Criteria for Use

Natalizumab in Multiple Sclerosis

VHA Pharmacy Benefits Management Service and Medical Advisory Panel

The following recommendations are based on current medical evidence and expert opinion from clinicians. The content of the document is dynamic and will be revised as new clinical data 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 situation. For a full discussion of natalizumab please refer to the monograph at http://vawww.national.cenop.va.gov/PBM/Clinical%20Guidance/Drug%20Monographs/Natalizumab.doc

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

- Patient has not been enrolled in and met all conditions of the TOUCH™ Prescribing Program
- Patient is diagnosed with primary progressive multiple sclerosis
- Patient has secondary progressive MS with no clinical or MRI evidence of relapses
- Patient is currently responsive to and tolerating another immunomodulatory treatment for MS
- Patient has current or prior history of progressive multifocal leukoencephalopathy (PML);
- Patient has a medical condition which significantly compromises the immune system including HIV infection or AIDS, leukemia, or lymphoma or organ transplantation;
- Patient is currently receiving or has received in the previous three months chronic antineoplastics or immunosuppressants (ie; adalimumab, alefacept alentuzumab, anakinra, azathioprine, cladribine, cyclophosphamide, cyclosporine, daclizumab, efalizumab, etanercept, fludarabine phosphate, infliximab, intravenous immunoglobulin leflunomide, mercaptopurine, methotrexate, mycophenolate mofetil, mycophenolic acid, pentametrexel, rituximab, trastuzumab.
- Patient is receiving concurrent immune system modifying drugs to treat MS (ie; interferon beta-1B, glatiramer acetate, interferon beta 1A, mitoxantrone)
- Providers may exclude patients with melanoma or at high risk of developing melanoma or other cancers if in their judgment treatment would pose a significant risk to the patient ( for more information refer to www.va.gov/ms)

Inclusion Criteria

- Patient has relapsing MS7 characterized by disease activity defined as one or more relapses in the one year prior to therapy or gadolinium positive lesions on MRI6, despite disease modifying therapy
- Patient has not demonstrated a clinical response during at least 4 weeks of therapy with glatiramer or interferon beta 1A or 1B ( rapidly progressive MS)
- Patient developed intolerance to therapy with both glatiramer and interferon beta
- Patients’ currently receiving immunosuppressants or antineoplastics (see list above in exclusion criteria) should generally have a washout period of at least 3 months prior to initiation of natalizumab.
- Patients receiving an interferon beta, glatiramer acetate, or corticosteroids should generally have a washout period of at least 2 weeks prior to initiation of natalizumab.
- Patient initial registry completed and FAXed to MS Center of Excellence

Dosage Recommendations

The recommended dose of natalizumab for relapsing forms of MS is 300 mg by IV infusion over one hour every four weeks

Monitoring

- Patients should be observed during the infusion and for one hour after the infusion is complete for signs or symptoms consistent with a hypersensitivity reaction. These reactions usually occur within 2 hours of the start of the infusion.
- There have been anecdotal reports of elevated hepatic transaminases and total bilirubin as early as six days post infusion. Liver enzymes and bilirubin should be monitored prior to each dose of natalizumab. ( for more information refer to www.va.gov/ms)
- Natalizumab induces increases in circulating leukocytes (including lymphocytes, monocytes, eosinophils, and basophils). It does not affect the number of circulating neutrophils.
- Since natalizumab has been causally linked with progressive multifocal leukoencephalopathy (PML) suspected cases should be investigated with a gadolinium enhanced MRI and when indicated a cerebrospinal fluid exam for JC viral DNA.
- Patients on natalizumab should be evaluated at 3 months and 6 months after the first infusion and every 6 months after that for any negative response, side effects, and any symptoms suggesting PML as well as a decision to continue natalizumab therapy.
- An annual brain MRI by CMSC Protocol (www.va.gov/ms) is highly recommended
- Registry update should be completed annually or as indicated (change in status, disease type or MRI findings, etc.)

---

*a Relapsing Forms of MS include: Relapsing, remitting MS: A clinical course of MS characterized by clearly defined, acute attacks with full or partial recovery and no disease progression between attacks. Secondary progressive MS with superimposed relapses: A clinical course of MS that shows steady progression but with superimposed acute relapses, after an initial relapsing-remitting course. Progressive-relapsing MS: A clinical course of MS that shows disease progression from the beginning, but with clear, acute relapses, with or without full recovery from those relapses

*b gadolinium should not be used in patients with CrCl ≤30 ml/min or those on dialysis

*c The risks of a shorter washout period should be weighed against the risks of another relapse.

Updated version may be found at www.pbm.va.gov or http://vawww.pbm.va.gov and the MS Center of Excellence site www.va.gov/ms

September 2008