialist will liaise with pharmacy regarding ofatumumab dispensing.

7.3 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 – ofatumumab administration must be delayed until the infection is resolved.
- Complete required vaccinations at least six weeks before treatment initiation

7.4 Side effects

Very common and common side effects:

- Injection site reactions (systemic and local)
- Infections and infestation:
  upper respiratory tract infection, urinary tract infection, oral herpes
- Blood immunoglobulin M decreased

8 Switching to ofatumumab from other therapies

When switching disease-modifying treatment the following breaks in treatment are required prior to commencing ofatumumab:

- **Beta interferon and glatiramer acetate** – start immediately, or after wash-out of one month.

- **Dimethyl fumarate** – start immediately or after wash-out of one month.

- **Fingolimod** – generally start when total lymphocyte count has increased to >0.8 (note however there is a risk of returning MS disease activity at 6 to 8 weeks after stopping fingolimod). Fingolimod should be stopped approximately four weeks prior to the planned ofatumumab treatment date. FBC and lymphocyte phenotypes should be checked two weeks prior to ofatumumab an MRI brain scan should be done before switching to exclude PML.

- **Natalizumab** – If JCV negative: wash-out 1 to 2 months and then as soon as lymphocyte count normal. If JCV positive: wash-out 2 to 3 months. MRI with last natalizumab infusion **and** repeated before starting ofatumumab with CSF for JCV DNA prior to starting ofatumumab.

9 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 ofatumumab (optional)
- Month 11 nurse clinic
- Year 2 doctor review (EDSS)
- Then continues to alternate nurse/ doctor if stable

Blood monitoring, to identify neutropenia, lymphopaenia and hypogammaglobinaemia, is done every twelve months and consists of:

- FBC and immunoglobulins

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. Currently no similar cases have been found with ofatumumab.

- 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 ofatumumab must be withheld. Evaluation including MRI scan preferably with contrast (compared with pre-treatment MRI), confirmatory CSF testing for JCV 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 childbearing potential should use contraception while receiving ofatumumab and for six months after the last infusion of ofatumumab.

10 Monitoring compliance with and the effectiveness of this document

(a) Process for monitoring compliance and effectiveness

- Patients will be assessed every six to 12 months 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 ofatumumab 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.

11 References

Cambridge University Hospitals (2021) Ofatumumab monograph

Novartis (2021) Kesimpta 20 mg solution for injection in pre-filled pen. Retrieved from: https://www.medicines.org.uk/emc/product/12433

NICE (2021) Ofatumumab for treating relapsing multiple sclerosis [TA699]. Manchester: NICE. https://www.nice.org.uk/guidance/ta699

12 Associated documents

- Multiple sclerosis (MS) disease modifying therapy (DMT) initiation and monitoring standard operating procedure

Equality and diversity statement

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

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Document management

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