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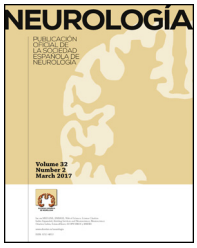

REVIEW ARTICLE

Consensus statement on the treatment of multiple sclerosis by the Spanish Society of Neurology in 2016☆

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Abstract With the advent of new disease-modifying drugs, the treatment of multiple sclerosis is becoming increasingly complex. Using consensus statements is therefore advisable. The present consensus statement, which was drawn up by the Spanish Society of Neurology's study group for demyelinating diseases, updates previous consensus statements on the disease.

The present study lists the medications currently approved for multiple sclerosis and their official indications, and analyses such treatment-related aspects as activity, early treatment, maintenance, follow-up, treatment failure, changes in medication, and special therapeutic situations.

This consensus statement includes treatment recommendations for a wide range of demyelinating diseases, from isolated demyelinating syndromes to the different forms of multiple sclerosis, as well as recommendations for initial therapy and changes in drug medication, and additional comments on induction and combined therapy and practical aspects of the use of these drugs.

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PALABRAS CLAVE
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Algoritmo

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Resumen La incorporación de nuevos medicamentos para modificar el curso de la esclerosis múltiple y la complejidad de su uso plantea la conveniencia de utilizar consensos terapéuticos. El consenso actual ha sido elaborado por el grupo de enfermedades desmielinizantes de la Sociedad Española de Neurología y actualiza consensos previamente publicados.

Se enumeran los medicamentos aprobados para la esclerosis múltiple con sus indicaciones oficiales. Se analizan aspectos relacionados con el tratamiento, como la presencia de actividad, la precocidad, el mantenimiento terapéutico, el seguimiento, el fallo terapéutico, los cambios de medicación y el tratamiento en situaciones especiales.

Se elaboran indicaciones de tratamiento desde el síndrome desmielinizante aislado a las distintas formas de esclerosis múltiple detallando recomendaciones de tratamiento inicial, cambios de medicación, con consideraciones sobre terapia combinada e inducción y aspectos prácticos del uso de medicamentos.

Introduction

Multiple sclerosis (MS) is a chronic disease of the central nervous system (CNS) characterised by inflammation, demyelination, glial scarring, and axonal damage leading to varying degrees of neurological impairment. MS usually affects young adults and is 2 to 3 times more frequent in women. It causes episodes of neurological dysfunction lasting a few days or weeks and known as relapses; they tend to resolve partially or completely, especially in the early stages of the disease. In a small percentage of patients (around 10%), MS leads to progressive neurological impairment without relapses.

The associated symptoms vary greatly. The first episode, known as clinically isolated syndrome (CIS), is associated with symptoms indicative of spinal cord, brainstem, or eye involvement. Although symptoms usually resolve, relapses leave permanent sequelae.

Disease progression also varies. The first stage, which usually lasts several years, is characterised by sporadic relapses. After 10 to 15 years, relapses become less frequent. Approximately half of all patients will develop progressive deterioration (this stage is called ''secondary progressive MS'').

MS has 2 distinct characteristics: autoimmune inflammation, which is typical of the initial stages and manifests as relapses and demyelinating lesions in white and grey matter on MR images; and degeneration, which is associated with irreversible damage to axons and neurons starting in the early stages of the disease and becoming more significant in later stages.

The personal and socio-economic impact of MS is considerable given its frequency, the associated disability it causes in young adults, its interference with work productivity, the associated need for care, and high treatment costs.

This document is an updated version of the 2010 consensus document published by the Spanish Society of Neurology's study group for demyelinating diseases.[1,2]

Approved drugs for multiple sclerosis

In the past 20 years, 11 drugs have been approved as MS treatments in the European Union, plus azathioprine in some individual countries including Spain.

All these drugs have had a positive impact on several clinical variables (by decreasing relapse frequency and, to a lesser extent, cumulative disability) and on MRI results. The first of these drugs, approved 20 years ago, was interferon beta 1b (Betaferon®), followed by intramuscular (IM) interferon beta 1a (Avonex®), subcutaneous (SC) interferon beta 1a (Rebif®), and glatiramer acetate (Copaxone®). Mitoxantrone (Novantrone®) was then approved, followed by the first monoclonal antibody, natalizumab (Tysabri®), a few years later. Fingolimod (Gilenya®) was the first drug to be administered orally. In 2014, the 4 most recent drugs were approved: oral drugs teriflunomide (Aubagio®) and dimethyl fumarate (Tecfidera®), monoclonal antibody alemtuzumab (Lemtrada®), and pegylated interferon beta 1a (Plegridy®). Each of these drugs was approved based on the results of clinical trials.[3–13]

They have all been proven effective for treating relapsing-remitting MS; several of these drugs are also effective against CIS given that they have been found to delay onset of further demyelinating episodes or new MRI lesions; others have been proved effective in patients with secondary progressive MS associated with relapses. According to the published clinical trials, none of these drugs has been shown to alter primary or secondary progression when MS is not associated with relapses (further explanation to follow).

Summary of official indications for treatment

Each of the approved drugs has been studied in clinical trials including patients with a certain clinical form of the disease;