**RESEARCH AERTICLE**

# Central American and Caribbean Consensus for the Treatment of Multiple Sclerosis and Therapeutic Attitudes Facing the COVID-19 Pandemic

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**Abstract**

Therapeutic decisions for multiple sclerosis have become more complex in the Central American and Caribbean region (CAC), with new treatments appearing every year but with well-known limitations in terms of access and application. Concomitantly, the advent of the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) pandemic, with an increasing number of cases in the region, has increased the need for a consensus on therapeutic decisions to be made for people with multiple sclerosis. Under these circumstances, a reference framework is needed to gather current information to assist neurologists in making therapeutic decisions.

An evidence-based consensus on the use of disease-modifying therapies for multiple sclerosis was proposed and accomplished by the Central American and Caribbean Multiple Sclerosis Forum (FOCEM), including recommendations for treatment during the pandemic. Using the consensus panel development methodology, after a bibliographic review of the best quality and actualized information, a final report was written; this includes statements that reached more than 70% consensus among the panel of experts.

The recommendations encompass indications for drugs available for multiple sclerosis, definitions of therapeutic failure, patient follow-up, factors of poor prognosis, discontinuation of treatment, treatment during pregnancy and lactation and specific recommendations to apply during the SARS-CoV-2 pandemic.

**Keywords:** COVID-19, SARS-CoV-2, multiple sclerosis, consensus, Central America.

# 1 | INTRODUCTION

Multiple sclerosis (MS) is a chronic, inflammatory, autoimmune, demyelinating, potentially neurodegenerative disease of the central nervous system, primarily affecting young adults. Its etiology is not been well established; however, genetic and environmental factors may contribute to the risk of developing this disease (1).

Epidemiological data from MS in Central America and the Caribbean show a prevalence between 0.9 and 19.8 per 100,000 inhabitants (2) In the region, the 2017 version of the McDonald Criteria (3) is utilized for diagnosis, retaining the clinical classification proposed by Lublin et al based on clinical and magnetic resonance imaging (MRI) activity (4): clinically isolated syndrome (CIS), relapsing-remitting multiple sclerosis (RRMS), secondary progressive multiple sclerosis (SPMS), and primary progressive multiple sclerosis (PPMS). Clinical activity implies the development of relapses; meanwhile, MRI activity is generally defined as the presence of gadolinium-enhancing T1 lesions and/or the appearance of a new T2 lesion or an enlarging signal with respect to previous MRI studies. The general recommendation is to use MRI equipment of at least 1.5 Tesla, which is readily available in our region.

Over the last two decades, diverse therapeutic agents for MS have been approved by international licensing agencies. In addition, although the region is an endemic area for various infections, it has not previously faced extreme circumstances, such as those caused by the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) pandemic. For this reason, the current situation requires the development of specific treatment guidelines for our region.

Treatment guidelines for Latin America have already been published (5). Nevertheless, at present, no specific document has been produced for the Central American and Caribbean region, which represents an unmet need for regional therapeutic recommendations.

A working and research group from the Central American and Caribbean region dedicated to MS-related research (Central American and Caribbean Forum on MS or FOCEM) was founded in Panama City on April 4th, 2018. The group aimed to develop a consensus on scientific evidence-based recommendations for therapeutic strategies for MS in the area. The document was also intended to provide support to physicians, patients, regulatory entities, and healthcare policy decision makers in each of these countries regarding the complexities of actual MS management.

# 2 | METHODS

To achieve consensus, a *consensus panel development* methodology was used (6). A project coordinator was appointed who formulated the questions addressing the items to develop for the common accord Table 1 The questions were emailed to an expert panel composed of 16 neurologists, two representatives from each participating country (all Hispanic Central American countries: Guatemala, El Salvador, Honduras, Nicaragua, Costa Rica and Panama, as well as the Dominican Republic and Cuba), who provided input for each question as well as amendments.

Based on the designed questions in the consensus, a literature search was conducted on the PubMed and Cochrane databases. Electronic alerts were activated in leading neurology journals publishing articles about multiple sclerosis, including papers up to April 2020.

Topics related to treatment efficacy, systematic reviews, phase 3 clinical trials, and high-quality cohort studies were included. To address safety issues, case reports were also included. Treatment guidelines

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**TABLE 1:** PICO questions for the consensus panel

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|---|
| 1. When should patients be started on approved drugs for remitting-relapsing Multiple sclerosis and for isolated clinical syndrome? |
| 2. Which drugs can be considered for progressive multiple sclerosis? |
| 3. How should therapeutic failure for a disease-modifying drug be defined? |
| 4. Which are the minimum variables to assess during follow-up for patients with multiple sclerosis? |
| 5. Are there variables that help define patients at a higher risk of disability progression in the early stages of multiple sclerosis? |
| 6. What are the guidelines to consider when sequencing treatment for Patients with remitting-relapsing multiple sclerosis? To become pregnant or currently lactating? |
| 7. Which should be the approach for patients with multiple sclerosis wishing |
| 8. For patients stable in the long term, is it prudent to discontinue drugs? |

published by the American and European Neurology Academies were reviewed.

In terms of information related to the SARS-CoV-2 pandemic, a review was carried out from expert recommendations provided by the World Health Organization, the Multiple Sclerosis International Federation, the Latin-American Committee for the Research and Treatment of Multiple Sclerosis, and others.

A data summary obtained from each question to be addressed in the consensus was provided to the experts' panel for review. In the context of the XVII Central American Congress on Neurology, May 25th 2018, the panel met for the initial proposed recommendations. Consensus was defined as a homogeneous vote from 70% of the participants. Later, the recommendations were completed in virtual meetings.

A final version was drafted with the recommendations obtained by consensus from the working group.

## 3 | CONSENSUS RECOMMENDATIONS

### A. USE OF DISEASE-MODIFYING DRUGS

There are multiple options available for disease-modifying drugs (DMDs) for patients with RRMS; most of them are available in the countries that contributed to the FOCEM. At the time of completion of this study, there was no commercial or institutional availability of dimethyl fumarate, pegylated interferon 1a, siponimod, diroximel fumarate or ozanimod in these countries.

Based on results obtained in terms of reduction of the annualized relapse rate in pivotal trials, approved drugs are generally classified as *high-efficacy* (>50%) or *moderate-efficacy*. High-efficacy drugs include fingolimod, cladribine, natalizumab, alemtuzumab and ocrelizumab, while the moderate-efficacy group includes interferon beta-1a 44 mg, interferon beta 1a 30 mg, interferon beta 1b, glatiramer acetate, fumarate and teriflunomide (7) Oral Siponimod, recently approved by the FDA, could be included among the high-efficacy drugs, and it is licensed as well for active SPMS (8, 9).

Patients with PPMS have fewer therapeutic options. The only medication currently approved for this phenotype is ocrelizumab (10) . International licensing agencies have approved the use of oral cladribine as a second-line drug in relapsing MS after an alternative therapy fails or is not tolerated. It is also indicated for the active SPMS phenotype but not for CIS in view of its safety profile (11).

**RECOMMENDATION 1:** Drugs approved for use for RRMS and CIS should be initiated as soon as the diagnosis is made. If available, physicians should prescribe drugs approved by the European Medicine Agency (EMA) and/or the United States Food and Drug Administration (FDA), as well as by their national health drug license-granting authorities.

**RECOMMENDATION 2:** Ocrelizumab should be considered for PPMS. The experts provided the caveat that the clinical trials show a higher effect on younger patients and with the presence of MRI activity.

**RECOMMENDATION 3:** In patients with SPMS with clinical and/or radiologic activity, the use of doriximel fumarate (12), ozanimod (13), siponimod (14) , cladribine and ocrelizumab could be considered.

## B. FOLLOW-ON THERAPEUTIC MOLECULES AND BIOSIMILARS IN THE MANAGEMENT OF MULTIPLE SCLEROSIS

There are numerous non-innovator drugs in the region, manufactured in Latin America and Asia. The proposed efficacy and safety profiles of these drugs are based on data obtained by controlled clinical trials accomplished by the innovator (brand or reference medication). Follow-on therapeutic molecules are those that have not been involved in controlled phase 3 clinical trials or comparative head-to-head studies with the original products. The lack of adequate assessments cannot guarantee safety and clinical efficacy similar to those of the reference product. Some of these molecules have been approved basically with no restrictions by national regulatory agencies, mostly with no evidence provided (15)

Considering this fact, it is urgent for national regulatory agencies to establish sufficiently stringent guidelines to guarantee that drugs used to treat MS populations in the region are safe, effective, and of adequate industrial and pharmacological quality. These guidelines must specify whether the drug in question is a chemically synthesized molecule, a biologic drug or a complex nonbiologic drug, as there are recognized differences in manufacturing characteristics and quality assessments for each of these three major drug groups (16). Bioequivalence under these circumstances may be compromised.

**RECOMMENDATION**: National regulatory entities are advised to revise their requirements for approval of small-molecule chemically synthesized drugs, biologic drugs, and nonbiologic complex drugs to ensure that only those drugs that can guarantee proper quality of production, safety, and efficacy are available in the market for use by patients with MS.

In this sense, the pharmaceutical industry, in producing biosimilars, must provide their own clinical data on efficacy and safety, risk-management plans, and adequate long-term quality controls and pharmacovigilance to detect, in a timely manner, any adverse effects unknown at the time of approval while ensuring a smooth quality level of the drug over time.

Physicians managing patients with multiple sclerosis must maintain updated knowledge of the definitions and therapeutic profiles of generic drugs and biosimilars offered locally or in their respective institutions.

## C. ASSESSING THE RISK OF EARLY DISABILITY PROGRESSION UPON INITIAL PRESENTATION

Treatment for each patient should be personalized from the initial approach, and an effort should be made to detect any characteristics that can predict the risk of early disability progression in patients.

Characteristics that can be assessed in daily clinical practice in the region and that have been associated with a higher risk of disability progression include the following (17–27) :

• Male sex

• Initial ataxia

• High rate of relapse within the first two years after onset of symptoms (>2)

• More than 10 lesions on brain MRI

• At least 2 infratentorial lesions (brain stem and spinal cord) on MRI

• Positive oligoclonal bands (OCBs)

• Presence of residual disability since initial presenta-tion

• Kurtzke's functional motor system impairment upon initial presentation

• Elevated annual relapse rate ($\geq$ 2 per year)

• Genetic African ancestry

• Older age at disease onset

• Delay in the start of immunomodulator therapy

**RECOMMENDATION 1:** If one or several of the above risk factors for poor prognosis are present, starting high-efficacy therapies is recommended, such as fingolimod, natalizumab, ocrelizumab, alemtuzumab, or cladribine, since, theoretically, induction therapy may reduce the risk of relapse and disability progression in patients with RRMS.

The clinician's decision-making therapy should be based on the assessment of risk factors considering the safety and tolerability of each drug in association with everyone's characteristics, including for instance, the presence of comorbidities Figure 1.

**RECOMMENDATION 2:** The patient should be educated and informed, and their opinion should be considered, as not all of them will have the same tolerance for managing the possible side effects of each drug, nor they do have the same expectations of treatment.

## D. DEFINITION OF THERAPEUTIC FAILURE AND GUIDELINES FOR SEQUENCING DISEASE-MODIFYING DRUGS

MS disease activity is assessed from clinical manifestations and MRI behavior. Several scoring systems have been proposed to define patients not responding to treatment and at risk for disability progression. Most of these scales have been assessed with short follow-up periods and only for patients using certain types of drugs. Tools to define nonresponders to treatment include the Rio score (27), the modified Rio score (28), and the Recommendations for Treatment Optimization in Latin America (5, 29, 30), among others. They all require a certain level of clinical and/or radiologic disease activity before a patient can be classified as a non-responder. Rio et al defined the concept of minimal evidence of disease activity (MEDA) as the presence of relapse not causing increased disability, the isolated presence of minimal radiologic activity (one or two new T2-weighted lesions or 1 new gadolinium-enhancing lesion), or minimal clinical and radiologic activity (one relapse and one new T2-weighted lesion on MRI) (31). Scoring can be employed periodically to assess changes.

The concept of no evidence of disease activity (NEDA) as a treatment goal to maintain the best possible disease control involves the use of effective drugs (32). In the Central American and Caribbean region, NEDA 3 assessment is available, defined as no relapses, no disability progression and no activity on sequential conventional MRI studies.

Because most available drugs show an effect on the disease circa three months after initiating therapy, the presence of a new clinical event during this period is not considered a therapeutic failure. Therefore, a brain MRI scan is recommended 3 to 6 months after starting treatment, and this can be considered the baseline for future comparisons throughout patient follow-up (33).

There are two main reasons why a treatment modification is warranted for a patient:

1. Presence of adverse effects preventing treatment continuity

2. Lack of therapeutic efficacy of the chosen drug

**RECOMMENDATION 1:** Given that an international consensus is not available on the best group of characteristics defining efficacy failure for a specific treatment in an individual patient, an evaluation from a neurologist with experience in the management of multiple sclerosis is recommended. In each specific case, consideration should be given to maintain NEDA (e.g., in cases of more aggressive presentation) or MEDA status, in which case assessment with the Rio or modified Rio score is recommended. For patients with a score of 1 on these scales, the recommendation is to reassess the 3 variables within 6 months. If the score is 2 or 3, a change in therapy should be considered.
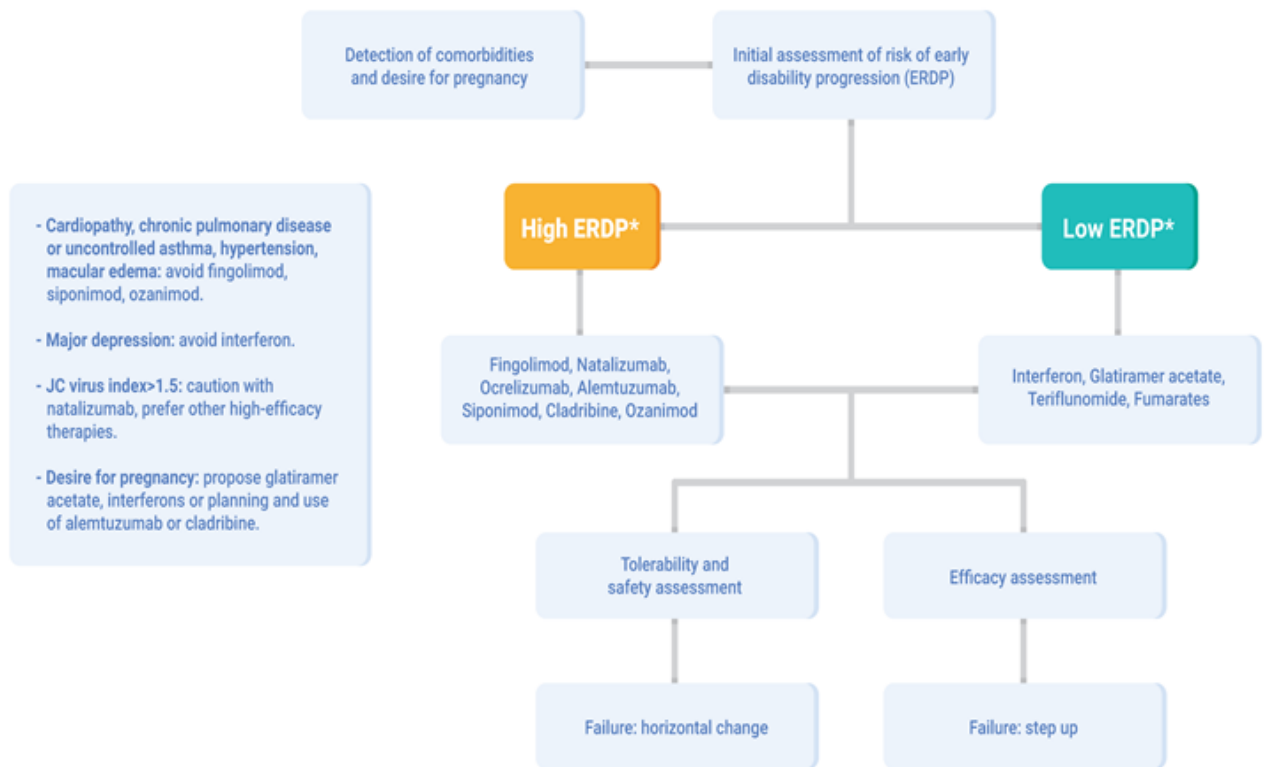
**RECOMMENDATION 2:** In the presence of therapeutic failure due to intolerance or the presence of adverse events, a drug of equal or superior efficacy (escalation approach) to the current drug is recommended, selecting an agent with features that make it unlikely to present the same adverse event detected.

**RECOMMENDATION 3:** If a lack of efficacy is detected, a drug with higher efficacy than the current one should be used, and the guidelines described in Figure 1 should be followed. The strategy of using induction therapy remains under study at present (34).

## E. CLINICAL VARIABLES TO ASSESS DURING FOLLOW-UP OF DISEASE ACTIVITY

Variables to assess during follow-up of patients with multiple sclerosis include

Relapses, clarifying if there is a need for steroid use or hospitalization, and whether they are associated with residual disability at 3 or 6 months.

- Cardiopathy, chronic pulmonary disease or uncontrolled asthma, hypertension, macular edema: avoid fingolimod, siponimod, ozanimod.

- Major depression: avoid interferon.

- JC virus index>1.5: caution with natalizumab, prefer other high-efficacy therapies.

- Desire for pregnancy: propose glatiramer acetate, interferons or planning and use of alemtuzumab or cladribine.

Detection of comorbidities and desire for pregnancy

Initial assessment of risk of early disability progression (ERDP)

High ERDP*

Low ERDP*

Fingolimod, Natalizumab, Ocrelizumab, Alemtuzumab, Siponimod, Cladribine, Ozanimod

Interferon, Glatiramer acetate, Teriflunomide, Fumarates

Tolerability and safety assessment

Efficacy assessment

Failure: horizontal change

Failure: step up

* Risk of disability progression determined by the presence of 1 clinical variable + 1 radiologic variable for poor prognosis, as outlined in the text.

**FIGURE 1:** The initial therapeuticdecision flowchart for MS patients.

MRI, conducted annually and recording any new or enlarging T2-weighted or T1 gadolinium-enhanced lesions. Disability assessment, recorded using EDSS scores and each functional scale score. This should be assess every 3 to 6 months.

Deeper knowledge of the disease has shown that disability goes beyond motor deficits and that other aspects are also affected even from early disease stages, as in the case of the cognitive domain, which is poorly evaluated by the EDSS scores (35).

It has been proposed to consider other variables to more accurately evaluate the patient's status. The working group defines mild impairment as 20% worsening in the results from the timed 25-foot walk test (T25W), the 9-hole peg test (9HPT), and visual acuity with the SLOAN chart or 4 fewer points in the symbol-digit modalities test (SDMT), while severe impairment involves 40% worsening in the above tests and 8 fewer points in the SDMT (36).

**RECOMMENDATION 1:** The number of relapses should be recorded annually, as should the number of new or enlarging T2-weighted lesions or T1-weighted gadolinium-enhanced lesions; the EDSS should be applied and its scores recorded every 3 to 6 months. Where logistics are appropriate, the T25W, 9HPT, SDMT, and low-contrast SLOAN tests should be administered.

**RECOMMENDATION 2:** If there are no abnormalities in the evaluation, it can be reviewed again in 6 months. If there is an impairment rated as mild in at least 1 test, a reassessment should take place in 3 months (33) .

**F. APPROACH TO PATIENTS WISHING TO BECOME PREGNANT OR BREASTFEEDING**

If there has been active disease during the preceding year, treatment continuity must be assessed at least until conception. In this case, glatiramer acetate, interferon beta, and natalizumab appear to be

safe, even during the first trimester of pregnancy. Continuation beyond that point must be considered with extreme care, especially for natalizumab, which has been associated with thrombocytopenia and hemolytic anemia in newborns from mothers using it in the third trimester (37, 38).

In patients with inactive MS, the recommendation is to suspend these drugs. In the case of fumarate, because its half-life is approximately 12 hours, the recommendation is to suspend it one week before conception. The recommended suspension time is 2 months prior to conception for fingolimod, 3 months for ozanimod, 10 days for siponimod and 4 months for alemtuzumab. In the case of teriflunomide, the recommendation is for the patient to undergo a drug clearance procedure, using cholestyramine 4 to 8 g every 8 hours for 11 days; it is considered to be safe for conception at serum levels of 0.02 mg/ml or lower. Furthermore, this drug has been detected in semen, and therefore, the same procedure is recommended for males. If cladribine is used, suspension is recommended 6 months before conception, both for men and women. In the case of ocrelizumab, women are advised to wait 6 months after the last dose to attempt pregnancy (7–14).

Lactation must be assessed individually, based on disease activity during pregnancy and in the $1^{st}$ month after birth and on access to supplementary lactation. A protective effect of exclusive lactation on the risk of postpartum relapse has been observed, but this effect is lost if lactation is combined with supplementary formula (39–41).

If the patient's MS has been inactive during pregnancy, they wish to nurse exclusively and have no evidence of disease activity on MRI in the first month after birth; they may breastfeed exclusively for 6 months without reinitiating DMDs. It is up to the clinician to perform a control brain MRI at 3 months to verify disease inactivity (42, 43).

In cases of patients with disease activity during pregnancy or on postpartum brain MRI, DMDs such as glatiramer acetate or interferon beta should be initiated, as they are preferred for their low expression in breast milk (44).

**RECOMMENDATION 1:** Patients with childbearing potential should be educated from the beginning of treatment about the need for planned pregnancy.

**RECOMMENDATION 2:** The use of drugs should be suspended (in accordance with the indicated withdrawal periods for each drug) before conception in patients with inactive disease. In cases of active disease and if the patient wishes to become pregnant, consider the use of glatiramer acetate during pregnancy or interferon beta or natalizumab during the first trimester; the decision should always be made together with the patient. Immune reconstituting drugs given in pulses (alemtuzumab, cladribine) can be proposed as an option in patients wishing for a planned pregnancy.

**RECOMMENDATION 3:** In patients who present with active disease during pregnancy or in the year prior to pregnancy, an immediate restart of treatment after giving birth can be proposed. In patients with inactive disease during pregnancy, a brain MRI is recommended in the first month after giving birth, with a clinical evaluation to determine the safety of continuing with exclusive breastfeeding and postponing the start of treatment.

## G. SUSPENSION OF DISEASE-MODIFYING TREATMENT

To date, available evidence on treatment suspension is controversial. Populations and methodologies used differ between studies conducted, so no definitive conclusion can be drawn about this issue (45–47).

**RECOMMENDATION 1:** Treatment should be continued as long as there are no adverse effects detected that could compromise the patient's quality of life beyond the benefit that they receive from the drug used.

**RECOMMENDATION 2:** In the presence of secondary progressive multiple sclerosis, suspension of disease-modifying treatment must be considered individually in patients with EDSS scores above 7.5 sustained for more than 2 years and who present with progression of $\geq 1$ point sustained for 12 months despite adequate use of high-efficacy drugs.

## H. THERAPIES FOR MS PATIENTS DURING THE COVID-19 PANDEMIC

The SARS-CoV-2 pandemic has forced social restriction and changes in lifestyles in all areas of daily living. Given its genetic characteristics of recombination and high contagiousness, the virus is able to generate mainly pulmonary infections, especially in vulnerable populations such as patients over 60 years of age, those with lung, cardiac, and metabolic morbidities, cancer and mainly immunosuppressed patients (48–50).

To date, there is no evidence that COVID-19 directly affects individuals suffering from MS; however, immunomodulatory treatments produce a degree of immunosuppression and increase the risk of infection in such a way that the start and continuation of the treatments should be assessed individually (51, 52).

The objective of these guidelines is to review the available evidence and serve as guidance and conduct that should be followed in different scenarios. We must take into consideration that they could vary over time, as the behavior of COVID-19 becomes better known (53–57)

*Precautionary measures (54) :*

● Surgical masks should be used when leaving the home.

● Hands should be washed with soap for 30 seconds or rubbed with 60% gel/alcohol.

● The eyes, nose or mouth should not be touched unless with clean hands.

● When coughing or sneezing, the mouth and nose should be covered with the inner corner of the elbow.

● At least 2 meters (approximately 6 feet) of distance should be maintained between individuals.

● Hygiene measures and food washing should be performed when and as appropriate.

● Public transportation should be avoided.

Medical consultations should be made virtually, avoiding visiting the hospital.

● For urgent or emergency hospital needs, preventive COVID-19 measures should be taken according to the standards established by the Ministries of Health.

● Telecommuting should be performed where possible. Work should be avoided if it can lead to exposure crowds.

● In cases of respiratory or febrile symptoms, doctors should be consulted early.

● Control and follow-up laboratory studies should not be postponed in patients who have received immunosuppressive therapy.

● Routine MRI studies should be postponed to avoid contact with the hospital, unless a therapeutic change depends on these tests; otherwise, safety should be assessed in the case of suspected progressive multifocal leukoencephalopathy.

● Precautionary measures must be taken by family and caregivers.

*Management of acute crisis (Relapse)*

The administration of corticosteroids is recommended for the treatment of an acute crisis. Methylprednisolone 1 gr a day intravenously for 3 to 5 days, depending on the patient and preferably at home. The relapse could also be treated with prednisone or methylprednisolone orally.

*Advice regarding immunomodulatory treatment for multiple sclerosis*

● Patients with a diagnosis of MS being treated with immunomodulators should continue with the treatment. More stringent isolation measures should be taken for patients being treated with alemtuzumab, cladribine, ocrelizumab, rituximab, fingolimod, fumarates, teriflunomide, ozanimod or siponimod.

● The newly diagnosed patient should be treated after an in-depth analysis and discussion of the therapeutic alternatives with the patient and their relatives, as well as the benefits and risks of these drugs with respect to the current situation of the pandemic.

● Patients should be started on a personalized treatment plan.

● Special considerations and controls must be taken when recommending medications that can reduce the immune system's response capacity to an infection and assess the benefits and risks.

● It is recommended to start treatment, particularly in cases of highly active MS.

*Additional considerations for patients under treatment:*

● Alemtuzumab: It is recommended to delay the second cycle by increasing the gap between the first and second cycles up to 18 months. It is contraindicated in the case of active infection with COVID-19

● Cladribine: In case the cycle has already started, the drug should be discontinued in cases of infection with COVID-19 unless the grade 4 lymphopenia is detected.

● Ocrelizumab: The next infusion can proceed. The drug should be suspended in case of active COVID-19 infection.

● Rituximab: The next infusion should proceed. The drug should be suspended in case of active COVID-19 infection

● Natalizumab: Each infusion should be extended to six weeks. Patients may continue with the drug in cases of infection with COVID-19.

● Fingolimod: Patients should be closely monitored for lymphopenia. The drug should be suspended in cases of severe active COVID-19 infection requiring hospitalization.

● Dimethyl fumarate: Patients should be closely monitored for lymphopenia. The drug should be suspended in case of active COVID-19 infection.

● Teriflunomide: The drug should be discontinued in cases of active infection with COVID-19.

● Interferons and glatiramer acetate: These drugs can be maintained during active infection with COVID-19.

## 4 | CONCLUSIONS

The recommendations given in this document originated from a collaborative consensus from the Central American and Caribbean Multiple Sclerosis Forum and sought to provide an updated guide on the use of disease-modifying drugs for multiple sclerosis to reduce variability in therapeutic decision-making and thus provide a better quality of life for patients.

It should be noted that the individual decision on the drug to be used for each patient must be made in consensus between the doctor and his patient. It will be necessary to include, in addition to efficacy and safety measures, those related to comorbidities and gestational desire as indicated, as well as others such as geographic access to health services, working hours and any other specific measures for each patient.

The influence of the SARS-CoV-2 pandemic on access to health services, patient follow-up procedures, and therapeutic decision-making has not yet been fully defined. Nevertheless, hygiene measures and certain precautions in the use of some drugs can be adopted while processing the information of the true impact that this virus can have on patients.

Finally, it is worth mentioning that the present recommendations should be updated periodically due to the rapid development of new drugs and information in the field of multiple sclerosis.

Alexander Parajeles Vindas has received speaker honoraria from Merck, Novartis and Roche.

Deyanira Ramírez Navarro has received speaker honoraria from Merck, Novartis, Genzyme and Roche; also has received research grants from Roche and Novartis.

Amado Díaz de la Fe nothing to disclose

Ligia Portillo Rivera has received speaker honoraria from Bayer pharmaceuticals, Genzyme, Merck, Novartis and Roche; also has received research grants from Roche.

Nidia Eunice Ramíres nothing to disclose

Victor M Rivera has received speaker honoraria from Merck, Biogen and Roche

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