



TYSABRI® ▼ (natalizumab) Update

December 2010

Dear Health Care Professional,

As part of Biogen Idec's ongoing commitment to educational guidance, please find enclosed an updated electronic Physician Pack containing the following elements;

- Physician information about TYSABRI (**updated**)
- Appendix 1 Summary of Product Characteristics (**updated**)
- Appendix 2 Package Leaflet (**updated**)
- Appendix 3 Patient alert card
- Appendix 4 Treatment initiation and treatment continuation forms (**new**)

This information replaces all previous versions.

Please keep for reference purposes and access as appropriate.

Summary of Main Changes to the Physician Pack;

- The risk of PML increases if the patient has received prior treatment with an immunosuppressant, independent of TYSABRI treatment duration.
- Informing patients about the risk of PML, via a new treatment /continuation information form
- Carefully reconsidering the benefit and risk of the treatment after 2 years together with the patient.
- Performing a Magnetic Resonance Image (MRI) within 3 months before initiation of treatment with TYSABRI, and repeating it on a yearly basis to update this reference.
- Continued clinical vigilance.
- Prompt discontinuation of TYSABRI when PML is suspected with subsequent appropriate evaluation, including a standardised magnetic resonance imaging (MRI) scan and lumbar puncture.
- Preferably treating patients as part of national registries or post-marketing studies.

I hope this information is of value.

Please do not hesitate to contact the Medical Information Helpline if you have any questions.

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Prescribing information: TYSABRI[®] ▼
(natalizumab)

Please refer to the Summary of Product Characteristics for full prescribing information.

Indications: Single disease modifying therapy in highly active relapsing remitting multiple sclerosis for the following patient groups: Patients with highly active relapsing remitting multiple sclerosis or patients with high disease activity despite treatment with interferon-beta.

Dosage and administration: TYSABRI therapy is to be initiated and continuously supervised by specialised physicians experienced in the diagnosis and treatment of neurological conditions; centres should have resources for the management of hypersensitivity reactions and timely access to MRI. TYSABRI 300mg is administered by IV infusion once every 4 weeks. Infuse the diluted solution over approximately 1 hour at 2ml/min. Observe patients during infusion and for 1 hour afterwards for signs and symptoms of hypersensitivity reactions.

Contraindications: Hypersensitivity to natalizumab or to any of the excipients; progressive multifocal leukoencephalopathy (PML); patients with increased risk of opportunistic infections, including immunocompromised patients (including those currently receiving immunosuppressive therapies or those immunocompromised by prior therapies, e.g. mitoxantrone or cyclophosphamide); combination with interferon-beta or glatiramer acetate; known active malignancies; children under 18 years. TYSABRI is not recommended for use in patients aged over 65 years. **Warnings and precautions:** PML; use of TYSABRI has been associated with increased risk of PML, this increases with treatment duration, especially beyond 2 years, and/or if the patient has received prior treatment with an immunosuppressant. Before initiation of treatment with TYSABRI, a recent (usually within 3 months) MRI should be available and should be repeated yearly. Patients must be monitored at regular intervals for any new or worsening neurological symptoms or signs suggestive of PML. If PML is suspected, further dosing must be suspended until PML has been excluded. If the symptoms are suggestive of PML, or if any doubt exists, further evaluation, including MRI (compared with pre-treatment MRI) and repeat neurological assessments should be considered. Once PML has been excluded, dosing of TYSABRI may resume. If patients develop PML, the dosing of TYSABRI must be

permanently discontinued. **Educational guidance;** all physicians who intend to prescribe TYSABRI must ensure they are familiar with the Physician Information and Management Guidelines. Physicians must discuss the benefits and risks of TYSABRI therapy with the patient, provide them with a Patient Alert Card and re-inform at 2 years. Patients and their caregiver should be instructed that if they develop any new or worsening symptoms they should inform their physician that they are being treated with TYSABRI. Physicians should counsel patients on the importance of uninterrupted dosing, particularly in the early months of treatment.

Hypersensitivity; hypersensitivity reactions have been associated with TYSABRI, including serious systemic reactions. These reactions usually occur during the infusion or up to 1 hour after completion of infusion. If a hypersensitivity reaction occurs TYSABRI must be permanently discontinued. **Immunogenicity;** in the case of disease exacerbations or infusion related events the presence of antibodies should be evaluated. Treatment should be discontinued if persistent antibodies develop. **Stopping therapy;** if therapy is discontinued the physician needs to be aware that TYSABRI has pharmacodynamic effects for up to 12 weeks **Pregnancy and lactation:** If patients become pregnant while taking TYSABRI, discontinuation of TYSABRI should be considered. Patients receiving TYSABRI should not breastfeed their infants. **Undesirable effects:** The most commonly reported symptoms are: **Nervous system disorders;** headache, dizziness. **Gastrointestinal disorders;** vomiting, nausea. **Musculoskeletal and connective tissue disorder;** arthralgia. **Infections and infestations;** urinary tract infection, nasopharyngitis. **General disorders and administration site conditions;** rigors, pyrexia, fatigue. **Immune system disorders;** urticaria. Other less common events include; infusion reactions, hypersensitivity reactions, immunogenicity, PML, other opportunistic infections and spontaneous cases of serious liver injuries. **Legal classification:** POM. **Pack size:** 1 vial/pack. **Price:** UK; £1130/vial. **Package quantities:** 300mg/15ml. **Marketing Authorisation Number;** EU/1/06/346/001. **Marketing Authorisation Holder:** Elan Pharma International Ltd., Monksland, Athlone, County Westmeath, Ireland. **Date of last revision of prescribing information:** Dec 2010.

Adverse events should be reported.
Reporting forms and information can be found at
www.yellowcard.gov.uk (UK) or www.imb.ie (Ireland).
Adverse events should also be reported to Biogen Idec
on 0800 008 7401 (UK) or 1800 812 719 (Ireland).