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## EPAR summary for the public

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# Tysabri

natalizumab

This document is a summary of the European public assessment report (EPAR) for Tysabri. It explains how the Committee for Medicinal Products for Human Use (CHMP) assessed the medicine to reach its opinion in favour of granting a marketing authorisation and its recommendations on the conditions of use for Tysabri.

### What is Tysabri?

Tysabri is a concentrate that is made up into a solution for infusion (drip into a vein). It contains the active substance natalizumab.

### What is Tysabri used for?

Tysabri is used to treat adults with highly active multiple sclerosis (MS). MS is a disease of the nerves, in which inflammation destroys the protective sheath surrounding the nerve cells. Tysabri is used in the type of MS known as 'relapsing-remitting' MS, when the patient has attacks (relapses) in between periods with no symptoms (remissions). It is used when the disease has failed to respond to a beta-interferon (another type of medicine used in MS), or is severe and getting worse rapidly.

The medicine can only be obtained with a prescription.

### How is Tysabri used?

Treatment with Tysabri should be started and continuously supervised by a doctor who is experienced in treating diseases of the nervous system and has access to a magnetic resonance imaging (MRI) scanner. This machine will enable the doctor to see inside the body to check for changes in the brain linked to MS or the rare brain infection called progressive multifocal leukoencephalopathy (PML).

Tysabri is given as a one-hour infusion every four weeks. Because the infusion can trigger an allergic reaction, the patient must be monitored during the infusion and for one hour afterwards. If there is no clear benefit for the patient after six months, the doctor will have to re-assess the treatment.



Patients who receive Tysabri must be given a special alert card that summarises the key safety information about the medicine. Patients should show this card to their partner or carer, as well as to other doctors treating them, because they may notice symptoms of PML that the patient is not aware of, such as changes in mood, behaviour or speech. Patients should also be informed about the risk of PML at the start of treatment. After two years, the benefits and risks of continued treatment should be re-assessed, and the patient should be informed about the increased risk of PML.

## **How does Tysabri work?**

The active substance in Tysabri, natalizumab, is a monoclonal antibody. A monoclonal antibody is an antibody (a type of protein) that has been designed to recognise and attach to a specific structure (called an antigen) that is found on certain cells in the body. Natalizumab has been designed to attach to a specific part of an 'integrin' called ' $\alpha\beta 1$  integrin'. This is found on the surface of most leucocytes (the white cells in the blood that are involved in the inflammation process). By blocking the integrin, natalizumab stops the leucocytes from going from the blood into the brain. This reduces inflammation, and the nerve damage caused by MS.

## **How has Tysabri been studied?**

Tysabri has been investigated in two studies, both lasting two years. One study compared Tysabri on its own with placebo (a dummy treatment) in 942 patients. The second study looked at the effect of adding Tysabri to interferon beta-1a (another medicine used in MS) in 1,171 patients. The main measures of effectiveness were the number of relapses, and the changes in the patients' level of disability measured using a standard scale (the Expanded Disability Status Scale).

## **What benefit has Tysabri shown during the studies?**

Tysabri used on its own was more effective than placebo in reducing the number of relapses. After a year, there was a decrease of about two-thirds in the number of MS attacks in Tysabri-treated patients, in comparison with the patients who received placebo. Tysabri was also more effective than placebo on the disabling effects of MS: over two years, the risk of disability getting worse was reduced by 42% in comparison with placebo. In the add-on study with interferon beta-1a, the risk of disability getting worse and the number of relapses were reduced, but the way the study was designed did not allow the clear identification of whether these results were due to Tysabri only or to the combination.

## **What is the risk associated with Tysabri?**

Patients, carers and doctors need to be aware that Tysabri can be associated with infections, including the brain infection PML. PML has symptoms that may be similar to those of an MS attack, and usually leads to severe disability or death. The risk of PML increases the longer a patient has been receiving Tysabri, especially in patients treated for more than two years. The risk of PML is also higher if the patient used immunosuppressant medicines before starting Tysabri, or if the patient has antibodies against the virus that causes PML. If PML is suspected, the doctor must stop treatment until it is certain that the patient does not have the infection.

In studies, the most common side effects with Tysabri (seen in between 1 and 10 patients in 100) were urinary tract infection (infection of the structures that carry urine), nasopharyngitis (inflammation of the nose and throat), urticaria (itchy rash), headache, dizziness, vomiting, nausea (feeling sick), arthralgia (joint pain), rigors (shaking chills), pyrexia (fever) and fatigue (tiredness). For the full list of all side effects reported with Tysabri, see the package leaflet.

About 6% of the patients in the studies developed long-lasting antibodies against natalizumab. This led to a decrease in the effectiveness of the medicine.

Tysabri should not be used in people who may be hypersensitive (allergic) to natalizumab or any of the other ingredients. It must not be given to patients who have PML or who are at risk of getting an infection, including patients whose immune systems are weakened. It must not be given with beta-interferon or glatiramer acetate (other medicines for MS), to patients who have cancer (unless it is a type of skin cancer called basal cell carcinoma) or to patients who are under 18 years of age.

### **Why has Tysabri been approved?**

The CHMP concluded that the effectiveness of Tysabri in MS had been clearly shown but because of its safety profile, it should only be used in patients who have a real need for the medicine either because they have failed to respond to a beta-interferon or because their disease is severe and getting worse rapidly. The Committee decided that Tysabri's benefits are greater than its risks and recommended that it be given marketing authorisation.

### **What measures are being taken to ensure the safe use of Tysabri?**

The company that makes Tysabri will agree on measures to further enhance the monitoring of patients with each Member State, such as registries and studies of patients receiving Tysabri. It will also supply all doctors in each Member State who prescribe Tysabri with an educational pack that includes information on the safety of Tysabri, including information on which patients may be at a higher and lower risk of PML, and forms for use with patients at the start of treatment and after two years to inform them of the risks associated with the medicine.

### **Other information about Tysabri:**

The European Commission granted a marketing authorisation valid throughout the European Union for Tysabri to Elan Pharma International Ltd on 27 June 2006. After five years, the marketing authorisation was renewed for a further five years.

The full EPAR for Tysabri can be found on the Agency's website: [ema.europa.eu/Find\\_medicine/Human\\_medicines/European\\_Public\\_Assessment\\_Reports](http://ema.europa.eu/Find_medicine/Human_medicines/European_Public_Assessment_Reports). For more information about treatment with Tysabri, read the package leaflet (also part of the EPAR) or contact your doctor or pharmacist.

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