Published by
Ministry of Health, Labour and Welfare

Translated by
Pharmaceuticals and Medical Devices Agency



# Revision of Precautions
# Natalizumab (genetical recombination)

September 13, 2016

**Non-proprietary name**

Natalizumab (genetical recombination)

**Safety measure**

Precautions should be revised in the package insert.

In the Important precautions section regarding the risk of progressive multifocal leukoencephalopathy (PML), the following texts should be revised (underlined parts are revised):

Risk factors of PML due to this drug include being positive for anti-JC virus (JCV) antibody, having a history of treatment with an immunosuppressive agent, and long-term administration. The risk of PML is reportedly higher in patients with all these factors or those with a high anti-JCV antibody titer and a history of long-term treatment with this drug despite no history of treatment with an immunosuppressive agent. To consider the risk and benefit, the latest incidence of PML by patients with each risk factor (shown in documents such as the Guide for Proper Use) should be confirmed.

The following text should be revised regarding the diagnosis of PML (underlined parts are revised):

The latest MRI images should be periodically obtained before the start of and during administration because they are useful for the diagnosis of PML. More frequent MRI scanning should be considered for patients with a high risk of PML.

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The following text should be added:

Acute retinal necrosis by administration of this drug has been reported bilaterally in some cases. Patients should be carefully monitored during administration of this drug because acute retinal necrosis may rapidly lead to blindness. Patients should be instructed to consult ophthalmologists immediately if symptoms such as reduced visual acuity, blurred vision, conjunctival hyperemia, and eye pain are observed.

In the Clinically significant adverse reaction subsection regarding PML of the Adverse reaction section, the following texts should be revised (underlined parts are revised):

Progressive multifocal leukoencephalopathy (PML), granule cell neuronopathy (GCN):
PML may occur. Patients should be carefully monitored during and after treatment with this drug. If symptoms such as hemiplegia, quadriplegia, cognitive impairment, aphasia, vision disorders, and cerebellar symptoms (including ataxia and nystagmus) are observed, administration of this drug should be discontinued immediately. The onset of PML should be confirmed through examinations such as imaging diagnostics with MRI and cerebrospinal fluid tests, and appropriate measures such as plasmapheresis should be adopted. In addition, cases of GCN caused by JCV have been reported in patients receiving this drug. If cerebellar symptoms occurred, potential GCN should be noted. Patients should be carefully monitored for the onset of immune reconstitution inflammatory syndrome after discontinuation of administration of the drug or after elimination of the drug by plasmapheresis.

Furthermore, the following text should be added:

Acute retinal necrosis (ARN):
Acute retinal necrosis may occur. If symptoms such as reduced visual acuity, blurred vision, conjunctival hyperemia, and eye pain are observed, administration of this drug should be discontinued immediately. The onset of ARN should be confirmed through ophthalmological examinations, and appropriate measures should be adopted.

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