Shared Care Guideline - GP monitoring bloods only (no prescribing required)
Alemtuzumab for treating relapsing-remitting multiple sclerosis

Executive summary

- Alemtuzumab will be prescribed according to NICE TAG 312 by a consultant neurologist at Cambridge University Hospitals NHS Foundation Trust.
- Alemtuzumab will be administered at Cambridge University Hospitals as daily infusions of 12mg per day for five consecutive days, followed 12 months later by three consecutive days (see note below with regards retreatment beyond this).
- **GPs will be asked to participate in shared care by ensuring monitoring is arranged and results (abnormal or normal) reported to the MS specialist team (add-tr.msnurses@nhs.net).**
- GPs need to confirm they accept the shared care guideline on an individual basis with the MS specialist team.
- Patients will be asked to participate in shared care by committing to 48 months of follow up (entry made in Epic recording consultation) after the last infusion of alemtuzumab (including retreatment).
- Shared care must not be assumed, confirmation of agreement must be received by all parties in order for shared care to happen.
- Serum creatinine and full blood count with differential must be carried out monthly in between infusions and for 48 months following the last infusion.
- Liver function tests and thyroid function test must be carried out three-monthly from the first dose and continued for 48 months following the last infusion.
- Further information regarding alemtuzumab can be found on the manufacturers summary of product characteristics
- Sharing of care depends on communication between the specialist, GP and the patient or their parent/carer. The intention to share care should be explained to the patient and accepted by them. Patients are under regular follow-up and this provides an opportunity to discuss drug therapy. The doctor/ healthcare professional who prescribes the medication has the clinical responsibility for the drug and the consequences of its use.

Planned first date of infusion:

Anticipated last date of infusion:

1. Scope

This document provides advice with regards administration and monitoring of alemtuzumab and defines the specifics of areas of shared care between the hospital and community.

2. Aim

To inform all parties involved in patient care about the prescribing and monitoring requirements for alemtuzumab when being used to treat active relapsing-remitting multiple sclerosis.

3. Introduction

Alemtuzumab is recommended as an option, within its marketing authorisation, for treating adults with active relapsing-remitting multiple sclerosis. NICE has appraised alemtuzumab in NICE TAG 312.

The MHRA released a statement in February 2020 providing a review of the benefits and risks of alemtuzumab in the treatment of MS. This statement details new contraindications, monitoring requirements and advice to patients. This guidance has been incorporated into the internal CUH protocol for using alemtuzumab:

https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/865491/Feb-2020-PDF.pdf

Alemtuzumab may be used as a single disease-modifying therapy in adults with relapsing remitting multiple sclerosis with: highly active disease despite a full and adequate course of treatment with at least one disease-modifying therapy or rapidly evolving severe disease defined by 2 or more disabling relapses in one year, and with one or more gadolinium-enhancing lesions on brain MRI or a significant increase in T2 lesion load compared to a recent MRI. Is given as two infusion courses, 12 months apart and requires monitoring and follow-up for 48 months after the last infusion. NHS England has commissioned a third cycle of three days if necessary once treatment is initiated.

RRMS is a chronic, disabling, neurological condition that, as it progresses, is life altering and has a large negative impact on quality of life. Prior to alemtuzumab first-line treatments for RRMS need to be injected weekly or several times per week and can be associated with unpleasant side effects.

Alemtuzumab is an antibody that binds to specific cells if the immune system, causing their destruction. The way in which alemtuzumab slows the decline of active RRMS is not fully understood.

4. Abbreviations

CUH	Cambridge University Hospitals NHS Foundation Trust
eGFR	estimated glomerular filtration rate
EMA	European Medicines Agency
FBC	full blood count
IV	intravenous
MS	multiple sclerosis

NICE	National Institute for Health and Care Excellence
RRMS	relapsing-remitting multiple sclerosis
SPC	summary of product characteristics
TAG	technology appraisal guidance
TFT	thyroid function test
VZV	varicella zoster virus

5. Dose and Administration

- Alemtuzumab will only be prescribed by a consultant neurologist and only be administered in a specialist centre (CUH).
- Alemtuzumab is given as an intravenous infusion at a dose of 12mg/day.
- The initial treatment course is for five consecutive days (60mg total dose).
- The second treatment course is for three consecutive days (36mg total dose) and is given 12 months after the first course.
- Following the initial two courses, a third cycle may be required as described in the NICE TAG 312 if a patient has further relapse(s). The retreatment dose should be 12mg/day for three consecutive days (36mg total dose).
- Any missed doses should not be given on the same day as a scheduled dose.

6. Specifics of Administration

Patients should be pre-treated with corticosteroids; 1000mg of IV methylprednisolone must be given for the first three days of the treatment course.

- Antihistamines (cetirizine) and antipyretics (paracetamol) should also be available and prescribed as per hospital protocol.
- Prophylaxis for herpes infection should be given to all patients starting on the first day of each treatment and should continue for at least one month following treatment with alemtuzumab. Aciclovir 200mg TWICE daily is used at CUH. Prophylaxis for listeria infection is also administered (Co-trimoxazole 960mg on alternate days for one month). The entire prophylactic courses are supplied by CUH.
- Observations are required for at least two hours after the infusion has finished.
- All staff involved in the administration of alemtuzumab must follow local procedure for administration.

7. Adverse effects

The adverse effects listed below are given as a guide only. These **must** be read alongside the summary of product characteristics.

Very common (≥ 1 in 10)

- Upper respiratory tract or urinary tract infection
- Lymphopenia or leukopenia
- Headache
- Flushing
- Nausea
- Urticaria, rash or pruritus
- Pyrexia or fatigue

Common (≥ 1 in 100 and < 1 in 10)

- Lower respiratory tract infections, herpes zoster, gastroenterotitis, oral herpes, oral candidiasis, influenza, ear infections.
- Lymphadenopathy
- Cytokine release syndrome
- Graves disease, thyroid dysfunction and deranged TFTs
- Insomia or anxiety
- Dizziness, MS relapse, hypoaesthesia, paraesthesia, tremor or change in taste.
- Blurred vision or vertigo
- Hyper or hypotension
- Cough
- Abdominal pain, vomiting diarrhea, dyspepsia
- Rash,
- Myalgia, muscle weakness or spasms
- Proteinuria or haematuria
- Menorrhagia or irregular menstruation
- Chest discomfort, chills, pain, peripheral oedema

Uncommon (≥ 1 in 1000 and < 1 in 100)

- Tooth infection, genital herpes, onychomycosis, conjunctivitis
- Immune thrombocytopenic purpura (ITP), thrombocytopenia, decreased haemoglobin or haematocrit.
- Depression, sensory disturbance, hyperaesthesia
- Throat tightness, hiccups
- Constipation, reflux, gum bleeding, dysphagia
- Blisters or night sweats
- Cervical dysplasia or amenorrhoea
- Decreased weight

8. Cautions

Only the main cautions are listed; these **must** be read alongside the summary of product characteristics.

- Concomitant use with or following antineoplastic or immunosuppressive therapies
- Patients known to be carriers of hepatitis B or C virus
- Pre-existing or ongoing malignancy
- Alemtuzumab should only be used in pregnancy if potential benefit justifies the potential risk to the foetus. See the summary of product characteristics for full advice.

9. Contraindications

- Hypersensitivity to the active substance, or to any of the excipients listed in the SPC
- Human immunodeficiency virus (HIV) Infection
- Severe active infection until complete resolution
- Uncontrolled hypertension
- A history of arterial dissection of the cervicocephalic arteries
- A history of stroke

- A history of angina or myocardial infarction
- Clotting abnormalities including treatment with antiplatelet or anticoagulant therapy
- Concomitant autoimmune diseases (apart from MS)

10. Interactions

- Only the main interactions are listed; these MUST be read alongside the summary of product characteristics.
- Treatment with all other disease modifying therapies should be stopped 28 days before the first alemtuzumab infusion.

Further information about dose and administration, adverse effects, cautions, contraindications and interactions can be found in the Summary of Product Characteristics.

11. Monitoring standards & actions to take in the event of abnormal test results/symptoms

- GP blood monitoring monthly (unless differently specified) for 48 months after last alemtuzumab infusion.
- GP practice and hospital to establish a robust system for copying blood results to MS specialist team (add-tr.msnurses@nhs.net).
- The MS specialist team will take responsibility for reviewing blood results and acting upon them.

12. Blood results communication process

1. When patients have had their scheduled blood tests, they will advise the service (email/telephone) of both the date when they were performed and the date when they were due, so that MS nurses are alerted.
2. The GP surgery, not the patient, will report the results to the MS nurses via email add-tr.msnurses@nhs.net within five working days of blood tests being performed.
3. The MS nurses will request the results from the GP surgery if they have not received them within three working days of the date on which they were either due or performed (if known), whichever is the later.
4. The results are reviewed by the team and acted on if abnormal. The MS nurse will inform the GP accordingly as soon as reasonably possible, but within no longer than eight working days.

Baseline monitoring of all tests listed in tables below are conducted by the hospital prior to initiation.

Monthly frequency:

Test	Comments
Serum creatinine 44-97 mmol/L	• eGFR less than 30, to be communicated on the same day to the patient please, ideally also to arrange urine dipstick for blood.

Test	Comments
Full Blood Count (with differential) • WBC 3.60-10.50 10*9/L • RBC 3.85-5.20 10*9/L • Hb 118-158 g/L • MCV 80.0-101.0 fL • MCH 27.0-34.0 pg • RCD 11.0-16.0 % • PLT count 160-370 10*9/L • MPV fL • Hct 0.355-0.455 L/L • Eosinophil count 0.02-0.50 10*9/L • Basophil count 0.00-0.20 10*9/L • Lymphocyte count 1.10-4.00 10*9/L • Monocyte count 0.10-0.90 10*9/L • Neutrophil count 1.50-7.70 10*9/L	• Platelet less than 100 10*9/L to be communicated to the specialist on the same day the results are reported. • The lymphocyte count always falls following treatment and is not a concern. • Neutrophil count less than 1.0 to be communicated to the specialist on the same day the results are reported.

3 monthly frequency:

Test	Comments
Liver Function Tests • ALP 30-130 U/L • Albumin 35-50 g/L • ALT 7-40 U/L • Total Bilirubin 0-20 umol/L	
Thyroid Function Tests • TSH 0.35-5.50 mU/L • Free T3 3.50-6.50 pmol/L • Free T4 10.0-19.80 pmol/L	• If thyroid disease has not already been diagnosed and free T4 is > 40, to be communicated to the specialist on the same day the results are reported.

13. Shared Care Responsibilities

a) Hospital specialist:

- Provide the patient with a Patient Alert Card, Patient guide and the Package Leaflet and request the patient to participate in shared care.
- Ensure baseline tests are conducted and reviewed as outlined in *Table 1* prior to treatment.
- Ensure pre and post treatment prophylactic medications are prescribed as per local policy and summary of product characteristics.
- Ensure patients without a history of chickenpox or without vaccination against varicella zoster virus (VZV) are tested for VZV and vaccinated as required.
- Ensure patient is advised to stop treatment with other disease modifying therapies 28 days before the first alemtuzumab infusion.
- Send a letter to the GP requesting shared care for the patient.
- Inform the GP after each clinic attendance if there is any change to treatment or monitoring.

- Inform GP of patients who do not attend clinic appointments, and advise of further actions required.
- Inform GP of the date of the last infusion (in year 2) and update the GP in case the patient requires re-treatment (as this means the date of the last infusion will change)
- To review blood results communicated by the GP practice and to act on any adverse result accordingly.
- To provide any advice to the patient/carer when requested.

b) General practitioner:

- Agreement to shared care guideline by the GP, agreement must be communicated in writing, fax or by email to the hospital specialist or MS nurse.
- Ensure that the medicine prescribed and supplied by secondary care is recorded and updated within the patient's record on the GP clinical system.
    - For Systm One this is within the 'Other Medication' category
    - For EMIS web this is within the 'Hospital Medication' category.
    - Please note medication prescribed and supplied by secondary care should **not** be added incorrectly as a repeat template.
- Arrange for bloods (TFT, FBC and creatinine) to be taken (as detailed in *Table 1).*
- Ensure all monitoring is arranged and results (abnormal or normal) reported to the MS specialist team (add-tr.msnurses@nhs.net).
- Report any adverse events to the hospital specialist, where appropriate.
- Request advice from the hospital specialist when necessary.

c) Patient or parent/carer:

- Commit to 48 months of follow up (entry made in Epic recording consultation) after the last infusion of alemtuzumab (including retreatment) to all of the following points:
- Ensure that they stop treatment with all disease modifying therapies 28 days before the first alemtuzumab infusion.
- Report to the hospital specialist or GP if they do not have a clear understanding of their treatment.
- Attend scheduled clinic and blood test appointments.
- Patients *may* receive the results of monitoring directly from the GP if requested (who arranged the blood tests.
- If a patient has signed up to use MyChart, results may be reported via this patient portal. Not all patients have access to this, and this remains optional.
- Must inform other clinical staff that they are receiving treatment with alemtuzumab.
- Report any adverse effects to the hospital specialist or GP.
- Seek advice from their GP, hospital specialist or pharmacist before purchasing any medication not prescribed by their doctor, including herbal or homeopathic medication.
- Report side effects such as bruising, rash, bleeding, heavy menstrual bleeding, blood in sputum or urine to the MS Specialist Team or GP.
- Female patients should use effective contraception measures during treatment and for **four** months afterward with alemtuzumab. Any concerns must be discussed promptly with a member of the MS team.

14. Contact numbers for advice and support

Cambridgeshire University Hospitals NHS Foundation Trust

Specialist	Post	Telephone
Professor Alasdair Coles	Consultant Neurologist	01223 256208
MS Nursing Team	MS Specialist Nurse	01223 257160 (add-tr.msnurses@nhs.net)
Medicines helpline	Medicines information	01223 217502/217478

15. Monitoring compliance with and the effectiveness of this document

The MS specialist team will continue to monitor feedback from GPs with regard to the guideline and the use of the drug on a regular basis (normally yearly) and make changes as appropriate.

16. Equality and diversity statement

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

17. Disclaimer

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

18. Document Management

Ratification Process	Details
Authored by:	Cambridge University Hospitals NHS Foundation Trust
Ratified by:	Cambridgeshire and Peterborough Joint Prescribing Group
Date ratified:	January 2023
Review date:	January 2026
Version number:	1

The information contained in this guideline is issued on the understanding that it is accurate based on the resources at the time of issue. For further information please refer to the most recent Summary of Product Characteristics for Lemtrada (Alemtuzmab) or www.medicines.org.uk.

Shared Care Guideline Title - Template Letter

{GP ADDRESS}

Dear Dr,

{PATIENT DETAILS}

Your patient was seen on ***{Insert date}*** with a diagnosis of ***{Insert diagnosis}***. He/she has relapsing remitting multiple sclerosis. I have therefore initiated alemtuzumab and am writing to ask you to participate in the shared care for this patient.

This medication and indication has been accepted as suitable for shared care by the Cambridgeshire and Peterborough Integrated Care System. I agree to the secondary care responsibilities set out in the shared care agreement for this medication. I am therefore requesting your agreement to share the care of this patient.

Medication name:	**Alemtuzumab**
Current dose:	Year 1: 12mg daily for 5 days Year 2: 12mg daily for 3 days Any subsequent years
Date medication started:	{Insert date}
Date after which GP to start prescribing:	Blood monitoring support only. Monthly blood tests as described in SCG document starting one month after treatment given.

{Insert if applicable - Last bloods were taken on {Insert date} and these show {Insert blood test details} within the normal range. The latest results are attached below.}

I confirm I have explained to the patient: the risks and benefits of treatment, the baseline tests conducted and the need for monitoring, how monitoring will be arranged, and the roles of the consultant/nurse specialist, GP and the patient in shared care.

I confirm the patient has understood and is satisfied with this shared care arrangement.

Yours sincerely

{Consultant name}

[1]This should be the date when the last prescription was issued. It is expected that patients will request a repeat prescription sometime after this date.