Natalizumab

Product:
NATALIZUMAB (Tysabri®) 300mg vial

Class of drugs:
Recombinant monoclonal antibody

Indication:
Treatment of multiple sclerosis (MS)

Manufacturer:
Biogen Idec Canada Inc.

Highlights of Recommendation:
◆ Natalizumab (Tysabri) is a laboratory-produced antibody used in the treatment of the relapsing-remitting form of multiple sclerosis (RRMS).
◆ In the AFFIRM study, natalizumab (Tysabri) was associated with a reduced risk of disability progression and fewer exacerbations (relapses) compared to placebo.
◆ There are currently no good quality studies comparing natalizumab (Tysabri) against other multiple sclerosis treatments. Hence, it is unknown how well natalizumab (Tysabri) works versus alternative therapies funded by the Ontario Public Drug Programs.
◆ Natalizumab (Tysabri) has been associated with the development of progressive multifocal leukoencephalopathy (PML), a rare viral disease affecting the brain and nervous system. PML can cause severe disability or death.
◆ Natalizumab (Tysabri) costs substantially more than other treatments for multiple sclerosis ($33,700 per year versus $16,000 - $22,000 per year).
◆ Overall, the Committee acknowledged the modest efficacy of natalizumab (Tysabri) in the treatment of RRMS. However, given the lack of evidence that this drug offers efficacy, safety or economic advantages over other available treatments, the Committee recommended that natalizumab (Tysabri) not be funded.

Background:
Multiple sclerosis (MS) is a disabling disease that affects the brain and spinal cord. The disease attacks myelin, an insulating material that protects critical portions of nerve cells. MS often destroys myelin in patches, causing swelling and interfering with the usual flow of signals along nerve fibres.

The effects of MS vary greatly from one person to another, depending on the way in which the disease strikes the nervous system. Symptoms include blurry vision, difficulties speaking, faulty short-term memory, bowel or bladder problems, extreme fatigue, loss of balance or coordination, muscle stiffness, and even partial or complete paralysis. Not all people with MS experience the same symptoms. With the relapsing-remitting form of MS, attacks are followed by complete or partial recovery.

Canada is a high risk region for MS, which occurs more often in countries further away from the equator. While there is no cure, some approved drugs can alter the course of the disease. Several treatments are based on interferon, a protein that is part of the immune response to foreign agents. Another treatment, glatiramer acetate, consists of some of the same biochemical building blocks found in myelin.

Natalizumab (Tysabri) is a laboratory-produced antibody. It is designed to impede the movement of potentially damaging immune cells from the bloodstream into the brain and spinal cord.

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Detailed Discussion:

- The Committee considered data from the AFFIRM study (Polman et al. *New England Journal of Medicine*, 2006). The AFFIRM trial found that natalizumab (Tysabri), versus placebo, is associated with statistically significant reductions in the mean rate of relapse at one year and at two years. Natalizumab (Tysabri) therapy is also associated with statistically significant reductions in the cumulative probability of sustained progression of disability at two years. Quality of life scores increased in the natalizumab (Tysabri) treatment group and decreased in the placebo group.

- A second study, the SENTINEL trial, evaluated the combination use of natalizumab (Tysabri) with interferon. The Committee noted that natalizumab (Tysabri) is approved only as monotherapy in Canada and that the efficacy and safety of natalizumab (Tysabri) in combination with other MS treatments have not been established.

- There are no randomized controlled trials comparing natalizumab (Tysabri) monotherapy with other systemic therapies for the treatment of MS (i.e. interferon beta products or glatiramer), all of which are currently funded by the Ontario Public Drug Programs. Therefore, the comparative efficacy of natalizumab (Tysabri) versus these alternate treatments is unknown.

- The most frequent adverse events reported with natalizumab (Tysabri) were infection and hypersensitivity reactions, including anaphylaxis.

- Natalizumab (Tysabri) therapy is also associated with progressive multifocal leukoencephalopathy (PML), a condition that can cause severe disability or death.

- The Committee had concerns with the potential off-label use of natalizumab (Tysabri) (e.g. use in other types of multiple sclerosis) where its efficacy has not been examined.

- The annual cost of natalizumab (Tysabri) therapy is approximately $33,000 per year. This is more costly than other available treatments for MS. Beta interferon products range from $18,000 - $22,000 per year, and glatiramer costs approximately $16,000 per year.

- The Committee noted that the manufacturer’s pharmacoeconomic analysis made questionable assumptions regarding clinical efficacy. Despite this limitation, natalizumab (Tysabri) was shown to be not cost-effective.

- Overall, the Committee acknowledged the modest efficacy associated with natalizumab (Tysabri) when used as monotherapy in RRMS. However, the Committee recommended that natalizumab (Tysabri) not be funded because comparative clinical efficacy of natalizumab versus alternate treatments is unknown and long-term data are not available. In addition, there are concerns regarding the risk for progressive multifocal leukoencephalopathy and the potential for off-label use. Lastly, value for money has not been demonstrated.

CEDAC Recommendation:

(http://www.cadth.ca/index.php/en/cdr/recommendations)

The Canadian Expert Drug Advisory Committee (CEDAC) recommended that natalizumab (Tysabri) not be listed.

For more information, please contact:

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or click: http://www.health.gov.on.ca/english/providers/program/drugs/ced_rec_table.html