Feidhmeannacht na Seirbhíse Sláinte
Health Service Executive

Alemtuzumab THERAPY

INDICATIONS FOR USE:

INDICATION	ICD10	Protocol Code
Treatment of adult patients with relapsing remitting multiple sclerosis (RRMS) with active disease defined by clinical or imaging features	G35	MS100

ELIGIBILTY:

- Indications as above
- Patient aged 18-55 (use with caution outside of this age range)
- Women of childbearing potential should use effective contraceptive measures during treatment and for 4 months following a course of alemtuzumab treatment

EXCLUSIONS:

- Hypersensitivity to alemtuzumab or to any of the known excipients
- HIV infection

USE with CAUTION:

- In patients with previous autoimmune conditions e.g. ITP, thyroid disorders, nephropathies
- In pregnancy and lactation

TESTS:

Baseline Measures:
MRI 3 months prior to treatment
Baseline tests:

- FBC, U&E, LFTs and TFT
- Unrinalysis and microscopy
- HIV test
- Varicella Zoster Virus (VZV) Serology

- All vaccinations must be completed 6 weeks prior to treatment
- Ensure cervical (HPV) screening has been carried out for female patients,
- Evaluation for active or latent TB as per local guidelines
- Screening patients at high risk of HBV and/or HCV infection before initiation of alemtuzumab should be considered. Caution should be exercised in prescribing alemtuzumb to patients identified as carriers of HBV and/or HCV as these patients may be at risk of irreversible liver damage relative to a potential virus reactivation as a consequence of their pre-existing status.
- Annual cervical (HPV) screening for female patients

Regular tests:
FBC, serum creatinine levels, urinalysis with microscopy at monthly intervals.
Thyroid Function Tests every 3 months.
A MRI scan should be performed within 3 months of each course of treatment to allow for assessment of disease response.

These laboratory tests should be conducted at periodic intervals for 48 months following the last treatment course of alemtuzumab in order to monitor for early signs of autoimmune disease:

Disease monitoring:
Disease monitoring should be in line with the patient's treatment plan and any other test/s as directed by the supervising Consultant. An annual MRI scan for disease activity should be carried out. An EDSS score should be included prior to each treatment or change to treatment.

TREATMENT:

Alemtuzumab therapy is recommended as 2 treatment courses, (Day 1-5 on Year 1 and Day 1-3 on Year 2) with safety follow-up of patients from initiation of treatment and until 48 months after the last infusion.

In the extension phases of the phase 3 clinical trials a 3rd cycle was given in patients if there was a single clinical relapse or two new MRI lesions. A third dose should not be used where the clinician considers the patient not to have fully responded to the

2nd treatment course i.e. in cases where there is breakthrough clinical or MRI activity at least 12 months since the last course.

Day	Drug	Dose	Route	Diluent & Rate	Cycle
1-5	Alemtuzumab	12mg	IV infusion	100ml 0.9% NaCl or 5% glucose over 4 hours	1
12 months later					
1-3	Alemtuzumab	12mg	IV infusion	100ml 0.9% NaCl or 5% glucose over 4 hours	2
Missed doses should not be given on the same day as a scheduled dose.					

Resources for the management of anaphylaxis or serious reactions should be available.

DOSE MODIFICATIONS:

- No recommended dose modifications

Renal and Hepatic impairment:
Alemtuzumab has not been studied in patients with renal or hepatic impairment

SUPPORTIVE CARE:

PREMEDICATIONS:
Patients should be pre-treated with corticosteroids (such as 1,000mg methylprednisolone) immediately prior to alemtuzumab administration on each of the first 3 days of any treatment course.
Additionally, pre-treatment with antihistamines and/or antipyretics prior to alemtuzumab administration may also be considered.

TAKE HOME MEDICATIONS:
Oral prophylaxis for herpes infection (such as acyclovir 200mg twice a day or equivalent) should be administered to all patients starting on the first day of each treatment course and continuing for a minimum of 1 month following treatment with alemtuzumab.

Listeriosis/*Listeria meningitis* has been reported in patients treated with alemtuzumab, generally within one month of infusion. To reduce this risk, patients receiving alemtuzumab should avoid ingestion of uncooked or undercooked meats, soft cheeses and unpasteurized dairy products for at least one month after treatment

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS

The adverse effects listed are not exhaustive. Please refer to the relevant Summary of Product Characteristics for full details.

This medicinal product is subject to additional monitoring. Healthcare professionals are asked to report any suspected adverse reactions.

Autoimmunity: Treatment may result in the formation of autoantibodies and increase the risk of autoimmune mediated conditions including immune thrombocytopenic purpura (ITP), thyroid disorders or, rarely, nephropathies (e.g. anti-glomerular basement membrane disease). Caution should be exercised in patients with previous autoimmune conditions other than MS, although available data suggests there is no worsening of pre-existing autoimmune conditions after alemtuzumab treatment.

Infusion-Associated Reactions (IARs): It is recommended that patients be premedicated to ameliorate the effects of infusion reactions as detailed above. IARs may occur in patients despite pretreatment. Observation for infusion reactions is recommended during and for 2 hours after alemtuzumab infusion. If an IAR occurs, provide the appropriate symptomatic treatment, as needed. If the infusion is not well tolerated, the infusion duration may be extended. If severe infusion reactions occur, immediate discontinuation of the intravenous infusion should be considered. Physicians should be aware of the patient's cardiac history as infusion-associated reactions can include cardiac symptoms such as tachycardia.

Infections: Infections may occur at a higher rate in patients treated with alemtuzumab. For more detail please refer to the SmPC.

Concurrent treatment with immunosuppressants: Alemtuzumab has not been administered for treatment of MS concomitantly with or following antineoplastic or immunosuppressive therapies. As with other immunomodulating therapies, potential combined effects on the patient's immune system should be taken into account when considering administration of alemtuzumab. Concomitant use of alemtuzumab with any of these therapies could increase the risk of immunosuppression.

DRUG INTERACTIONS:

- No formal drug interaction studies have been conducted with alemtuzumab using the recommended dose in patients with MS.
- Current drug interaction databases should be consulted for more information.

SUPPORT RESOURCES:

Please note that this is for information only and does not constitute endorsement by the NDMP

LEMTRADA: Health Professional Guide. Available at http://www.hpra.ie/img/uploaded/swedocuments/edumat_auto_472ee9c2-89ef-4282-a92b-6e290a88a976.pdf

ATC CODE:

Alemtuzumab L04AA34

REIMBURSEMENT CATEGORY:

National Drugs Management Scheme (NDMS)

PRESCRIPTIVE AUTHORITY:

The treatment plan must be initiated by a Consultant Neurologist experienced in the treatment of MS.

REFERENCES:

1. CAMMS223 Trial Investigators, Coles AJ, Compston DA, Selmaj KW, Lake SL, Moran S, Margolin DH, Norris K, Tandon PK. Alemtuzumab vs. interferon beta-1a in early multiple sclerosis. N Engl J Med. 2008;359:1786-801
2. Cohen JA et al. Alemtuzumab versus interferon beta 1a as first-line treatment for patients with relapsing-remitting multiple sclerosis: a randomised controlled phase 3 trial Lancet 2012; 380: 1819–28
3. Coles AJ et al. Alemtuzumab for patients with relapsing multiple sclerosis after disease-modifying therapy: a randomised controlled phase 3 trial. Lancet 2012; 380: 1829–39
4. LEMTRADA 12 mg concentrate for solution for infusion Accessed Dec 2016 Available at http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Product_Information/human/003718/WC500150521.pdf

Version	Date	Amendment	Approved By

Comments and feedback welcome at ndmp@hse.ie.