Guidelines to be followed by centres, services and units in order to be designated as Reference Centres, Services and Units of the National Health System, as agreed by the Interterritorial Board

43. MULTIPLE SCLEROSIS

Multiple Sclerosis (MS) has been known as a clinical-pathological condition for more than 130 years, although its aetiology is still unknown. MS is characterized by focal lesions of the central nervous system, called "plaques", with inflammation being the most prominent aspect as well as myelin loss (demyelination), axon loss (neurodegeneration) and gliosis. Usually there are multiple lesions extended all through the central nervous system.

MS clinical condition is a consequence of the neuropathological processes mentioned above. The demyelination process causes an alteration in the normal myelin transmission method, slowing down the transmission and even blocking it, causing the disease symptoms to appear. Transitory symptoms are related to the inflammation/demyelination and the permanent symptoms are linked to the axon/neural loss and gliosis.

The most striking characteristic of MS is its high variability; symptoms and signs are determined by the location of the damage. The lesions show preference for certain parts of the central nervous system (periventricular, optic nerve and chiasm, brain stem, cerebellar peduncles, spinal cord), causing symptom clusters: weakness, paraesthesia, vision changes, diplopia, nystagmus, dysarthria, tremor, ataxia, deep sensibility alterations, vesical dysfunction, paraparesis, emotional changes and cognitive impairment.

A pre clinical stage of the disease may be distinguished, in which damage may be detected unexpectedly through MRI without having taken place any clinical symptoms. Later, in 90% of the cases, numerous relapses start (relapsing remitting type – RRMS). After some years, there is a transitional stage (when the patient reaches a 3-4 disability in the EDSS) and later it evolves to the secondary progressive stage (PPMS). There are 10% of the patients with a progressive course since the beginning, the primary progressive type (PPMS).

Clinical diagnosis of MS is performed by taking into consideration clinical criteria in terms of spatial (symptoms and signs indicating the existence of two independent lesions in the central nervous system) and temporal distribution (two or more episodes of neurological dysfunction). Nowadays, with clinical techniques and help from paraclinical research methods (CSF, evoked potentials, magnetic resonance), it is possible to rule out with high confidence other diseases and reach increasingly earlier a MS diagnosis with certainty. There are diagnosis criteria as well as disability scales being commonly used.

Diagnosis and, specially, treatment of the disease are more and more complex, justifying the need for reference units, since nowadays, without being acknowledge, they do exist and patients must transfer without guarantees. Frequency of the disease seems to be increasing.

The type of cases that would be cared for in these units would be those patients who, from the onset of disease, show a more aggressive progression than usual and are difficult to control in general neurological care, since either great experience in this type of cases is required or specialized training in diagnosis techniques (cerebrospinal fluid analysis, evoked potentials, MRI) and differential diagnosis are required. Despite these diagnostic requirements, these units must have, either on the unit itself or in its centres, all therapeutic modalities, including the possibility for complex treatment, such as bone marrow transplantation, and great experience in the use of immunomodulatory/ immunosupressants treatments, only used in units with a high number of patients and which require support from studies on antibody used instead of drugs or studies of pharmacogenetics/pharmacogenomics or proteomics in order to lead the treatments.

A. Rationale for the proposal

► Epidemiological data on multiple sclerosis (incidence and prevalence).	MS is the most common chronic neurological disease in young adults in Europe and North America. Incidence of 3-4 cases/100,000 population. Prevalence of 80 cases/100,000 population. Although MS is considered a rare disease, this condition is changing, since both incidence and prevalence are increasing, currently being Spain a medium-high risk area.

B. Guidelines to be followed by Centres, Services and Units in order to be designated as Reference Centres, Services and Units treating patients with multiple sclerosis

► Experience of the Reference Centres, Services	

and Units: - Activity: • Number of patients with multiple sclerosis that should be assisted in a year to ensure an adequate care. • Number of procedures similar to those specific to the designation requested that should be performed in a year. - Other data: research on the subject, postgraduate teaching, continuing training, publications, etc.	 - 500-1,000 patients (new and being monitored) per year, of these at least 25-30 new patients. - Procedures in patients with multiple sclerosis: ● 50 lumbar punctures / cerebrospinal fluid. ● 250 MRI. ● 100 evoked potentials. ● 25 optical coherence tomography. - Accredited postgraduate teaching: Unit participation in the internship and residency programme of the Centre. - Participation in research projects and publications in the field[a]. - Continuing training programme standardized and authorized by the centre's board of directors. - Clinical multidisciplinary sessions, at least once a month, in order to make clinical decisions and coordinate treatments.
► Specific resources of the Reference Centres, Services and Units: - Human resources required for the adequate care of multiple sclerosis. - Basic education of the team members[b].	 - 2 neurologists. - 1 clinical psychologist and/or psychiatrist. - Nursing staff. - Neurologists with, at least, 3 year experience in patients with multiple sclerosis. - Clinical psychologist and/or psychiatrist with, at least, 3 year experience in patients

	with multiple sclerosis. - Nursing staff with experience in patients with multiple sclerosis.
- Specific equipment required for the adequate care of multiple sclerosis.	- Day hospital within the unit or available in the centre, for immunomodulatory/ immunosupressants IV outpatient treatments. - Premises for extractions and handling of body fluids (blood, CSF). - 1 outpatient care area, exclusive to the unit. - CSF/Serum Bank: 70 ºC, aliquoted, serum and plasma samples. Required for immunologic studies, genetic studies, etc. - System for communication with patients, for extraordinary care in cases of relapses or complications (telephone, e-mail, website).
► Resources from other units and services besides those belonging to the Reference Centres, Services and Units required for the adequate care of multiple sclerosis.	- Radiodiagnosis services/unit, with neuroradiology, 1.5 Tesla MRI or higher. - Neurophysiology services/unit, performing visual, auditory, somatosensory and motor evoked potentials. - Nuclear medicine services/unit, with SPECT, required for differential diagnosis. - Immunology services/unit, performing detection of oligoclonal IgG and IgM bands. - Rehabilitation services/unit with experience in patients with multiple sclerosis. - Ophthalmology services/unit, performing optical coherence tomography (OCT) and with experience in patients with multiple sclerosis. - Urology services/unit with experience in patients with multiple sclerosis. - Genetics services/unit, with the possibility to storage DNA samples for genetic studies. - Bone marrow transplantation unit availability.
► Procedure and clinical results indicators of the Reference Centres, Services and Units [c]:	**The indicators will be agreed with the Units that will be designated.**
► Existence of an adequate IT system (Type of data that the IT system must include to allow identification of the activity and evaluation	- Filling up the complete MBDS of hospital discharge. - The unit must have a *registry of patients with multiple sclerosis* which at least must

of the quality of the services provided)	include: - Medical record number. - Date of birth. - Sex. - Patient's habitual region of residence. - Admission date and discharge date. - Type of admission (Emergency, planned, other). - Type of discharge (Home, hospital transfer, voluntary, death, transfer to a healthcare centre, other.) - Service in charge of patient's discharge. - Main diagnosis (ICD-9-CM). Date of diagnosis and date of relapses. - Other diagnosis (ICD-9-CM). - Diagnostic procedures provided to the patient (ICD-9-CM): Type of procedure and date when it was provided. - Therapeutic procedures provided to the patient (ICD-9-CM): Type of procedure and date when it was provided. ◆ Immunomodulatory treatment. ◆ Immunosupressants treatment. ◆ Bone marrow transplantation. ◆ Other therapeutic procedures. - Complications (ICD-9-CM). - Monitoring: number of recurrences (relapses). Disability progression, patients' degree of satisfaction. - The unit must have the required data which should be sent to the Spanish National Health Service Reference Centres, Services and Units Appointment Commission Secretariat for yearly reference unit monitoring.

[a] *Criteria to be assessed by the Appointment Commission.*

[b] *Experience will be accredited by certification from the hospital manager.*

[c] *Clinical results standards, agreed to by the experts group, will be assessed, initially by the Appointment Commission, while in the qualification process, as more information from the Reference Centres, Services and Units is being obtained. Once qualified by the Appointment Commission, the Quality Agency will authorize its compliance, as for the rest of guidelines.*

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