Cambridge University Hospitals NHS
NHS Foundation Trust

NHS
Cambridgeshire and Peterborough
Clinical Commissioning Group

# 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.
- Alemtuzumab will be administered at Cambridge University Hospitals as daily infusions of 12mg per day for 5 consecutive days, followed 12 months later by 3 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 patient.**
- 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 ensuring all blood results are communicated back to the MS Specialist Team, Cambridge University Hospitals.
- 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.
- Thyroid function test must be carried out 3 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: http://www.medicines.org.uk/emc/medicine/28917
- The responsibilities of the hospital specialist, GP and patient for this Shared Care Guideline can be found within this document here


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. Further information about the general responsibilities of the hospital specialist and GP can be found here

**Planned first date of infusion:**

**Anticipated last date of infusion:**

## 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.

## 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.

## 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 technology appraisal guidance 312.

Alemtuzumab has a UK marketing authorisation for treating adults with RRMS with active disease defined by clinical or imaging features defined by clinical or imaging features. It is given as 2 infusion courses, 12 months apart and requires monitoring and follow-up for 48 months after the last infusion.

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.

## Abbreviations

| | |
|---|---|
| TAG | Technology appraisal guidance |
| NICE | National Institute for Health and Clinical Excellence |
| SPC | Summary of product characteristics |
| MS | Multiple sclerosis |
| RRMS | Relapsing-Remitting Multiple Sclerosis |
| IV | Intravenous |
| CUH | Cambridge University Hospitals |
| VZV | Varicella Zoster Virus |
| TFT | Thyroid Function Test |
| FBC | Full Blood Count |
| eGFR | Estimated Glomerular Filtration Rate |

## 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 5 consecutive days (60mg total dose).
- The second treatment course is for 3 consecutive days (36mg total dose) and is given 12 months after the first course.
- Retreatment following the initial two courses 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 3 consecutive days (36mg total dose).
- Any missed doses should not be given on the same day as a scheduled dose.

Further information can be found in the summary of product characteristics:
http://www.medicines.org.uk/emc/medicine/28917

## Specifics of Administration

Patients should be pre-treated with corticosteroids; 1000mg of IV methylprednisolone must be given for the first 3 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 1 month following treatment with alemtuzumab. Aciclovir 200mg TWICE daily is used at CUHFT. Prophylaxis for Listeria infection is also administered (Co-trimoxazole 960mg on alternate days for one month). The entire prophylactic courses are supplied by CUHFT.
- Observations are required for at least 2 hours after the infusion has finished.
- All staff involved in the administration of alemtuzumab must follow local procedure for administration.

## 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

Further information can be found in the summary of product characteristics:
http://www.medicines.org.uk/emc/medicine/28917

## Cautions

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

- Previous autoimmune conditions other than MS
- Previous thyroid disorder – should only be used if benefits justify potential risks
- Active infection
- Concomitant use with or following antineoplastic or immunosuppressive therapies
- Patients known to be carriers of hepatitis B or C virus
- Pre-existing or on-going 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.

Further information can be found in the summary of product characteristics:
http://www.medicines.org.uk/emc/medicine/28917

## Contraindications

- Hypersensitivity to the active substance, or to any of the excipients listed in the SPC
- Human Immunodeficiency Virus (HIV) Infection

Further information can be found in the summary of product characteristics:
http://www.medicines.org.uk/emc/medicine/28917

## 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 can be found in the summary of product characteristics:
http://www.medicines.org.uk/emc/medicine/28917

## Monitoring Standards & Actions to take in the event of abnormal test results/symptoms

*Table 1*

| **Baseline monitoring** | **Monthly until 48 months after last alemtuzumab infusion.** | **Every 3 months until 48 months after last alemtuzumab infusion.** |
|---|---|---|
| Hospital responsibility to take and review bloods | GP responsibility to ensure bloods are taken and communicate results to patient (abnormal and normal). Patient to | [redacted] |

| | | |
|---|---|---|
| | communicate results to MS Specialist Team. MS Specialist Team to review bloods. | |
| Serum creatinine: 44-97 mmol/L | Serum creatinine. Serum creatinine or eGFR outside the normal range to be communicated on the same day to patient. | |
| Thyroid function test:<br>• **TSH:** 0.35-5.50 mU/L<br>• **Free T3**: 3.50-6.50 pmol/L<br>• **Free T4:** 10.0-19.80 pmol/L. | | Thyroid function test. |
| Full blood count with differential<br>• **WBC:** 3.60-10.50 10*9/L<br>• **RBC:** 3.85-5.20 10*9/L<br>• **Hb:** 118-158 g/L<br>• **MCV:** 80.0-101.0 fL<br>• **MCH:** 27.0-34.0 pg<br>• **RCD:** 11.0-16.0 %<br>• **PLT count:** 160-370 10*9/L<br>• **MPV:** fL<br>• **Hct:** 0.355-0.455 L/L<br>• **Lymphocyte count:** 1.10-4.00 10*9/L<br>• **Basophil count:** 0.00-0.20 10*9/L<br>• **Eosinophil count:** 0.02-0.50 10*9/L<br>• **Monocyte count:** 0.10-0.90 10*9/L<br>• **Neutrophil count:** 1.50-7.70 10*9/L | Full blood count with differential.<br><br>The lymphocyte count always falls following treatment and is not a concern. Reduced neutrophil count or platelet count below the normal range or platelet count fallen by >100 10*9/L to be communicated on the same day to the patient. | |

## 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: http://www.medicines.org.uk/emc/medicine/28917
- 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.

- 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 patient 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.
- Arrange for bloods (TFT, FBC and creatinine) to be taken (as detailed in *Table 1).*
- Ensure all results (abnormal and normal) are communicated to the patient and any abnormal results are highlighted (those outside the reference values).
- 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 will receive the results of monitoring directly from the GP (who arranged the blood tests). Patients must inform the MS Specialist Team **ASAP** (see number below) if the result was normal or abnormal. If abnormal (especially if platelet count falling or below the normal range) the Specialist team will follow up and review.
- 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.

## Contact numbers for advice and support

| **Cambridgeshire University Hospitals NHS Foundation Trust** | | |
|---|---|---|
| **Specialist** | **Post** | **Telephone** |
| Dr John Thorpe | Consultant Neurologist | 01223 256208; 01733 673549 |
| Dr Paul Molyneux | Consultant Neurologist | 01223 256208; 01284 712897 |
| MS Nursing Team | MS Specialist Nurse | 01223 257160 |
| | Neurology fax number | **Fax**: 01223 336941<br>(FAO MS Team) |
| Medicines helpline | Medicines information | 01223 217502/217478 |

## 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.

## Equality and Diversity Statement

This document complies with the Cambridge University Hospital service Equality and Diversity statement.

## Disclaimer

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

## Document Management

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| Authors: | Frances Smith – Lead Pharmacist for Neurosciences<br>Katherine Bongaerts – Medicines optimisation pharmacist NHSE<br>Approved by Dr John Thorpe (Consultant Neurologist) |
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**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** http://www.medicines.org.uk/emc/medicine/28917