Guidelines for the use of Ublituximab in Relapsing Multiple Sclerosis

Background:
Ublituximab is a monoclonal antibody that selectively targets CD20-expressing B cells resulting in a reduction in the number and function of these cells. It is administered by IV infusion.

Innate immunity and total T-cell numbers are virtually unaffected.

Ublituximab is indicated for the treatment of adult patients with relapsing forms of multiple sclerosis (RMS) with active disease defined by clinical or imaging features.

Funding Status of Ublituximab
Ublituximab is funded by NHS England for patients who satisfy the following criteria:

- The patient has a diagnosis of relapsing multiple sclerosis defined as active by clinical or imaging features.
- Use of ublituximab has been discussed and agreed at a multi-disciplinary (MDT) meeting

Pre-treatment assessments:
The following must be completed prior to treatment with ublituximab:

- Tuberculosis (TB) screening – rule out active and latent TB before starting treatment.
    - TB Elispot – ensure clear of latent TB
    - Chest X-ray – ensure clear and no signs of infection. Accepted up to 6 months prior to treatment, provided there is no change in clinical status, such as no history of chronic chest infection or exposure to tuberculosis.
- Negative pregnancy test (in women of child bearing potential)
- Hepatitis B virus screening complete with no evidence of active/latent active disease
- No signs or symptoms of progressive multifocal leukoencephalopathy (PML)

The following contra-indications for treatment with ublituximab need to be ruled out:

- Hypersensitivity to ublituximab or any of the excipients
- Severe active infection
- Patients in a severely immunocompromised state
- Known active malignancies

Administration must be delayed in patients with an active infection until the infection is resolved.

Dosing information
A proforma prescription can be found in appendix 1 of this document.

Cycle 1:
150mg of ublituximab on day 1 and 450mg on day 15.

Subsequent cycles:
450mg of ublituximab every 24 weeks (after day 1 of cycle 1). The minimum dosing interval should be 5 months (20 weeks), between each dose of ublituximab.

Premedication to prevent/ameliorate infusion related reactions
Premedication must be administered prior to each infusion to reduce the frequency and severity of infusion related reactions:

- 100mg methylprednisolone sodium succinate IV – administered 30 minutes prior to each infusion
- 10mg chlorphenamine IV – administered 30 – 60 minutes prior to each infusion
- 1g paracetamol oral – given as an antipyretic 30 – 60 minutes prior to each infusion.

Storage

Ublituximab vials should be stored at 2 – 8° C (in a refrigerator). Once diluted, the IV infusion should be used immediately once the contents of the infusion bag has reached room temperature. **The contents of the bag must be at room temperature to avoid/reduce the likelihood of an infusion reaction due to the administration of the solution at low temperatures.**

Administration of the infusion
Cycle 1 dose of 150mg on day 1:
150mg of ublituximab (one vial) is placed into a 250ml sodium chloride 0.9% infusion bag.

Subsequent doses of 450mg on day 15 of cycle 1 and then every 24 weeks:
450mg of ublituximab (three vials) are placed in 250ml sodium chloride 0.9% infusion bag.

The infusion rate should increase incrementally depending on which infusion is being administered.

Infusion rate for cycle 1 doses of 150mg
150mg ublituximab in 250ml 0.9% sodium chloride (will take approximately 4 hours)

Time	Maximum infusion rate (as tolerated)
Start	10ml / hour
30 min	20ml / hour
60 min	35ml / hour
120 min	100ml / hour

Infusion rate for subsequent doses of 450mg
450mg ublituximab in 250ml 0.9% sodium chloride (will take approximately 1 hour)

Time	Maximum infusion rate (as tolerated)
Start	100ml / hour
30 min	400ml / hour

Patients should be observed for at least 1 hour after completion of the first two ublituximab infusions (cycle 1). Subsequent infusions do not require the post infusion monitoring, unless infusion related reaction or hypersensitivity have occurred.

Patients should be warned that these may still occur within 24 hours after ublituximab infusion.

Managing Infusion Related Reactions
Reactions are most common with the first ublituximab infusion; the risk decreases significantly with subsequent doses.

Reactions include:
- Pruritus, rash, urticarial, erythema, flushing, hypotension, pyrexia, fatigue, headache, dizziness, throat irritation, oropharyngeal pain, dyspnoea, pharyngeal or laryngeal oedema, nausea, tachycardia

Severity of reaction	Initial action	Further action
Mild to moderate eg headache	Reduce infusion rate to half that at the onset of the event and maintain for at least 30 minutes	If tolerated, increase the infusion rate according to the initial schedule
Severe eg dyspnoea or complex of flushing, fever and throat pain symptoms	Interrupt the infusion immediately and provide symptomatic treatment	The infusion should be restarted only after all the symptoms have resolved. When restarting the infusion rate should be at half of the infusion rate at the time of stopping the infusion. If that rate is tolerated, the rate can be increased slowly to the maximum of 100ml/hour for doses of 150mg and maximum of 400ml/hour for 450mg doses.
Life-threatening eg acute hypersensitivity, acute respiratory distress syndrome	Immediately STOP the infusion and provide the appropriate treatment	Treatment should be discontinued permanently in these patients

Advice on Pregnancy and Breastfeeding

Prior to ublituximab treatment, female patients should be advised of risks and benefits around the advised wash out period of 4 months. In line with other antiCD20 medications, the wash out period may be shortened but this should be on a case-by-case basis and on discussion with the Consultant in charge of the patients care. Ublituximab should be avoided during pregnancy.

Breast feeding should be avoided/discontinued for the first few days after an ublituximab infusion. Potential risks and benefits of breastfeeding on treatment should be discussed with patients.

Advice on vaccinations

All relevant vaccinations should occur at least 4 weeks prior to their first infusion of ublituximab for live or live-attenuated vaccines, and at least 2 weeks prior to the first infusion for inactivated vaccines. Subsequent non-live vaccinations can and should still be obtained, for example against seasonal flu, even after treatment has commenced. Live vaccinations should not be given whilst the patient is taking ublituximab.

Monitoring

Ublituximab is dosed every 24 weeks with no routine monitoring between doses. However, routine monitoring of multiple sclerosis should occur, with vigilance for early symptoms and/or signs of PML, which can include any new onset, or worsening of neurological signs or symptoms.

For continued funding of ublituximab an annual EDSS score should be recorded in the patients' records every 12 months.

Responsibilities:

Neurology Consultant

- Identify patients suitable for ublituximab; provide patient name and hospital number to the MDT co-ordinator for inclusion in a virtual or non-virtual MDT.
- Record the following in the electronic health record (Cerner Millennium CRS):
    - Details of prior treatment
    - EDSS score (at initiation and at least annually)
- Review referrals to the MDT by other consultants
- Support medical and nursing staff in any adverse event management should they occur
- Discussion of treatment approaches around pregnancy and breastfeeding, where indicated
- Review the patients at least every 12 months.

Neurosciences Pharmacist

- Confirm the patient's suitability for ublituximab
- Submit the Blueteq request to NHSE
- Ensure the prescription is signed by a member of the neurology team
- Once date of treatment is confirmed, ordering of medication
- Review patients as part of the MDT
- Be available for advice as required on medication related queries.

MS Specialist Nurse

- Co-ordinate the screening checklist and baseline measurements
- Provide the patient with an information pack and confirm understanding
- Co-ordinate the stopping of current prior MS therapy, if applicable
- Refer the patient to the infusion nurse(s) for infusion dates to be arranged
- Ensure communication with the GP is complete at all stages of the therapy
- Review the patient at regular time points and arrange blood safety monitoring
- Review patients as part of the MDT.

Neurology Infusion Nurses

- Co-ordinate the doses of ublituximab with the patient and organise the schedule in the day care unit.
- Administer the drug in line with the prescription
- Ensure the patient fully understands the therapy on discharge and the requirements for monitoring for infusion related reactions

References:

1 Ublituximab Summary of Product Characteristics, Roche (accessed January 2025)
2 Treatment protocol Briumvi, Neurax (emailed January 2025)

Guideline written by Joela Mathews, reviewed by Prof Klaus Schmierer and Prof Ruth Dobson January 2025 (and Barts MS team, January 2025)

Ublituximab Prescription Cycle 1: 150mg dose

Barts Health NHS Trust

Patient:	Hosp. No.:	DOB:
Cycle No:	Consultant:	Date of last dose:

Cycle 1: Day 1: 150mg of ublituximab

Subsequent doses: 450mg on day 15 and then every 24 weeks.

DATE	DRUG	ROUTE	DOSE	DURATION	TIME GIVEN	NURSE ADMINISTRING	NURSE CHECKING
	Methylprednisolone sodium succinate	IV	125mg	As per MEDUSA monographs on intranet			
	Chlorphenamine	IV	10mg				
	Paracetamol	PO	1g	n/a			n/a
	Ublituximab	IV	150mg	See below			

Administration details:
Cycle 1: day 1
150mg of ublituximab (1vial) added to 250ml 0.9% sodium chloride bag

Time	Maximum infusion rate (as tolerated)
Start	10ml / hour
30 min	20ml / hour
60 min	35ml / hour
120 min	100ml / hour

To manage infusion relation reactions, see the full protocol of summary of product characteristics but in severe or life threatening reactions the infusion must be immediately stopped. For mild to moderate reactions the infusion rate can be halved for at least 30 minutes.

PRESCRIBER: Sign & date below if prescription is **CONFIRMED**:	Pharmacist Check: sign & date:

Proforma drawn by (sign & date)	Proforma Checked & Approved By: (sign & date)		Review Date
Joela Mathews (January 2025)	**Klaus Schmierer (January 2025)**		**January 2030**

Ublituximab Prescription infusion 2 onwards

Barts Health NHS Trust

Patient:	Hosp. No.:	DOB:
Cycle No:	Consultant:	Date of last dose:

Subsequent doses: 450mg at day 15 of cycle 1 then every 24 weeks

DATE	DRUG	ROUTE	DOSE	DURATION	TIME GIVEN	NURSE ADMINISTRING	NURSE CHECKING
	Methylprednisolone sodium succinate	IV	125mg	As per MEDUSA monographs on intranet			
	Chlorphenamine	IV	10mg				
	Paracetamol	PO	1g	n/a			n/a
	Ublituximab	IV	450mg	See below			

Administration details:
Infusion 2 onwards 450mg of ublituximab (3 vials) added to 250ml 0.9% sodium chloride bag

Time	Maximum infusion rate (as tolerated)
Start	100ml / hour
30 min	400ml / hour

To manage infusion relation reactions, see the full protocol of summary of product characteristics but in severe or life threatening reactions the infusion must be immediately stopped. For mild to moderate reactions the infusion rate can be halved for at least 30 minutes.

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