Alemtuzumab (Lemtrada®)
Criteria for Use

VHA Pharmacy Benefits Management Services, Medical Advisory Panel and VISN Pharmacist Executives

The following recommendations are based on medical evidence, clinician input, and expert opinion. The content of the document is dynamic and will be revised as new information becomes available. The purpose of this document is to assist practitioners in clinical decision-making, to standardize and improve the quality of patient care, and to promote cost-effective drug prescribing. **THE CLINICIAN SHOULD UTILIZE THIS GUIDANCE AND INTERPRET IT IN THE CLINICAL CONTEXT OF THE INDIVIDUAL PATIENT. INDIVIDUAL CASES THAT ARE EXCEPTIONS TO THE EXCLUSION AND INCLUSION CRITERIA SHOULD BE ADJUDICATED AT THE LOCAL FACILITY ACCORDING TO THE POLICY AND PROCEDURES OF ITS P&T COMMITTEE AND PHARMACY SERVICES.**

The Product Information should be consulted for detailed prescribing information.

See the VA National PBM-MAP-VPE Monograph on this drug at www.pbm.va.gov or http://vaww.pbm.va.gov for further information.

Exclusion Criteria (if any box is checked the patient DOES NOT qualify for alemtuzumab)

- ☐ Secondary progressive MS and no clinical or MRI evidence of relapses
- ☐ Concurrent use of immune system modifying drugs (DMT) to treat MS (i.e.; interferon beta-1B, glatiramer acetate, interferon beta 1A, natalizumab, mitoxantrone) unless the previous agent will be discontinued when alemtuzumab is initiated.
- ☐ Infection with Human Immunodeficiency Virus
- ☐ No documented baseline testing including (within 30 days prior to alemtuzumab); CBC with differential, LFT, and skin exam.
- ☐ Positive test for tuberculosis. Active and latent tuberculosis cases occurred in 0.3% of alemtuzumab-treated patients, most often in endemic regions

Inclusion Criteria

Patients with relapsing MS characterized by clearly defined acute attacks with full or partial recovery.". Alemtuzumab must be prescribed and monitored by a VA neurologist or locally designated MS Specialist.

AND

- ☐ Loss of clinical response or intolerance to at least two DMT (options include injectable: interferon beta 1a, interferon beta 1b, glatiramer; oral; dimethyl fumarate, fingolimod, teriflunomide) and if serum JCV Ab negative, a trial of natalizumab.

OR

- ☐ Currently on natalizumab therapy with development of risk factors for PML (duration of therapy > 24 months, anti JC virus antibody positive or received immunosuppressant therapy prior to natalizumab)

OR

- ☐ Highly aggressive disease as demonstrated by heavy burden of MRI T2 lesions, presence of multiple enhancing lesions at onset of disease, high burden of gadolinium enhancing lesions or rapid accrual of disability

Dosage Recommendations

- The recommended dosage of alemtuzumab is 12 mg/day administered by intravenous infusion for 5 consecutive days, followed by three consecutive daily infusions 1 year later. Following the second treatment course, subsequent treatment courses of 12 mg per day on 3 consecutive days (36 mg total dose) may be administered, as needed, at least 12 months after the last dose of any prior treatment courses.
- Patients require premedication with the following:

Corticosteroids

- Premedicate patients with high dose corticosteroids (1,000 mg methylprednisolone or equivalent) immediately prior to alemtuzumab infusion and for the first 3 days of each treatment course

Herpes Prophylaxis

- Administer anti-viral prophylaxis for herpetic viral infections starting on the first day of each treatment course and continue for a minimum of two months following treatment with alemtuzumab or until the CD4+ lymphocyte count is > 200 cells per microliter, whichever occurs later

Issues for Consideration

- Serious and life-threatening stroke (including ischemic and hemorrhagic stroke) has been reported within 3 days of alemtuzumab administration. Instruct patients to seek immediate medical attention if symptoms of stroke occur
- Patients without a documented history of varicella zoster virus infection or vaccination against it should be evaluated for vaccination against varicella prior to alemtuzumab initiation. Zostavax® should not be used in these individuals. In these patients vaccination with the live varicella virus product (Varivax®) should be undertaken and these patients should not initiate alemtuzumab therapy until at least six weeks after the two doses of vaccine are completed. Consult the CDC website for guidance. (2 doses of the vaccine must be given at least 4 weeks apart) www.cdc.gov/vaccines/recs/schedules/adult-schedule.htm
- Do not administer live viral vaccines for at least 2 months after a course of alemtuzumab or until the CD4+ lymphocyte count is > 200 cells per microliter, whichever occurs later.
- Consider delaying alemtuzumab in persons with active infection until the infection is fully controlled.
- Fungal infections and Listeria meningitis have occurred with increased frequency in patients receiving alemtuzumab for the treatment of multiple sclerosis
- There have been 21 reported cases of Listeria Monocytogenes with alemtuzumab. Symptoms of infection can be difficult to distinguish from infusion reactions. Patients should be counseled to not consume foods associated with Listeria prior to alemtuzumab infusion.
- During postmarketing use, cases of pulmonary alveolar hemorrhage have been reported with onset within 48 hours of alemtuzumab infusion.

- **<u>The FDA approval for Alemtuzumab includes a Black Box Warning</u>** because of the risk of autoimmunity, infusion reactions, and malignancies, alemtuzumab is available only through restricted distribution under a Risk Evaluation Mitigation Strategy (REMS) program. http://www.fda.gov/Alemtuzumab
  - Alemtuzumab causes serious, sometimes fatal, autoimmune conditions such as immune thrombocytopenia and antiglomerular basement membrane disease.
- Patients with anti-GBM disease may develop end-stage renal disease requiring dialysis or renal transplantation. Urgent evaluation and treatment is required, because early treatment can improve the preservation of renal function. Anti-GBM disease can be life-threatening if left untreated. Alveolar hemorrhage, manifested as hemoptysis, is a common component of anti-GBM disease and has been reported in postmarketing cases. Cases of anti-GBM disease have been diagnosed up to 40 months after the last dose of alemtuzumab.
  - Alemtuzumab causes serious and life-threatening infusion reactions; therefore it must be administered in a setting with appropriate equipment and personnel to manage anaphylaxis or serious infusion reactions. Monitor patients for 2 hours after each infusion. Make patients aware that serious infusion reactions can also occur after the 2-hour monitoring period.
  - Alemtuzumab has been associated with an increased risk of malignancies, including thyroid cancer, melanoma, and lymphoproliferative disorders.

Monitoring

- HPV (human papillomavirus) screening is recommended for female patients on an annual basis.
- Complete blood counts with differential, serum creatinine levels, and urinalysis with urine cell counts and urine protein to creatinine ratio should be obtained prior to initiation of treatment and at monthly intervals until 48 months after the last infusion of alemtuzumab.
- Thyroid function tests should be obtained prior to the initiation of treatment and every 3 months until 48 months after the last infusion. Monitoring may need to continue past 48 months based on clinical findings of autoimmune conditions in postmarketing studies.
- Skin examination for melanoma should be performed prior to treatment and yearly thereafter.
- An annual brain MRI by CMSC Protocol (www.va.gov/ms) is recommended