CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT TO BE IMPLEMENTED BY THE MEMBER STATES

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The National Competent Authorities in each Member State shall discuss and agree with the Marketing Authorisation Holder (MAH) measures to enhance further the monitoring of patients treated with Tysabri (e.g. registries, post-marketing surveillance studies) as appropriate and must ensure that the MAH implements the agreed measures within an agreed time frame.

The Member States shall discuss and agree the physician pack with the MAH and ensure that:

The Marketing Authorisation provides all physicians who intend to prescribe TYSABRI with a physician pack containing the following elements:

- Summary of Product Characteristics and Package Leaflet
- Physician information about TYSABRI
- Patient alert card
- Treatment initiation and treatment continuation forms

The physician information about TYSABRI shall contain the following key elements:

- That TYSABRI therapy is to be initiated and continuously supervised by specialised physicians experienced in the diagnosis and treatment of neurological conditions, in centres with timely access to MRI.
- Information that atypical/opportunistic infections, and in particular PML, may occur with TYSABRI and include:
    - That the risk of PML increases with increasing duration of treatment and that treatment beyond 24 months carries additional risk
    - Other factors associated with an increased risk for the development of PML
        - Immunosuppressant treatment prior to the use of Tysabri
        - Presence of anti-JC virus antibodies
    - A stratification of the risk of developing PML based on the three identified risk factors
    - Diagnosis of PML including differentiation between PML and MS relapse
    - PML management algorithm
    - Possibility of other opportunistic infections
    - The recommendation that patients should have MRI scans at the following times
        - Within 3 months prior to starting TYSABRI
        - Annually during treatment with TYSABRIi
        - At the first sign of any symptoms indicative of the possibility of PML.
    - The need to inform patients about the benefits and risk of TYSABRI and provide them with:
        - A copy of the treatment initiation form
        - A patient alert card including a core text agreed by the CHMP
    - If treatment is to be continued for longer than 24 months, the need to inform patients about the increased risk of PML and provide them with a copy of the treatment continuation form
    - The need to inform the National Competent Authority about any cases of PML

- Information about the following adverse reactions:
    - Infusion reactions
    - Hypersensitivity reactions
    - Antibody formation

- Information about any registry or other monitoring system set up in the Member State and how to enter patients

The treatment initiation form should contain the following elements:

- That the aim of the treatment initiation form is to provide patients with information on PML and IRIS
- Information on PML and IRIS including the risk of developing PML during Tysabri treatment stratified by prior treatment with immunosuppressants and JC virus infection.
- Confirmation that the doctor has discussed the risks of PML and the risk of IRIS if treatment is discontinued following suspicion of PML
- Confirmation of patient understanding of the risks of PML and that they have received a copy of the form and a patient alert card
- Patient details, signature and date
- Prescriber name, signature and date
- Date treatment started

The treatment continuation form should contain the elements of the treatment initiation form and, in addition, a statement that the risks of PML increase with duration of treatment and that treatment beyond 24 months carries additional risk.